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DESCRIPTION

FIELD OF THE INVENTION

[0001] The invention relates to medicine. In particular the invention relates to the diagnosis, prophylaxis and/or treatment of infection by staphylococci.

BACKGROUND OF THE INVENTION

[0002] *Staphylococcus* is a genus of gram-positive bacteria and a member of the micrococcaceae family. Staphylococci are spherical bacteria that are found primarily on the skin and in the mucous membranes of humans and other warm-blooded animals, and aggregate into small, grape-like clumps. Staphylococci can be divided into two groups, *i.e.* coagulase-positive and coagulase-negative staphylococci. Overall, there are about thirty species of staphylococci.

[0003] Staphylococci can cause a wide variety of diseases in humans either through toxin production or invasion. *Staphylococcus aureus* (*S. aureus*) has been recognized as one of the most important and lethal human bacterial pathogens since the beginning of the previous century. Until the antibiotic era, more than 80% of the patients growing *S. aureus* from their blood died. Through infections caused by coagulase-positive *S. aureus* were generally known to be potentially lethal, coagulase-negative staphylococci has been dismissed as avirulent skin commensals incapable of causing human disease. However, over the past 30 years, coagulase-negative staphylococcal infections have emerged as one of the major complications of medical progress. They are currently the pathogens most commonly isolated from infections of indwelling foreign devices and are the leading cause of nosocomial (hospital-acquired) bacteremias in US hospitals. Staphylococcal infections are commonly treated with antimicrobial agents. However, the ascendancy of staphylococci as pre-eminent nosocomial pathogens also has been associated with a major increase in the proportion of these isolates that are resistant to (multiple) antimicrobial agents. Of the estimated 2 million hospital infections in the US in 2004, 70% was resistant to at least one antibiotic, thereby causing major medical and consequently economic problems. Ninety percent of the staphylococci strains are penicillin resistant, leaving only methicillin and vancomycin to treat the majority of infections. However, with increasing numbers of reports of methicillin-resistant *Staphylococcus aureus* (MRSA) chemists are faced with the daunting task of generating new antibiotics with novel modes of action. Despite the urgent need for the development of new antibiotics, the major pharmaceutical companies appear to have lost interest in the antibiotic market. In 2002, only 5 out of the more than 500 drugs in phase II or phase III clinical development were new antibiotics. In the last 6 years only 10 antibiotics have been registered and only 2 of those did not exhibit cross-reactivity with existing drugs (and thus not subject to the same patterns of drug resistance). This trend has been attributed to several factors: the cost of new drug development and the relatively small return on investment that infectious disease treatments yield compared to drugs against hypertension, arthritis and lifestyle drugs *e.g.* for impotence. Another contributing factor is the increasing difficulty in finding new targets, further driving up development costs. Therefore, investigation into novel therapies or preventative measures for (multi-drug-resistant) bacterial infections is urgently needed to meet this impending healthcare crisis.

[0004] Active immunization with vaccines and passive immunization with immunoglobulins are promising alternatives to classical small molecule therapy. A few bacterial diseases that once caused widespread illness, disability, and death can now be prevented through the use of vaccines. The vaccines are based on weakened (attenuated) or dead bacteria, components of the bacterial surface or on inactivated toxins. The immune response raised by a vaccine is mainly directed to immunogenic structures, a limited number of proteins or sugar structures on the bacteria that are actively processed by the immune system. Since these immunogenic structures are very specific to the organism, the vaccine needs to comprise the immunogenic components of all variants of the bacteria against which the vaccine should be protective. As a consequence thereof, vaccines are very complex, take long and are expensive to develop. Further complicating the design of vaccines is the phenomenon of 'antigen replacement'. This occurs when new strains become prevalent that are serologically and thus antigenically distinct from those strains covered by the vaccines. The immune status of the populations at risk for nosocomial infections further complicates vaccine design. These patients are inherently unwell and may even be immunocompromised (due to the effect of immunosuppressive drugs) resulting in delayed or insufficient immunity against the infecting pathogens. Furthermore, except in the case of certain elective procedures, it may not be possible to identify and vaccinate the at risk patients in time to give them sufficient immune protection from infection.

[0005] Direct administration of therapeutic immunoglobulins, also referred to as passive immunization, does not require an immune response from the patient and therefore gives immediate protection. In addition, passive immunization can be directed to bacterial structures that are not immunogenic and that are less specific to the organism. Passive immunization against pathogenic organisms has been based on immunoglobulins derived from sera of human or non-human donors. However, blood-derived

products have potential health risks inherently associated with these products. In addition, the immunoglobulins can display batch-to-batch variation and may be of limited availability in case of sudden mass exposures. Recombinantly produced antibodies do not have these disadvantages and thus offer an opportunity to replace immunoglobulins derived from sera.

[0006] Marine monoclonal antibodies directed against staphylococci are known in the art (see WO 03/059259 and WO 03/059260). However, marine antibodies are limited for their use *in vivo* due to problems associated with administration of murine antibodies to humans, such as short serum half life, an inability to trigger certain human effector functions and elicitation of an unwanted dramatic immune response against the murine antibody in a human (HAMA).

[0007] In WO 03/059259 and WO 03/059260 the attempts have been made to overcome the problems associated with the use of fully murine antibodies in humans by preparing chimeric antibodies. A disadvantage of these chimeric antibodies is however that they still retain some murine sequences and therefore still elicit an unwanted immune reaction, especially when administered for prolonged periods.

[0008] WO 2004/043405 relates to polysaccharide vaccines for staphylococcal infections, prepared from poly N-acetylglucosamine (PNAG) surface polysaccharide from *Staphylococci*, and the deacetylated form thereof (dPNAG). WO 2004/043405 also discloses rabbit antiserum to PNAG and dPNAG, coupled to Diphtheria Toxoid (DTm).

[0009] WO 98/57994 discloses a chimeric antibody MAb 96-110 which binds to *S. aureus* strains 5 and 8. WO 98/57994 is silent about antibody MAb 96-110 binding to *S. aureus* strains Newman, Cowan, Smith, 29213 and Wood.

[0010] Although WO 03/059259, WO 03/059260 and WO 2004/043405 refer to human antibodies as desired molecules, the antibodies actually disclosed and used therein are partly of murine or completely of rabbit origin, and none of these documents actually discloses any human antibodies, nor sequences thereof.

[0011] In view of their therapeutic benefit in humans, there is thus still a need for human monoclonal antibodies against *Staphylococci*. The present invention provides these antibodies and their sequences, and shows that they can be used in medicine, in particular for diagnosis, prevention and/or treatment of staphylococcal infections.

DESCRIPTION OF THE FIGURES

[0012]

Figure 1 shows antibody-mediated phagocytosis of *S. aureus* strain Cowan harvested during the log phase of growth in the absence of complement with the antibodies CR2430 (white dot), CR5132 (black triangle), CR5133 (black dot), and a negative control monoclonal antibody (white square).

Figure 2 shows antibody-mediated phagocytosis of *S. aureus* strain Cowan harvested during the stationary phase of growth in the absence of complement with the antibodies CR2430 (white dot), CR5132 (black triangle), CR5133 (black dot), and a negative control monoclonal antibody (white square).

Figure 3 shows antibody-mediated phagocytosis of *S. aureus* strain SA125 harvested during the stationary phase of growth in the absence of complement with the antibodies CR5132 (black triangle), CR5133 (black dot), and a negative control monoclonal antibody (white square).

Figure 4 shows antibody-mediated phagocytosis of *S. epidermidis* strain SE131 harvested during the stationary phase of growth in the absence of complement with the antibodies CR5132 (black triangle), CR5133 (black dot), and a negative control monoclonal antibody (white square).

DESCRIPTION OF THE INVENTION

[0013] Here below follow definitions of terms as used in the invention.

DEFINITIONS

Amino acid sequence

[0014] The term "amino acid sequence" as used herein refers to naturally occurring or synthetic molecules and to a peptide, oligopeptide, polypeptide or protein sequence.

Binding molecule

[0015] As used herein the term "binding molecule" refers to an intact immunoglobulin including monoclonal antibodies, such as chimeric, humanized or human monoclonal antibodies, or to an antigen-binding and/or variable domain comprising fragment of an immunoglobulin that competes with the intact immunoglobulin for specific binding to the binding partner of the immunoglobulin, e.g. staphylococci. Regardless of structure, the antigen-binding fragment binds with the same antigen that is recognized by the intact immunoglobulin. An antigen-binding fragment can comprise a peptide or polypeptide comprising an amino acid sequence of at least 2 contiguous amino acid residues, at least 5 contiguous amino acid residues, at least 10 contiguous amino acid residues, at least 15 contiguous amino acid residues, at least 20 contiguous amino acid residues, at least 25 contiguous amino acid residues, at least 30 contiguous amino acid residues, at least 35 contiguous amino acid residues, at least 40 contiguous amino acid residues, at least 50 contiguous amino acid residues, at least 60 contiguous amino acid residues, at least 70 contiguous amino acid residues, at least 80 contiguous amino acid residues, at least 90 contiguous amino acid residues, at least 100 contiguous amino acid residues, at least 125 contiguous amino acid residues, at least 150 contiguous amino acid residues, at least 175 contiguous amino acid residues, at least 200 contiguous amino acid residues, or at least 250 contiguous amino acid residues of the amino acid sequence of the binding molecule.

[0016] The term "binding molecule", as used herein includes all immunoglobulin classes and subclasses known in the art. Depending on the amino acid sequence of the constant domain of their heavy chains, binding molecules can be divided into the five major classes of intact antibodies: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgA1, IgA2, IgG1, IgG2, IgG3 and IgG4.

[0017] Antigen-binding fragments include, *inter alia*, Fab, F(ab'), F(ab')₂, Fv, dAb, Fd, complementarity determining region (CDR) fragments, single-chain antibodies (scFv), bivalent single-chain antibodies, single-chain phage antibodies, diabodies, triabodies, tetrabodies, (poly)peptides that contain at least a fragment of an immunoglobulin that is sufficient to confer specific antigen binding to the (poly)peptide, etc. The above fragments may be produced synthetically or by enzymatic or chemical cleavage of intact immunoglobulins or they may be genetically engineered by recombinant DNA techniques. The methods of production are well known in the art and are described, for example, in *Antibodies: A Laboratory Manual*, Edited by: E. Harlow and D. Lane (1988), Cold Spring Harbor Laboratory, Cold Spring Harbor, New York. A binding molecule or antigen-binding fragment thereof may have one or more binding sites. If there is more than one binding site, the binding sites may be identical to one another or they may be different.

[0018] The binding molecule can be a naked or unconjugated binding molecule but can also be part of an immunoconjugate. A naked or unconjugated binding molecule is intended to refer to a binding molecule that is not conjugated, operatively linked or otherwise physically or functionally associated with an effector moiety or tag, such as *inter alia* a toxic substance, a radioactive substance, a liposome, an enzyme. It will be understood that naked or unconjugated binding molecules do not exclude binding molecules that have been stabilized, multimerized, humanized or in any other way manipulated, other than by the attachment of an effector moiety or tag. Accordingly, all post-translationally modified naked and unconjugated binding molecules are included herewith, including where the modifications are made in the natural binding molecule-producing cell environment, by a recombinant binding molecule-producing cell, and are introduced by the hand of man after initial binding molecule preparation. Of course, the term naked or unconjugated binding molecule does not exclude the ability of the binding molecule to form functional associations with effector cells and/or molecules after administration to the body, as some of such interactions are necessary in order to exert a biological effect. The lack of associated effector group or tag is therefore applied in definition to the naked or unconjugated binding molecule *in vitro*, not *in vivo*.

Biological sample

[0019] As used herein, the term "biological sample" encompasses a variety of sample types, including blood and other liquid

samples of biological origin, solid tissue samples such as a biopsy specimen or tissue cultures, or cells derived therefrom and the progeny thereof. The term also includes samples that have been manipulated in any way after their procurement, such as by treatment with reagents, solubilization, or enrichment for certain components, such as proteins or polynucleotides. The term encompasses various kinds of clinical samples obtained from any species, and also includes cells in culture, cell supernatants and cell lysates.

Complementarity determining regions (CDR)

[0020] The term "complementarity determining regions" as used herein means sequences within the variable regions of binding molecules, such as immunoglobulins, that usually contribute to a large extent to the antigen binding site which is complementary in shape and charge distribution to the epitope recognized on the antigen. The CDR regions can be specific for linear epitopes, discontinuous epitopes, or conformational epitopes of proteins or protein fragments, either as present on the protein in its native conformation or, in some cases, as present on the proteins as denatured, *e.g.*, by solubilization in SDS. Epitopes may also consist of posttranslational modifications of proteins.

Deletion

[0021] The term "deletion", as used herein, denotes a change in either amino acid or nucleotide sequence in which one or more amino acid or nucleotide residues, respectively, are absent as compared to the parent, often the naturally occurring, molecule.

Expression-regulating nucleic acid sequence

[0022] The term "expression-regulating nucleic acid sequence" as used herein refers to polynucleotide sequences necessary for and/or affecting the expression of an operably linked coding sequence in a particular host organism. The expression-regulating nucleic acid sequences, such as *inter alia* appropriate transcription initiation, termination, promoter, enhancer sequences; repressor or activator sequences; efficient RNA processing signals such as splicing and polyadenylation signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (*e.g.*, ribosome binding sites); sequences that enhance protein stability; and when desired, sequences that enhance protein secretion, can be any nucleic acid sequence showing activity in the host organism of choice and can be derived from genes encoding proteins, which are either homologous or heterologous to the host organism. The identification and employment of expression-regulating sequences is routine to the person skilled in the art.

Functional variant

[0023] The term "functional variant", as used herein, refers to a binding molecule that comprises a nucleotide and/or amino acid sequence that is altered by one or more nucleotides and/or amino acids compared to the nucleotide and/or amino acid sequences of the parent binding molecule and that is still capable of competing for binding to the binding partner, *e.g.* staphylococci, with the parent binding molecule. In other words, the modifications in the amino acid and/or nucleotide sequence of the parent binding molecule do not significantly affect or alter the binding characteristics of the binding molecule encoded by the nucleotide sequence or containing the amino acid sequence, *i. e.* the binding molecule is still able to recognize and bind its target. The functional variant may have conservative sequence modifications including nucleotide and amino acid substitutions, additions and deletions. These modifications can be introduced by standard techniques known in the art, such as site-directed mutagenesis and random PCR-mediated mutagenesis, and may comprise natural as well as non-natural nucleotides and amino acids.

[0024] Conservative amino acid substitutions include the ones in which the amino acid residue is replaced with an amino acid residue having similar structural or chemical properties. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, asparagine, glutamine, serine, threonine, tyrosine, cysteine, tryptophan), nonpolar side chains (*e.g.*, glycine, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan). It will be clear to the skilled artisan that other classifications of amino acid residue families than the one used above can also be employed. Furthermore, a variant may have non-conservative amino acid substitutions, *e.g.*, replacement of an

amino acid with an amino acid residue having different structural or chemical properties. Similar minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which amino acid residues may be substituted, inserted, or deleted without abolishing immunological activity may be found using computer programs well known in the art.

[0025] A mutation in a nucleotide sequence can be a single alteration made at a locus (a point mutation), such as transition or transversion mutations, or alternatively, multiple nucleotides may be inserted, deleted or changed at a single locus. In addition, one or more alterations may be made at any number of loci within a nucleotide sequence. The mutations may be performed by any suitable method known in the art.

Host

[0026] The term "host", as used herein, is intended to refer to an organism or a cell into which a vector such as a cloning vector or an expression vector has been introduced. The organism or cell can be prokaryotic or eukaryotic. It should be understood that this term is intended to refer not only to the particular subject organism or cell, but to the progeny of such an organism or cell as well. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent organism or cell, but are still included within the scope of the term "host" as used herein.

Human

[0027] The term "human", when applied to binding molecules as defined herein, refers to molecules that are either directly derived from a human or based upon a human sequence. When a binding molecule is derived from or based on a human sequence and subsequently modified, it is still to be considered human as used throughout the specification. In other words, the term human, when applied to binding molecules is intended to include binding molecules having variable and constant regions derived from human germline immunoglobulin sequences or based on variable or constant regions occurring in a human or human lymphocyte and modified in some form. Thus, the human binding molecules may include amino acid residues not encoded by human germline immunoglobulin sequences, comprise substitutions and/or deletions (e.g., mutations introduced by for instance random or site-specific mutagenesis *in vitro* or by somatic mutation *in vivo*). "Based on" as used herein refers to the situation that a nucleic acid sequence may be exactly copied from a template, or with minor mutations, such as by error-prone PCR methods, or synthetically made matching the template exactly or with minor modifications. Semi-synthetic molecules based on human sequences are also considered to be human as used herein.

Insertion

[0028] The term "insertion", also known as the term "addition", denotes a change in an amino acid or nucleotide sequence resulting in the addition of one or more amino acid or nucleotide residues, respectively, as compared to the parent sequence.

Intrinsic activity

[0029] The term "intrinsic activity", when applied to binding molecules as defined herein, refers to binding molecules that are capable of binding to certain protein or carbohydrate antigens on the surface of pathogens such as bacteria and that can inhibit the ability of the pathogen to grow and divide normally. Such binding molecules can for example block the entry of specific nutrients required for growth or the transport of toxic waste elements from the bacteria. Through the latter action they may also increase the sensitivity of bacteria to the action of antibiotic drugs.

Isolated

[0030] The term "isolated", when applied to binding molecules as defined herein, refers to binding molecules that are substantially free of other proteins or polypeptides, particularly free of other binding molecules having different antigenic specificities, and are also substantially free of other cellular material and/or chemicals. For example, when the binding molecules are recombinantly produced, they are preferably substantially free of culture medium, and when the binding molecules are

produced by chemical synthesis, they are preferably substantially free of chemical precursors or other chemicals, *i.e.*, they are separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. The term "isolated" when applied to nucleic acid molecules encoding binding molecules as defined herein, is intended to refer to nucleic acid molecules in which the nucleotide sequences encoding the binding molecules are free of other nucleotide sequences, particularly nucleotide sequences encoding binding molecules that bind binding partners other than staphylococci. Furthermore, the term "isolated" refers to nucleic acid molecules that are substantially separated from other cellular components that naturally accompany the native nucleic acid molecule in its natural host, *e.g.*, ribosomes, polymerases, or genomic sequences with which it is naturally associated. Moreover, "isolated" nucleic acid molecules, such as cDNA molecules, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized.

Monoclonal antibody

[0031] The term "monoclonal antibody" as used herein refers to a preparation of antibody molecules of single molecular composition. A monoclonal antibody displays a single binding specificity and affinity for a particular epitope. Accordingly, the term "human monoclonal antibody" refers to an antibody displaying a single binding specificity which has variable and constant regions derived from or based on human germline immunoglobulin sequences or derived from completely synthetic sequences. The method of preparing the monoclonal antibody is not relevant.

Naturally occurring

[0032] The term "naturally occurring" as used herein as applied to an object refers to the fact that an object can be found in nature. For example, a polypeptide or polynucleotide sequence that is present in an organism that can be isolated from a source in nature and which has not been intentionally modified by man in the laboratory is naturally occurring.

Nucleic acid molecule

[0033] The term "nucleic acid molecule" as used in the present invention refers to a polymeric form of nucleotides and includes both sense and anti-sense strands of RNA, cDNA, genomic DNA, and synthetic forms and mixed polymers of the above. A nucleotide refers to a ribonucleotide, deoxynucleotide or a modified form of either type of nucleotide. The term also includes single- and double-stranded forms of DNA. In addition, a polynucleotide may include either or both naturally occurring and modified nucleotides linked together by naturally occurring and/or non-naturally occurring nucleotide linkages. The nucleic acid molecules may be modified chemically or biochemically or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those of skill in the art. Such modifications include, for example, labels, methylation, substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as uncharged linkages (*e.g.*, methyl phosphonates, phosphotriesters, phosphoramidates, carbamates, etc.), charged linkages (*e.g.*, phosphorothioates, phosphorodithioates, etc.), pendent moieties (*e.g.*, polypeptides), intercalators (*e.g.*, acridine, psoralen, etc.), chelators, alkylators, and modified linkages (*e.g.*, alpha anomeric nucleic acids, etc.). The above term is also intended to include any topological conformation, including single-stranded, double-stranded, partially duplexed, triplex, hairpinned, circular and padlocked conformations. Also included are synthetic molecules that mimic polynucleotides in their ability to bind to a designated sequence via hydrogen bonding and other chemical interactions. Such molecules are known in the art and include, for example, those in which peptide linkages substitute for phosphate linkages in the backbone of the molecule. A reference to a nucleic acid sequence encompasses its complement unless otherwise specified. Thus, a reference to a nucleic acid molecule having a particular sequence should be understood to encompass its complementary strand, with its complementary sequence. The complementary strand is also useful, *e.g.*, for anti-sense therapy, hybridization probes and PCR primers.

Operably linked

[0034] The term "operably linked" refers to two or more nucleic acid sequence elements that are usually physically linked and are in a functional relationship with each other. For instance, a promoter is operably linked to a coding sequence, if the promoter is able to initiate or regulate the transcription or expression of a coding sequence, in which case the coding sequence should be understood as being "under the control of" the promoter.

Opsonic activity

[0035] "Opsonic activity" refers to the ability of an opsonin (generally either a binding molecule, *e.g.* an antibody, or serum complement factors) to bind to the surface of a pathogen either by specific antigenic recognition (in the case of antibodies) or through the catalytic effect of surface bound molecules (*e.g.* the increased deposition of C3b as a result of surface bound antibodies). Phagocytosis of opsonized pathogens is enhanced due to the specific recognition of receptors on the phagocyte for the opsonin (the Fc receptor in case the antibodies themselves are the opsonins and the complement receptor in case complement is the opsonin). Certain bacteria, especially encapsulated bacteria that resist phagocytosis due to the presence of the capsule, become extremely attractive to phagocytes such as neutrophils and macrophages when coated with an opsonic antibody and their rate of clearance from the bloodstream and infected organs is strikingly enhanced. Opsonic activity may be measured in any conventional manner (*e.g.* the opsonic phagocytic killing assay).

Pharmaceutically acceptable excipient

[0036] By "pharmaceutically acceptable excipient" is meant any inert substance that is combined with an active molecule such as a drug, agent, or binding molecule for preparing an agreeable or convenient dosage form. The "pharmaceutically acceptable excipient" is an excipient that is non-toxic to recipients at the dosages and concentrations employed, and is compatible with other ingredients of the formulation comprising the drug, agent or binding molecule.

Specifically Binding

[0037] The term "specifically binding", as used herein, in reference to the interaction of a binding molecule, *e.g.* an antibody, and its binding partner, *e.g.* an antigen, means that the interaction is dependent upon the presence of a particular structure, *e.g.* an antigenic determinant or epitope, on the binding partner. In other words, the antibody preferentially binds or recognizes the binding partner even when the binding partner is present in a mixture of other molecules or organisms. The binding may be mediated by covalent or non-covalent interactions or a combination of both. In yet other words, the term "specifically binding" means immunospecifically binding to an antigen or a fragment thereof and not immunospecifically binding to other antigens. A binding molecule that immunospecifically binds to an antigen may bind to other peptides or polypeptides with lower affinity as determined by, *e.g.*, radioimmunoassays (RIA), enzyme-linked immunosorbent assays (ELISA), BIACORE, or other assays known in the art. Binding molecules or fragments thereof that immunospecifically bind to an antigen may be cross-reactive with related antigens. Preferably, binding molecules or fragments thereof that immunospecifically bind to an antigen do not cross-react with other antigens.

Substitutions

[0038] A "substitution", as used herein, denotes the replacement of one or more amino acids or nucleotides by different amino acids or nucleotides, respectively.

Therapeutically effective amount

[0039] The term "therapeutically effective amount" refers to an amount of the binding molecule as defined herein that is effective for preventing, ameliorating and/or treating a condition resulting from infection with *Staphylococcus*.

Treatment

[0040] The term "treatment" refers to therapeutic treatment as well as prophylactic or preventative measures to cure or halt or at least retard disease progress. Those in need of treatment include those already inflicted with a condition resulting from infection with *Staphylococcus* as well as those in which infection with *Staphylococcus* is to be prevented. Subjects partially or totally recovered from infection with *Staphylococcus* might also be in need of treatment. Prevention encompasses inhibiting or reducing

the spread of *Staphylococcus* or inhibiting or reducing the onset, development or progression of one or more of the symptoms associated with infection with *Staphylococcus*.

Vector

[0041] The term "vector" denotes a nucleic acid molecule into which a second nucleic acid molecule can be inserted for introduction into a host where it will be replicated, and in some cases expressed. In other words, a vector is capable of transporting a nucleic acid molecule to which it has been linked. Cloning as well as expression vectors are contemplated by the term "vector", as used herein. Vectors include, but are not limited to, plasmids, cosmids, bacterial artificial chromosomes (BAC) and yeast artificial chromosomes (YAC) and vectors derived from bacteriophages or plant or animal (including human) viruses. Vectors comprise an origin of replication recognized by the proposed host and in case of expression vectors, promoter and other regulatory regions recognized by the host. A vector containing a second nucleic acid molecule is introduced into a cell by transformation, transfection, or by making use of viral entry mechanisms. Certain vectors are capable of autonomous replication in a host into which they are introduced (e.g., vectors having a bacterial origin of replication can replicate in bacteria). Other vectors can be integrated into the genome of a host upon introduction into the host, and thereby are replicated along with the host genome.

SUMMARY OF THE INVENTION

[0042] The invention provides human binding molecules capable of specifically binding to staphylococci and exhibiting killing and/or growth inhibiting activity against staphylococci. The invention also pertains to nucleic acid molecules encoding at least the binding region of the human binding molecules. The invention further provides for the use of the human binding molecules of the invention in the prophylaxis and/or treatment of a subject having, or at risk of developing, a *Staphylococcus* infection. Besides that, the invention pertains to the use of the human binding molecules of the invention in the diagnosis/detection of *Staphylococcus*.

DETAILED DESCRIPTION OF THE INVENTION

[0043] In a first aspect the present invention encompasses binding molecules capable of specifically binding to staphylococci. Preferably, the binding molecules are human binding molecules. Preferably, the binding molecules of the invention exhibit killing activity against staphylococci. In a further aspect the binding molecules of the invention are capable of specifically binding to and/or have killing activity against at least two different *Staphylococcus* species. Preferably the binding molecules of the invention are capable of specifically binding to and/or have killing activity against at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least sixteen, at least seventeen, at least eighteen, at least nineteen, at least twenty, at least twenty-one, at least twenty-two, at least twenty-three, at least twenty-four, at least twenty-five, at least twenty-six, at least twenty-seven, at least twenty-eight, at least twenty-nine, at least thirty different *Staphylococcus* species. *Staphylococcus* species that the binding molecules of the invention are capable of specifically binding to and/or have killing activity against are selected from the group consisting of *S. aureus*, *S. auricularis*, *S. capitis*, *S. caprae*, *S. caseolyticus*, *S. chromogenes*, *S. cohnii*, *S. epidermidis*, *S. haemolyticus*, *S. hominis*, *S. hyicus*, *S. intermedius*, *S. lentus*, *S. lugdunensis*, *S. saprophyticus*, *S. schleiferi*, *S. sciuri*, *S. simulans*, *S. warneri*, and *S. xylosus*. In an embodiment the binding molecules of the invention are capable of specifically binding to and have killing activity against different strains within one *Staphylococcus* species. In a further embodiment the binding molecules of the invention are capable of specifically binding to and have killing activity against a *Staphylococcus* strain in the lag phase, log phase, stationary phase and/or death phase. Preferably, they specifically bind to and have killing activity against a *Staphylococcus* strain in the log phase and stationary phase. In another embodiment, the binding molecules of the invention may even be capable of specifically binding to and/or have killing activity against at least one other Gram-positive bacterium and/or Gram-negative bacterium including, but not limited to, Group A streptococci; *streptococcus pyrogenes*, Group B streptococci; *streptococcus agalactiae*, *streptococcus milleri*, *streptococcus pneumoniae*, Viridans streptococci; *streptococcus mutans*, Enterococcus; *Enterococcus faecalis* and *Enterococcus faecium*, *Corynebacterium diphtheria*, *Corynebacterium ulcerans*, *Corynebacterium pseudotuberculosis*, *Corynebacterium jeikeium*, *Corynebacterium xerosis*, *Corynebacterium pseudodiphtheriticum*, *Bacillus anthracis*, *Bacillus cereus*, *Listeria monocytogenes*, *Clostridium perfringens*, *Clostridium tetani*, *Clostridium botulinum*, *Clostridium difficile*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Actinomyces israelii*, *Nocardia asteroides*, *Nocardia brasiliensis*, *Escherichia coli*, *Proteus mirabilis*, *Proteus vulgaris*, *Klebsiella pneumonia*, *Salmonella typhi*, *Salmonella paratyphi A, B & C*, *Salmonella enteritidis*, *Salmonella cholerae-suis*, *Salmonella virchow*, *Salmonella typhimurium*,

Shigella dysenteriae, *Shigella boydii*, *Shigella flexneri*, *Shigella sonnei*, *Pseudomonas aeruginosa*, *Pseudomonas mallei*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificus*, *Vibrio alginolyticus*, *Campylobacter pylori*, *Helicobacter pylori*, *Campylobacter jejuni*, *Bacteroides fragilis*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Branhamella catarrhalis*, *Haemophilus influenzae*, *Haemophilus ducreyi*, *Bordetella pertarssis*, *Brarcella abortus*, *Brarcella abortus*, *Brarcella melitensis*, *Legionella pneumophila*, *Treponema pallidum*, *Treponema carateum*, *Leptospira interrogans*, *Leptospira biflexa*, *Borrelia recurrentis*, *Borrelia burgdorferi*, *Mycoplasma pneumonia*, *Coxiella burnetii*, *Clamydia trachomatis*, *Clamydia psittaci*, *Clamydia pneumoniae*. The binding molecules of the invention may be capable of specifically binding to staphylococci and optionally other Gram-positive and/or Gram-negative bacteria that are viable, living and/or infective or that are in inactivated/attenuated form. Methods for inactivating/attenuating bacteria are well known in the art and include, but are not limited to, antibiotic treatment, UV treatment, formaldehyde treatment, etc.

[0044] The binding molecules of the invention may also be capable of specifically binding to one or more fragments of staphylococci (and other Gram-positive and/or Gram-negative bacteria) such as *inter alia* a preparation of one or more proteins and/or (poly)peptides derived from staphylococci or one or more recombinantly produced staphylococci proteins and/or polypeptides. For methods of treatment and/or prevention of staphylococcal infections the binding molecules are preferably capable of specifically binding to surface accessible proteins of staphylococci. For diagnostical purposes the binding molecules may also be capable of specifically binding to proteins not present on the surface of staphylococci. The nucleotide and/or amino acid sequence of proteins of various *Staphylococcus* species and strains can be found in the GenBank-database, EMBL-database and/or other databases. It is well within the reach of the skilled person to find such sequences in the respective databases.

[0045] Alternatively, binding molecules of the invention may also be capable of specifically binding to other staphylococcal molecules including, but not limited to, surface factors that inhibit phagocytic engulfment; factors that enhance their survival in phagocytes; invasins that lyse eukaryotic cell membranes; exotoxins that damage host tissues or otherwise provoke symptoms of disease; polysaccharides; other cell wall components such as teichoic acid, lipoteichoic acid, ribitol, peptidoglycan, pentaglycine oligopeptide, *N*-acetylglucosamine, *N*-acetylmuramic acid, *N*-acetylgalactosaminuronic acid, *N*-acetylglucosaminuronic acid, *N*-acetylmannosaminuronic acid, *O*-acetyl, glucosamine, muramic acid, galactosaminuronic acid, fucosamine, glucosaminuronic acid, mannosaminuronic acid and linkage units between any of these components.

[0046] In another embodiment the binding molecules of the invention are capable of specifically binding to a fragment of the above-mentioned proteins and/or other molecules, wherein the fragment at least comprises an antigenic determinant recognized by the binding molecules of the invention. An "antigenic determinant" as used herein is a moiety that is capable of binding to a binding molecule of the invention with sufficiently high affinity to form a detectable antigen-binding molecule complex.

[0047] The binding molecules of the invention can be intact immunoglobulin molecules such as polyclonal or monoclonal antibodies or the binding molecules can be antigen-binding fragments including, but not limited to, Fab, F(ab'), F(ab')₂, Fv, dAb, Fd, complementarity determining region (CDR) fragments, single-chain antibodies (scFv), bivalent single-chain antibodies, single-chain phage antibodies, diabodies, triabodies, tetrabodies, and (poly)peptides that contain at least a fragment of an immunoglobulin that is sufficient to confer specific antigen binding to staphylococci or a fragment thereof. In a preferred embodiment the binding molecules of the invention are human monoclonal antibodies.

[0048] The binding molecules of the invention can be used in non-isolated or isolated form. Furthermore, the binding molecules of the invention can be used alone or in a mixture comprising at least one binding molecule (or variant or fragment thereof) of the invention. In other words, the binding molecules can be used in combination, e.g., as a pharmaceutical composition comprising two or more binding molecules of the invention, variants or fragments thereof. For example, binding molecules having different, but complementary activities can be combined in a single therapy to achieve a desired prophylactic, therapeutic or diagnostic effect, but alternatively, binding molecules having identical activities can also be combined in a single therapy to achieve a desired prophylactic, therapeutic or diagnostic effect. Optionally, the mixture further comprises at least one other therapeutic agent. Preferably, the therapeutic agent such as e.g. an antibiotic is useful in the prophylaxis and/or treatment of a staphylococcal infection.

[0049] Typically, binding molecules according to the invention can bind to their binding partners, i.e. staphylococci or fragments thereof, with an affinity constant (K_D -value) that is lower than $0.2 \cdot 10^{-4}$ M, $1.0 \cdot 10^{-5}$ M, $1.0 \cdot 10^{-6}$ M, $1.0 \cdot 10^{-7}$ M, preferably lower than $1.0 \cdot 10^{-8}$ M, more preferably lower than $1.0 \cdot 10^{-9}$ M, more preferably lower than $1.0 \cdot 10^{-10}$ M, even more preferably lower than $1.0 \cdot 10^{-11}$ M, and in particular lower than $1.0 \cdot 10^{-12}$ M. The affinity constants can vary for antibody isotypes. For example, affinity binding for an IgM isotype refers to a binding affinity of at least about $1.0 \cdot 10^{-7}$ M. Affinity constants can for instance be measured

using surface plasmon resonance, for example using the BIACORE system (Pharmacia Biosensor AB, Uppsala, Sweden).

[0050] The binding molecules according to the invention may bind to staphylococci or a fragment thereof in soluble form such as for instance in a sample or in suspension or may bind to staphylococci or a fragment thereof bound or attached to a carrier or substrate, e.g., microtiter plates, membranes and beads, etc. Carriers or substrates may be made of glass, plastic (e.g., polystyrene), polysaccharides, nylon, nitrocellulose, or Teflon, etc. The surface of such supports may be solid or porous and of any convenient shape. Furthermore, the binding molecules may bind to staphylococci in purified/isolated or non-purified/non-isolated form.

[0051] The binding molecules of the invention exhibit killing activity. Killing activity as meant herein includes, but is not limited to, opsonic activity or any other activity increasing/augmenting/enhancing phagocytosis and/or phagocytic killing of bacteria, e.g. staphylococci; intrinsic (killing) activity, e.g. reduce or inhibit bacterial growth or directly kill bacteria; increase the sensitivity of bacteria to antibiotic treatment; or any combination thereof. Opsonic activity can for instance be measured as described herein. Alternative assays measuring opsonic activity are described in for instance Manual of Molecular and Clinical Laboratory Immunology, 7th Edition. Assays to measure the other mentioned activities are also known.

[0052] The binding molecules disclosed herein comprise at least a CDR3 region, preferably a heavy chain CDR3 region, comprising the amino acid sequence selected from the group consisting of SEQ ID NO:9 and SEQ ID NO:15. The CDR regions of the binding molecules of the invention are shown in Table 12. CDR regions are according to Kabat *et al.* (1991) as described in Sequences of Proteins of Immunological Interest, US Dept. Health and Human Services, NIH, USA (fifth edition). In an embodiment binding molecules may comprise two, three, four, five or even all six CDR regions of the binding molecules of the invention.

[0053] The binding molecules according to the invention comprise a heavy chain comprising the variable heavy chain of the amino acid sequence SEQ ID NO:30. In a further embodiment, the binding molecules according to the invention comprise a light chain comprising the variable light chain of the amino acid sequence SEQ ID NO:36. Table 13 specifies the heavy and light chain variable regions of the binding molecule of the invention.

[0054] In another aspect the binding molecules of the invention are capable of specifically binding to one specific *Staphylococcus* species, preferably one specific *Staphylococcus* strain. In other words, they are species- and even strain-specific. Preferably, the binding molecules of the invention exhibit killing activity against the specific *Staphylococcus* species/strain. In a preferred embodiment the *Staphylococcus* species is *S. aureus* and the strain is *S. aureus* strain Cowan. The binding molecules of the invention may be capable of specifically binding to and exhibit killing activity against the specific *Staphylococcus* species/strain in any phase, e.g. log and/or stationary phase. The binding molecules disclosed herein comprise at least a CDR3 region, preferably a heavy chain CDR3 region, comprising the amino acid sequence of SEQ ID NO:3. The CDR regions of the binding molecules are shown in Table 12. CDR regions are according to Kabat *et al.* (1991) as described in Sequences of Proteins of Immunological Interest, US Dept. Health and Human Services, NIH, USA (fifth edition). In an embodiment binding molecules may comprise two, three, four, five or even all six CDR regions of the binding molecules of the invention. Also disclosed herein are binding molecules comprising a heavy chain comprising the variable heavy chain of the amino acid sequence of SEQ ID NO:26 and a light chain comprising the variable light chain of the amino acid sequence of SEQ ID NO:32. Table 13 specifies the heavy and light chain variable regions of the binding molecule disclosed herein.

[0055] Also disclosed herein are functional variants of the binding molecules as defined herein. Molecules are considered to be functional variants of a binding molecule, if the variants are capable of competing for specifically binding to staphylococci (or other Gram-positive and/or Gram-negative bacteria) or a fragment thereof with the parent human binding molecules. In other words, when the functional variants are still capable of binding to staphylococci or a fragment thereof. Preferably, the functional variants are capable of competing for specifically binding to the at least two (or more) different *Staphylococcus* species or fragments thereof that are specifically bound by the parent human binding molecules. Furthermore, molecules are considered to be functional variants of a binding molecule according to the invention, if they have killing activity against staphylococci, preferably against the at least two (or more) *Staphylococcus* species against which the parental binding molecule exhibits killing activity. In another embodiment the functional variants of a binding molecule according to the invention also have killing activity against other Gram-positive and/or Gram-negative bacteria. Functional variants include, but are not limited to, derivatives that are substantially similar in primary structural sequence, but which contain e.g. *in vitro* or *in vivo* modifications, chemical and/or biochemical, that are not found in the parental binding molecule. Such modifications include *inter alia* acetylation, acylation, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, cross-linking, disulfide bond formation, glycosylation, hydroxylation, methylation, oxidation, pegylation, proteolytic processing, phosphorylation, and the like.

[0056] Alternatively, functional variants can be binding molecules as defined in the present invention comprising an amino acid

sequence containing substitutions, insertions, deletions or combinations thereof of one or more amino acids compared to the amino acid sequences of the parent binding molecules. Furthermore, functional variants can comprise truncations of the amino acid sequence at either or both the amino or carboxyl termini. Functional variants as described herein may have the same or different, either higher or lower, binding affinities compared to the parental binding molecule but are still capable of binding to staphylococci or a fragment thereof. For instance, functional variants may have increased or decreased binding affinities for staphylococci or a fragment thereof compared to the parent binding molecules. Preferably, the amino acid sequences of the variable regions, including, but not limited to, framework regions, hypervariable regions, in particular the CDR3 regions, are modified. Generally, the light chain and the heavy chain variable regions comprise three hypervariable regions, comprising three CDRs, and more conserved regions, the so-called framework regions (FRs). The hypervariable regions comprise amino acid residues from CDRs and amino acid residues from hypervariable loops. Functional variants as disclosed herein have at least about 50% to about 99%, preferably at least about 60% to about 99%, more preferably at least about 70% to about 99%, even more preferably at least about 80% to about 99%, most preferably at least about 90% to about 99%, in particular at least about 95% to about 99%, and in particular at least about 97% to about 99% amino acid sequence homology with the parent human binding molecules as defined herein. Computer algorithms such as *inter alia* Gap or Bestfit known to a person skilled in the art can be used to optimally align amino acid sequences to be compared and to define similar or identical amino acid residues. Functional variants can be obtained by altering the parent binding molecules or parts thereof by general molecular biology methods known in the art including, but not limited to, error-prone PCR, oligonucleotide-directed mutagenesis, site-directed mutagenesis and heavy nad/or light chain shuffling. The functional variants as disclosed herein have killing activity against staphylococci. The killing activity may either be identical, or be higher or lower compared to the parent binding molecules. Furthermore, the functional variants having killing activity may have a further activity suitable in staphylococcal control. Other activities are mentioned above. Henceforth, when the term (human) binding molecule is used, this also encompasses functional variants of the (human) binding molecule.

[0057] Disclosed herein is a panel of useful human monoclonal antibodies that have opsonic phagocytic killing activity against Staphylococci, said antibodies comprising the heavy and light chain variable regions of any one of the antibodies named CR2430, CR5132, CR5133, CR6166, CR6171, CR6176, CR6187, CR6193, CR6249, CR6273, CR6389, CR6403, CR6406, CR6410, CR6446, CR6450, CR6452, CR6453, CR6464, CR6471, CR6516, CR6517, CR6526, CR6528, CR6531, CR6533, CR6536, CR6537, CR6538, CR6540, CR6544, CR6566, or CR6625, or comprising variable regions with sequences that are at least 80%, preferably at least 90%, more preferably at least 95%, identical thereto. Preferably the sequences of the complete antibodies are at least 80%, more preferably at least 90%, still more preferably at least 95% identical to the sequences of these antibodies as disclosed herein. The antibodies fell into five distinct groups, based on a target competition assay. Group A consisted of CR5132, CR5133, CR6187 and CR6453; Group B consisted of CR5140 and CR6171; Group C consisted of CR6176; Group D consisted of CR6526; and Group E consisted of the rest of the panel CR6166, CR6193, CR6249, CR6273, CR6403, CR6406, CR6410, CR6446, CR6450, CR6452, CR6464, CR6471, CR6516, CR6517, CR6528, CR6531, CR6533, CR6536, CR6537, CR6538, CR6540, CR6544, CR6566, CR6625. Based on the potency, one antibody from each group was identified as preferred antibody, and the preferred antibodies are: CR5133, CR6166, CR6171, CR6176 and CR6526. These antibodies were all shown to bind and have opsonic phagocytic killing activity against at least two different *Staphylococcus* species (*S. aureus* and *S. epidermidis*), and against at least 3 different strains of *S. aureus* (502, Mn8, Newman). Also disclosed herein are compositions comprising at least 2, at least 3, at least 4, at least 5, or more, of the human monoclonal antibodies of the invention. In preferred embodiments, at least 2 of said antibodies in the composition are from different target groups. This has the advantage that different targets on the staphylococci are recognized and thus the chances of killing the bacteria are increased. Of course, higher affinity mutants or mutants with other advantageous properties can be prepared according to routine methods, based on the sequences of the antibodies as disclosed herein. Such improved antibodies are included within the scope of the present invention, when the variable regions of heavy and light chain are at least 80%, preferably at least 90%, still more preferably at least 95% identical to the sequences of the variable regions of the antibodies disclosed herein.

[0058] Also disclosed herein are immunoconjugates, *i.e.* molecules comprising at least one binding molecule as defined herein and further comprising at least one tag, such as *inter alia* a detectable moiety/agent. Also contemplated in the present invention are mixtures of immunoconjugates according to the invention or mixtures of at least one immunoconjugates according to the invention and another molecule, such as a therapeutic agent or another binding molecule or immunoconjugate. In a further embodiment, the immunoconjugates of the invention may comprise more than one tag. These tags can be the same or distinct from each other and can be joined/conjugated non-covalently to the binding molecules. The tag(s) can also be joined/conjugated directly to the human binding molecules through covalent bonding. Alternatively, the tag(s) can be joined/conjugated to the binding molecules by means of one or more linking compounds. Techniques for conjugating tags to binding molecules are well known to the skilled artisan.

[0059] The tags of the immunoconjugates of the present invention may be therapeutic agents, but they can also be detectable

moieties/agents. Tags suitable in therapy and/or prevention may be toxins or functional parts thereof, antibiotics, enzymes, other binding molecules that enhance phagocytosis or immune stimulation. Immunoconjugates comprising a detectable agent can be used diagnostically to, for example, assess if a subject has been infected with a *Staphylococcus* species or monitor the development or progression of a staphylococcal infection as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. However, they may also be used for other detection and/or analytical and/or diagnostic purposes. Detectable moieties/agents include, but are not limited to, enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals, and non-radioactive paramagnetic metal ions. The tags used to label the binding molecules for detection and/or analytical and/or diagnostic purposes depend on the specific detection/analysis/diagnosis techniques and/or methods used such as *inter alia* immunohistochemical staining of (tissue) samples, flow cytometric detection, scanning laser cytometric detection, fluorescent immunoassays, enzyme-linked immunosorbent assays (ELISA's), radioimmunoassays (RIA's), bioassays (e.g., phagocytosis assays), Western blotting applications, etc. Suitable labels for the detection/analysis/diagnosis techniques and/or methods known in the art are well within the reach of the skilled artisan.

[0060] Furthermore, the human binding molecules or immunoconjugates of the invention can also be attached to solid supports, which are particularly useful for *in vitro* immunoassays or purification of staphylococci or a fragment thereof. Such solid supports might be porous or nonporous, planar or non-planar. The binding molecules of the present invention can be fused to marker sequences, such as a peptide to facilitate purification. Examples include, but are not limited to, the hexa-histidine tag, the hemagglutinin (HA) tag, the myc tag or the flag tag. Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate. In another aspect the binding molecules of the invention may be conjugated/attached to one or more antigens. Preferably, these antigens are antigens which are recognized by the immune system of a subject to which the binding molecule-antigen conjugate is administered. The antigens may be identical, but may also differ from each other. Conjugation methods for attaching the antigens and binding molecules are well known in the art and include, but are not limited to, the use of cross-linking agents. The binding molecules of the invention will bind to staphylococci and the antigens attached to the binding molecules will initiate a powerful T-cell attack on the conjugate, which will eventually lead to the destruction of the staphylococci.

[0061] Next to producing immunoconjugates chemically by conjugating, directly or indirectly, via for instance a linker, the immunoconjugates can be produced as fusion proteins comprising the binding molecules of the invention and a suitable tag. Fusion proteins can be produced by methods known in the art such as, e.g., recombinantly by constructing nucleic acid molecules comprising nucleotide sequences encoding the binding molecules in frame with nucleotide sequences encoding the suitable tag(s) and then expressing the nucleic acid molecules.

[0062] It is another aspect of the present invention to provide a nucleic acid molecule encoding at least a binding molecule, or immunoconjugate according to the invention. Such nucleic acid molecules can be used as intermediates for cloning purposes, e.g. in the process of affinity maturation as described above. In a preferred embodiment, the nucleic acid molecules are isolated or purified.

[0063] The skilled man will appreciate that functional variants of these nucleic acid molecules are also disclosed herein. Functional variants are nucleic acid sequences that can be directly translated, using the standard genetic code, to provide an amino acid sequence identical to that translated from the parent nucleic acid molecules.

[0064] The nucleic acid molecules disclosed herein encode binding molecules comprising a CDR3 region, preferably a heavy chain CDR3 region, comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:9 and SEQ ID NO:15. In a further embodiment the nucleic acid molecules encode binding molecules comprising two, three, four, five or even all six CDR regions of the binding molecules of the invention.

[0065] In another embodiment, the nucleic acid molecules encode binding molecules comprising a heavy chain comprising the variable heavy chain of the amino acid sequence SEQ ID NO:30. In another embodiment the nucleic acid molecules encode binding molecules comprising a light chain comprising the variable light chain of the amino acid sequence SEQ ID NO:36.

[0066] It is another aspect of the invention to provide vectors, *i. e.* nucleic acid constructs, comprising one or more nucleic acid molecules according to the present invention. Vectors can be derived from plasmids such as *inter alia* F, R1, RP1, Col, pBR322, TOL, Ti, etc; cosmids; phages such as lambda, lambdoid, M13, Mu, P1, P22, Q β , T-even, T-odd, T2, T4, T7, etc; plant viruses. Vectors can be used for cloning and/or for expression of the binding molecules of the invention and might even be used for gene therapy purposes. Vectors comprising one or more nucleic acid molecules according to the invention operably linked to one or more expression-regulating nucleic acid molecules are also covered by the present invention. The choice of the vector is dependent on the recombinant procedures followed and the host used. Introduction of vectors in host cells can be effected by *inter alia* calcium phosphate transfection, virus infection, DEAE-dextran mediated transfection, lipofectamin transfection or

electroporation. Vectors may be autonomously replicating or may replicate together with the chromosome into which they have been integrated. Preferably, the vectors contain one or more selection markers. The choice of the markers may depend on the host cells of choice, although this is not critical to the invention as is well known to persons skilled in the art. They include, but are not limited to, kanamycin, neomycin, puromycin, hygromycin, zeocin, thymidine kinase gene from Herpes simplex virus (HSV-TK), dihydrofolate reductase gene from mouse (dhfr). Vectors comprising one or more nucleic acid molecules encoding the human binding molecules as described above operably linked to one or more nucleic acid molecules encoding proteins or peptides that can be used to isolate the human binding molecules are also covered by the invention. These proteins or peptides include, but are not limited to, glutathione-S-transferase, maltose binding protein, metal-binding polyhistidine, green fluorescent protein, luciferase and beta-galactosidase.

[0067] Hosts containing one or more copies of the vectors mentioned above are an additional subject of the present invention. Preferably, the hosts are host cells. Host cells include, but are not limited to, cells of mammalian, plant, insect, fungal or bacterial origin. Bacterial cells include, but are not limited to, cells from Gram-positive bacteria or Gram-negative bacteria such as several species of the genera *Escherichia*, such as *E. coli*, and *Pseudomonas*. In the group of fungal cells preferably yeast cells are used. Expression in yeast can be achieved by using yeast strains such as *inter alia* *Pichia pastoris*, *Saccharomyces cerevisiae* and *Hansenula polymorpha*. Furthermore, insect cells such as cells from *Drosophila* and Sf9 can be used as host cells. Besides that, the host cells can be plant cells such as *inter alia* cells from crop plants such as forestry plants, or cells from plants providing food and raw materials such as cereal plants, or medicinal plants, or cells from ornamentals, or cells from flower bulb crops. Transformed (transgenic) plants or plant cells are produced by known methods, for example, *Agrobacterium*-mediated gene transfer, transformation of leaf discs, protoplast transformation by polyethylene glycol-induced DNA transfer, electroporation, sonication, microinjection or bolistic gene transfer. Additionally, a suitable expression system can be a baculovirus system. Expression systems using mammalian cells such as Chinese Hamster Ovary (CHO) cells, COS cells, BHK cells or Bowes melanoma cells are preferred in the present invention. Mammalian cells provide expressed proteins with posttranslational modifications that are most similar to natural molecules of mammalian origin. Since the present invention deals with molecules that may have to be administered to humans, a completely human expression system would be particularly preferred. Therefore, even more preferably, the host cells are human cells. Examples of human cells are *inter alia* HeLa, 911, AT1080, A549, 293 and HEK293T cells. In preferred embodiments, the human producer cells comprise at least a functional part of a nucleic acid sequence encoding an adenovirus E1 region in expressible format. In even more preferred embodiments, said host cells are derived from a human retina and immortalized with nucleic acids comprising adenoviral E1 sequences, such as 911 cells or the cell line deposited at the European Collection of Cell Cultures (ECACC), CAMR, Salisbury, Wiltshire SP4 OJG, Great Britain on 29 February 1996 under number 96022940 and marketed under the trademark PER.C6® (PER.C6 is a registered trademark of Crucell Holland B.V.). For the purposes of this application "PER.C6" refers to cells deposited under number 96022940 or ancestors, passages up-stream or downstream as well as descendants from ancestors of deposited cells, as well as derivatives of any of the foregoing. Production of recombinant proteins in host cells can be performed according to methods well known in the art. The use of the cells marketed under the trademark PER.C6® as a production platform for proteins of interest has been described in WO 00/63403.

[0068] A method of producing a binding molecule according to the invention is an additional part of the invention. The method comprises the steps of a) culturing a host according to the invention under conditions conducive to the expression of the binding molecule, and b) optionally, recovering the expressed binding molecule. The expressed binding molecules or immunoconjugates can be recovered from the cell free extract, but preferably they are recovered from the culture medium. The above method of producing can also be used to make functional variants of the binding molecules and/or immunoconjugates of the present invention. Methods to recover proteins, such as binding molecules, from cell free extracts or culture medium are well known to the man skilled in the art. Binding molecules, functional variants and/or immunoconjugates as obtainable by the above-described method are also a part of the present invention.

[0069] Alternatively, next to the expression in hosts, such as host cells, the binding molecules and immunoconjugates of the invention can be produced synthetically by conventional peptide synthesizers or in cell-free translation systems using RNA nucleic acid derived from DNA molecules according to the invention. Binding molecules and immunoconjugates as obtainable by the above described synthetic production methods or cell-free translation systems are also a part of the present invention.

[0070] In yet another embodiment, binding molecules of the present invention can also be produced in transgenic, non-human, mammals such as *inter alia* rabbits, goats or cows, and secreted into for instance the milk thereof.

[0071] In yet another alternative embodiment, binding molecules according to the present invention, preferably human binding molecules specifically binding to staphylococci or a fragment thereof, may be generated by transgenic non-human mammals, such as for instance transgenic mice or rabbits, that express human immunoglobulin genes. Preferably, the transgenic non-

human mammals have a genome comprising a human heavy chain transgene and a human light chain transgene encoding all or a portion of the human binding molecules as described above. The transgenic non-human mammals can be immunized with a purified or enriched preparation of staphylococci or a fragment thereof. Protocols for immunizing non-human mammals are well established in the art. See *Using Antibodies: A Laboratory Manual*, Edited by: E. Harlow, D. Lane (1998), Cold Spring Harbor Laboratory, Cold Spring Harbor, New York and *Current Protocols in Immunology*, Edited by: J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober (2001), John Wiley & Sons Inc., New York. Immunization protocols often include multiple immunizations, either with or without adjuvants such as Freund's complete adjuvant and Freund's incomplete adjuvant, but may also include naked DNA immunizations. In another embodiment, the human binding molecules are produced by B cells or plasma cells derived from the transgenic animals. In yet another embodiment, the human binding molecules are produced by hybridomas, which are prepared by fusion of B cells obtained from the above-described transgenic non-human mammals to immortalized cells. B cells, plasma cells and hybridomas as obtainable from the above-described transgenic non-human mammals and human binding molecules as obtainable from the above-described transgenic non-human mammals, B cells, plasma cells and hybridomas are also a part of the present invention.

[0072] Also disclosed herein is a method of identifying a binding molecule, such as a human binding molecule, *e.g.* a human monoclonal antibody or fragment thereof, specifically binding to at least two different bacterial organisms or nucleic acid molecules encoding such binding molecules and comprises the steps of: (a) contacting a collection of binding molecules on the surface of replicable genetic packages with a first bacterial organism under conditions conducive to binding, (b) selecting at least once for a replicable genetic package binding to the first bacterial organism, (c) optionally, separating the replicable genetic package binding to the first bacterial organism from replicable genetic packages that do not bind to the first bacterial organism, contacting the separated replicable genetic packages with a second bacterial organism under conditions conducive to binding and selecting at least once for a replicable genetic package binding to the second bacterial organism, and (d) separating and recovering the replicable genetic package binding to the first and/or second bacterial organism from replicable genetic packages that do not bind to the first and/or second bacterial organism. Of course, the above methods extended with selections on third and further bacterial organisms are also part of the present invention.

[0073] A replicable genetic package as used herein can be prokaryotic or eukaryotic and includes cells, spores, yeasts, bacteria, viruses, (bacterio)phage, ribosomes and polysomes. A preferred replicable genetic package is a phage. The binding molecules, such as for instance single chain Fvs, are displayed on the replicable genetic package, *i. e.* they are attached to a group or molecule located at an exterior surface of the replicable genetic package. The replicable genetic package is a screenable unit comprising a binding molecule to be screened linked to a nucleic acid molecule encoding the binding molecule. The nucleic acid molecule should be replicable either *in vivo* (*e.g.*, as a vector) or *in vitro* (*e.g.*, by PCR, transcription and translation). *In vivo* replication can be autonomous (as for a cell), with the assistance of host factors (as for a virus) or with the assistance of both host and helper virus (as for a phagemid). Replicable genetic packages displaying a collection of binding molecules is formed by introducing nucleic acid molecules encoding exogenous binding molecules to be displayed into the genomes of the replicable genetic packages to form fusion proteins with endogenous proteins that are normally expressed from the outer surface of the replicable genetic packages. Expression of the fusion proteins, transport to the outer surface and assembly results in display of exogenous binding molecules from the outer surface of the replicable genetic packages.

[0074] The selection step(s) in the method according to the present invention can be performed with bacterial organisms that are live and still infective or inactivated. Inactivation of bacterial organism may be performed by bacterial inactivation methods well known to the skilled artisan such as *inter alia* treatment with low pH, *i.e.* pH 4 for 6 hours to 21 days; treatment with organic solvent/detergent, *i.e.* addition of organic solvents and detergents (Triton X-100 or Tween-80) to the bacterium; UV/light irradiation; gamma-irradiation; and treatment with relevant antibiotics. Methods to test, if a bacterial organism is still alive, infective and/or viable or partly or completely inactivated are well known to the person skilled in the art. The bacterial organisms used in the above method may be non-isolated, *e.g.* present in serum and/or blood of an infected individual. The bacterial organisms used may also be isolated as discrete colonies after overnight culture at 37°C on a suitable medium such as sheep blood agar.

[0075] In an embodiment the first and/or second bacterial organisms are in suspension when contacted with the replicable genetic packages. Alternatively, they may also be coupled to a carrier when contact takes place. In another embodiment the first and second bacterial organism are from a different bacterial family, *e.g.* the first is from a Gram-negative bacterium and the second is from a Gram-positive bacterium. This way, binding molecules capable of specifically binding to Gram-positive and Gram-negative bacteria can be found. Preferably, the first and second bacterial organism are both Gram-positive bacteria. The first and second bacterial organism can both be staphylococci. In one embodiment the first and second bacterial organism are different strains from the same bacterial species, *e.g.* a *Staphylococcus* species such as *S. aureus* or *S. epidermidis*. This way, species-specific binding molecules can be found that are capable of specifically binding to different strains within one species. In another embodiment the first and second bacterial organism are each a member of a different *Staphylococcus* species, *e.g.* the first and second *Staphylococcus* species are selected from the group consisting of *S. aureus* and *S. epidermidis*. This way,

binding molecules capable of specifically binding to different species within one bacterial genus can be found. Alternatively, first and second bacterial organisms can both be enterococci. In one embodiment the first and second bacterial organism are different strains from the same bacterial species, e.g. an *Enterococcus* species such as *E. faecalis* or *E. faecium*. This way, species-specific binding molecules can be found that are capable of specifically binding to different strains within one species. In another embodiment the first and second bacterial organism are each a member of a different *Enterococcus* species, e.g. the first and second *Enterococcus* species are selected from the group consisting of *E. faecalis* and *E. faecium*.

[0076] Alternatively, the selection step may be performed in the presence of a fragment of the bacterial organisms such as e.g. cell membrane preparations, cell membrane preparations that have been enzymically treated to remove proteins (e.g. with protease K), cell membrane preparations that have been enzymically treated to remove carbohydrate moieties (e.g. with periodate), recombinant proteins or polysaccharides. In yet another embodiment, the selection step may be performed in the presence of one or more proteins or (poly)peptides derived from the bacterial organisms, fusion proteins comprising these proteins or (poly)peptides, and the like. Extracellularly exposed parts of these proteins can also be used as selection material. The live or inactivated bacterial organisms or fragments thereof may be immobilized to a suitable material before use. Alternatively, live or inactivated bacteria in suspension are used. In an embodiment the selection can be performed on different materials derived from bacterial organisms. For instance, the first selection round can be performed on live or inactivated bacterial organisms in suspension, while the second and third selection round can be performed on recombinant bacterial proteins and polysaccharides, respectively. Of course, other combinations are also contemplated herein. Different bacterial materials can also be used during one selection/panning step. In a further aspect the invention provides methods wherein the bacterial organisms used in the selection step(s) are derived from the same or different growth phases of the bacteria, e.g. the lag phase, log phase, stationary phase or death phase. This way, phase-specific anti-bacterial binding molecules may be found. For instance, the first bacterial organism may be a *S. atreus* in stationary phase, while the second bacterial organism is a *S. atreus* in log phase or the first bacterial organism may be a *S. aureus* in lag phase, while the second bacterial organism is a *S. epidermidis* in lag phase. Further combinations are well within the reach of the skilled artisan.

[0077] Also disclosed herein is a method as described above wherein, if the first and/or second *Staphylococcus* species is a *S. aureus* strain, Protein A present on the surface of the *S. aureus* strain is blocked before the *S. aureus* strain is contacted with replicable genetic packages. Suitable blocking agent may be rabbit serum, purified rabbit immunoglobulin, fetal calf serum, pooled human serum

[0078] Also disclosed herein is a method of obtaining a binding molecule specifically binding to at least two different bacterial organisms or a nucleic acid molecule encoding such a binding molecule, wherein the method comprises the steps of a) performing the above described method of identifying binding molecules, and b) isolating from the recovered replicable genetic package the binding molecule and/or the nucleic acid molecule encoding the binding molecule. The collection of binding molecules on the surface of replicable genetic packages can be a collection of scFvs or Fabs. Once a new scFv or Fab has been established or identified with the above-mentioned method of identifying binding molecules or nucleic acid molecules encoding the binding molecules, the DNA encoding the scFv or Fab can be isolated from the bacteria or phages and combined with standard molecular biological techniques to make constructs encoding bivalent scFvs or complete human immunoglobulins of a desired specificity (e.g. IgG, IgA or IgM). These constructs can be transfected into suitable cell lines and complete human monoclonal antibodies can be produced (see Huls *et al.*, 1999; Boel *et al.*, 2000).

[0079] As mentioned before the preferred replicable genetic package is a phage. Phage display methods for identifying and obtaining (human) binding molecules, e.g. (human) monoclonal antibodies, are by now well-established methods known by the person skilled in the art. They are e.g. described in US Patent Number 5,696,108; Burton and Barbas, 1994; de Kruif *et al.*, 1995b; and Phage Display: A Laboratory Manual. Edited by: CF Barbas, DR Burton, JK Scott and GJ Silverman (2001), Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York.. For the construction of phage display libraries, collections of human monoclonal antibody heavy and light chain variable region genes are expressed on the surface of bacteriophage, preferably filamentous bacteriophage, particles, in for example single-chain Fv (scFv) or in Fab format (see de Kruif *et al.*, 1995b). Large libraries of antibody fragment-expressing phages typically contain more than $1.0 \cdot 10^9$ antibody specificities and may be assembled from the immunoglobulin V regions expressed in the B-lymphocytes of immunized- or non-immunized individuals. The phage library of binding molecules, preferably scFv phage library, is prepared from RNA isolated from cells obtained from a subject that has been vaccinated against a bacterium, recently vaccinated against an unrelated pathogen, recently suffered from a chronic or acute bacterial infection, e.g. staphylococcal infection, or from a healthy individual. RNA can be isolated from *inter alia* bone marrow or peripheral blood, preferably peripheral blood lymphocytes or on isolated B cells or even on subpopulations of B cells. The subject can be an animal vaccinated against a bacterium or an animal that has or has had a bacterial infection. Preferably, the animal is a human subject that has been vaccinated against a bacterium or has or has had a chronic bacterial infection or an acute bacterial infection. Preferably, the human subject has recently recovered from the bacterial

infection.

[0080] Alternatively, phage display libraries may be constructed from immunoglobulin variable regions that have been partially assembled *in vitro* to introduce additional antibody diversity in the library (semi-synthetic libraries). For example, *in vitro* assembled variable regions contain stretches of synthetically produced, randomized or partially randomized DNA in those regions of the molecules that are important for antibody specificity, e.g. CDR regions. Phage antibodies specific for bacteria such as staphylococci can be selected from the library by exposing the bacteria or material thereof to a phage library to allow binding of phages expressing antibody fragments specific for the bacteria or material thereof. Non-bound phages are removed by washing and bound phages eluted for infection of *E.coli* bacteria and subsequent propagation. Multiple rounds of selection and propagation are usually required to sufficiently enrich for phages binding specifically to the bacteria or material thereof. If desired, before exposing the phage library to the bacteria or material thereof the phage library can first be subtracted by exposing the phage library to non-target material such as bacteria of a different family, species and/or strain or bacteria in a different growth phase or material of these bacteria. These subtractor bacteria or material thereof can be bound to a solid phase or can be in suspension. Phages may also be selected for binding to complex antigens such as complex mixtures of bacterial proteins or (poly)peptides optionally supplemented with bacterial polysaccharides or other bacterial material. Host cells expressing one or more proteins or (poly)peptides of bacteria such as staphylococci may also be used for selection purposes. A phage display method using these host cells can be extended and improved by subtracting non-relevant binders during screening by addition of an excess of host cells comprising no target molecules or non-target molecules that are similar, but not identical, to the target, and thereby strongly enhance the chance of finding relevant binding molecules. Of course, the subtraction may be performed before, during or after the screening with bacterial organisms or material thereof. The process is referred to as the Mabstrac® process (Mabstrac® is a registered trademark of Crucell Holland B.V., see also US Patent Number 6,265,150).

[0081] Also disclosed herein is a method of obtaining a binding molecule potentially having killing activity against at least two different bacterial organisms, wherein the method comprises the steps of (a) performing the method of obtaining a binding molecule specifically binding to at least two different bacterial organisms or a nucleic acid molecule encoding such a binding molecule as described above, and (b) verifying if the binding molecule isolated has killing activity against at least two different bacterial organisms. Assays for verifying if a binding molecule has killing activity such as opsonic activity are well known in the art (see for instance Manual of Molecular and Clinical Laboratory Immunology, 7th Edition). In a further embodiment the binding molecule is also tested for any other activity. Other useful activities are mentioned above.

[0082] In a further aspect the invention pertains to a binding molecule having killing activity against at least two, preferably at least three or more, different bacterial organisms, such as e.g. staphylococci, and being obtainable by the methods as described above. A pharmaceutical composition comprising the binding molecule, the pharmaceutical composition further comprising at least one pharmaceutically acceptable excipient is also an aspect of the present invention. Pharmaceutically acceptable excipients are well known to the skilled person. The pharmaceutical composition according to the invention may further comprise at least one other therapeutic agent. Suitable agents are also well known to the skilled artisan.

[0083] In yet a further aspect, the invention provides compositions comprising at least one binding molecule preferably a human monoclonal antibody according to the invention, at least one immunoconjugate according to the invention or a combination thereof. In addition to that, the compositions may comprise *inter alia* stabilizing molecules, such as albumin or polyethylene glycol, or salts. Preferably, the salts used are salts that retain the desired biological activity of the binding molecules and do not impart any undesired toxicological effects. If necessary, the human binding molecules of the invention may be coated in or on a material to protect them from the action of acids or other natural or non-natural conditions that may inactivate the binding molecules.

[0084] In yet a further aspect, the invention provides compositions comprising at least one nucleic acid molecule as defined in the present invention. The compositions may comprise aqueous solutions such as aqueous solutions containing salts (e.g., NaCl or salts as described above), detergents (e.g., SDS) and/or other suitable components.

[0085] Furthermore, the present invention pertains to pharmaceutical compositions comprising at least one binding molecule such as a human monoclonal antibody of the invention (or functional fragment or variant thereof), at least one immunoconjugate according to the invention, at least one composition according to the invention, or combinations thereof. The pharmaceutical composition of the invention further comprises at least one pharmaceutically acceptable excipient.

[0086] In an embodiment the pharmaceutical compositions may comprise two or more binding molecules that have killing activity against a bacterial organism, e.g. a *Staphylococcus* species. In an embodiment, the binding molecules exhibit synergistic killing activity, when used in combination. In other words, the compositions comprise at least two binding molecules having killing activity, characterized in that the binding molecules act synergistically in killing a bacterial organism such as e.g. a *Staphylococcus* species. As used herein, the term "synergistic" means that the combined effect of the binding molecules when used in

combination is greater than their additive effects when used individually. The synergistically acting binding molecules may bind to different structures on the same or distinct fragments of the bacterial organism. In an embodiment the binding molecules acting synergistically in killing a bacterial organism may also be capable of killing other bacterial organisms synergistically. A way of calculating synergy is by means of the combination index. The concept of the combination index (CI) has been described by Chou and Talalay, 1984. The two or more binding molecules having synergistic activity have distinct modes of action. For instance a first binding molecule may have opsonizing activity, while the second binding molecule has another activity increasing/augmenting/enhancing phagocytosis or a first binding molecule may have intrinsic (killing) activity, *e.g.* reduce or inhibit bacterial growth or directly kill bacteria, while the second binding molecule increases the sensitivity of bacteria to antibiotic treatment. It is to be understood that other combinations are also contemplated herein.

[0087] A pharmaceutical composition according to the invention can further comprise at least one other therapeutic, prophylactic and/or diagnostic agent. Preferably, the pharmaceutical composition comprises at least one other prophylactic and/or therapeutic agent. Preferably, said further therapeutic and/or prophylactic agents are agents capable of preventing and/or treating a bacterial, *e.g.* staphylococcal, infection and/or a condition resulting from such an infection. Therapeutic and/or prophylactic agents include, but are not limited to, anti-bacterial agents. Such agents can be binding molecules, small molecules, organic or inorganic compounds, enzymes, polynucleotide sequences, antimicrobial peptides, etc. Other agents that are currently used to treat patients infected with bacterial infections such as staphylococcal infections are antibiotics such as methicillin, 2nd and 3rd generation cephalosporins, aminoglycosides, Carbapenems, Macrolides, Ketolides, Quinolones and miscellaneous antibiotics such as daptomycin, linezolid, nitrofurantoin, quinupristin/dalfopristin, trimethoprim/sulfa, vancomycin. These can be used in combination with the binding molecules of the invention. Agents capable of preventing and/or treating an infection with bacteria and/or a condition resulting from such an infection that are in the experimental phase might also be used as other therapeutic and/or prophylactic agents useful in the present invention.

[0088] The binding molecules or pharmaceutical compositions of the invention can be tested in suitable animal model systems prior to use in humans. Such animal model systems include, but are not limited to, murine sepsis and peritonitis models, rat sepsis and endocarditis models, and rabbit endocarditis models.

[0089] Typically, pharmaceutical compositions must be sterile and stable under the conditions of manufacture and storage. The binding molecules, immunoconjugates, nucleic acid molecules or compositions of the present invention can be in powder form for reconstitution in the appropriate pharmaceutically acceptable excipient before or at the time of delivery. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying (lyophilization) that yield a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

[0090] Alternatively, the binding molecules, immunoconjugates, nucleic acid molecules or compositions of the present invention can be in solution and the appropriate pharmaceutically acceptable excipient can be added and/or mixed before or at the time of delivery to provide a unit dosage injectable form. Preferably, the pharmaceutically acceptable excipient used in the present invention is suitable to high drug concentration, can maintain proper fluidity and, if necessary, can delay absorption.

[0091] The choice of the optimal route of administration of the pharmaceutical compositions will be influenced by several factors including the physico-chemical properties of the active molecules within the compositions, the urgency of the clinical situation and the relationship of the plasma concentrations of the active molecules to the desired therapeutic effect. For instance, if necessary, the binding molecules of the invention can be prepared with carriers that will protect them against rapid release, such as a controlled release formulation, including implants, transdermal patches, and microencapsulated delivery systems. Biodegradable, biocompatible polymers can *inter alia* be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Furthermore, it may be necessary to coat the binding molecules with, or co-administer the binding molecules with, a material or compound that prevents the inactivation of the human binding molecules. For example, the binding molecules may be administered to a subject in an appropriate carrier, for example, liposomes or a diluent.

[0092] The routes of administration can be divided into two main categories, oral and parenteral administration. The preferred administration route is intravenous.

[0093] Oral dosage forms can be formulated *inter alia* as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard capsules, soft gelatin capsules, syrups or elixirs, pills, dragees, liquids, gels, or slurries. These formulations can contain pharmaceutically acceptable excipients including, but not limited to, inert diluents, granulating and disintegrating agents, binding agents, lubricating agents, preservatives, colouring, flavoring or sweetening agents, vegetable or mineral oils, wetting agents, and thickening agents.

[0094] The pharmaceutical compositions of the present invention can also be formulated for parenteral administration. Formulations for parenteral administration can be *inter alia* in the form of aqueous or non-aqueous isotonic sterile non-toxic injection or infusion solutions or suspensions. The solutions or suspensions may comprise agents that are non-toxic to recipients at the dosages and concentrations employed such as 1,3-butanediol, Ringer's solution, Hank's solution, isotonic sodium chloride solution, oils, fatty acids, local anesthetic agents, preservatives, buffers, viscosity or solubility increasing agents, water-soluble antioxidants, oil-soluble antioxidants, and metal chelating agents.

[0095] In a further aspect, the binding molecules such as human monoclonal antibodies (functional fragments and variants thereof), immunoconjugates, compositions, or pharmaceutical compositions of the invention can be used as a medicament. So, a method of treatment and/or prevention of a bacterial (Gram-positive and/or Gram-negative), *e.g.* a staphylococcal, infection using the binding molecules, immunoconjugates, compositions, or pharmaceutical compositions of the invention is another part of the present invention. The above-mentioned molecules can *inter alia* be used in the diagnosis, prophylaxis, treatment, or combination thereof, of a bacterial infection. They are suitable for treatment of yet untreated patients suffering from a bacterial infection and patients who have been or are treated for a bacterial infection. They may be used for patients such as hospitalized infants, premature infants, burn victims, elderly patients, immunocompromised patients, immunosuppressed patients, patient undergoing an invasive procedure, and health care workers. Each administration may protect against further infection by the bacterial organism for up to three or four weeks and/or will retard the onset or progress of the symptoms associated with the infection. The binding molecules of the invention may also increase the effectiveness of existing antibiotic treatment by increasing the sensitivity of the bacterium to the antibiotic, may stimulate the immune system to attack the bacterium in ways other than through opsonization. This activation may result in long lasting protection to the infection bacterium. Furthermore, the binding molecules of the invention may directly inhibit the growth of the bacterium or inhibit virulence factors required for its survival during the infection.

[0096] The above-mentioned molecules or compositions may be employed in conjunction with other molecules useful in diagnosis, prophylaxis and/or treatment. They can be used *in vitro*, *ex vivo* or *in vivo*. For instance, the binding molecules such as human monoclonal antibodies (or functional variants thereof), immunoconjugates, compositions or pharmaceutical compositions of the invention can be co-administered with a vaccine against the bacterial organism (if available). Alternatively, the vaccine may also be administered before or after administration of the molecules of the invention. Instead of a vaccine, anti-bacterial agents can also be employed in conjunction with the binding molecules of the present invention. Suitable anti-bacterial agents are mentioned above.

[0097] The molecules are typically formulated in the compositions and pharmaceutical compositions of the invention in a therapeutically or diagnostically effective amount. Alternatively, they may be formulated and administered separately. For instance the other molecules such as the anti-bacterial agents may be applied systemically, while the binding molecules of the invention may be applied intrathecally or intraventricularly.

[0098] Dosage regimens can be adjusted to provide the optimum desired response (*e.g.*, a therapeutic response). A suitable dosage range may for instance be 0.1-100 mg/kg body weight, preferably 0.5-15 mg/kg body weight. Furthermore, for example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation. The molecules and compositions according to the present invention are preferably sterile. Methods to render these molecules and compositions sterile are well known in the art. The other molecules useful in diagnosis, prophylaxis and/or treatment can be administered in a similar dosage regimen as proposed for the binding molecules of the invention. If the other molecules are administered separately, they may be administered to a patient prior to (*e.g.*, 2 minutes, 5 minutes, 10 minutes, 15 minutes, 30 minutes, 45 minutes, 60 minutes, 2 hours, 4 hours, 6 hours, 8 hours, 10 hours, 12 hours, 14 hours, 16 hours, 18 hours, 20 hours, 22 hours, 24 hours, 2 days, 3 days, 4 days, 5 days, 7 days, 2 weeks, 4 weeks or 6 weeks before), concomitantly with, or subsequent to (*e.g.*, 2 minutes, 5 minutes, 10 minutes, 15 minutes, 30 minutes, 45 minutes, 60 minutes, 2 hours, 4 hours, 6 hours, 8 hours, 10 hours, 12 hours, 14 hours, 16 hours, 18 hours, 20 hours, 22 hours, 24 hours, 2 days, 3 days, 4 days, 5 days, 7 days, 2 weeks, 4 weeks or 6 weeks after) the administration of one or more of the human binding molecules or pharmaceutical compositions of the invention. The exact dosing regimen is usually sorted out during clinical trials in human patients.

[0099] Human binding molecules and pharmaceutical compositions comprising the human binding molecules are particularly useful, and often preferred, when to be administered to human beings as *in vivo* therapeutic agents, since recipient immune response to the administered antibody will often be substantially less than that occasioned by administration of a monoclonal murine, chimeric or humanized binding molecule.

[0100] In another aspect, the invention concerns the use of the binding molecules such as killing human monoclonal antibodies

(functional fragments and variants thereof), immunoconjugates, nucleic acid molecules, compositions or pharmaceutical compositions according to the invention in the preparation of a medicament for the diagnosis, prophylaxis, treatment, or combination thereof, of a bacterial (Gram-positive and/or Gram-negative), e.g. staphylococcal infection.

[0101] Next to that, kits comprising at least one binding molecule such as a killing human monoclonal antibody (functional fragments and variants thereof), at least one immunoconjugate, at least one nucleic acid molecule, at least one composition, at least one pharmaceutical composition, at least one vector, at least one host according to the invention or a combination thereof are also a part of the present invention. Optionally, the above-described components of the kits of the invention are packed in suitable containers and labeled for diagnosis, prophylaxis and/or treatment of the indicated conditions. The above-mentioned components may be stored in unit or multi-dose containers as an aqueous, preferably sterile, solution or as a lyophilized, preferably sterile, formulation for reconstitution. The containers may be formed from a variety of materials such as glass or plastic and may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). The kit may further comprise more containers comprising a pharmaceutically acceptable buffer. It may further include other materials desirable from a commercial and user standpoint, including other buffers, diluents, filters, needles, syringes, culture medium for one or more of the suitable hosts and, possibly, even at least one other therapeutic, prophylactic or diagnostic agent. Associated with the kits can be instructions customarily included in commercial packages of therapeutic, prophylactic or diagnostic products, that contain information about for example the indications, usage, dosage, manufacture, administration, contra-indications and/or warnings concerning the use of such therapeutic, prophylactic or diagnostic products.

[0102] The binding molecules of the invention may also be used to coat medical devices or polymeric biomaterials.

[0103] Also disclosed herein is a method of detecting a bacterial organism (Gram-positive and/or Gram-negative) in a sample, wherein the method comprises the steps of (a) contacting a sample with a diagnostically effective amount of a binding molecule (functional fragments and variants thereof) or an immunoconjugate according to the invention, and (b) determining whether the binding molecule or immunoconjugate specifically binds to a molecule of the sample. Preferably, the method is used to detect a *Staphylococcus* in a sample. The sample may be a biological sample including, but not limited to blood, serum, urine, tissue or other biological material from (potentially) infected subjects, or a non-biological sample such as water, drink, etc. The (potentially) infected subjects may be human subjects, but also animals that are suspected as carriers of such a bacterial organism might be tested for the presence of the organism using the human binding molecules or immunoconjugates of the invention. The sample may first be manipulated to make it more suitable for the method of detection. Manipulation means *inter alia* treating the sample suspected to contain and/or containing the bacterial organism in such a way that the organism will disintegrate into antigenic components such as proteins, (poly)peptides or other antigenic fragments. Preferably, the human binding molecules or immunoconjugates of the invention are contacted with the sample under conditions which allow the formation of an immunological complex between the human binding molecules and the bacterial organism or antigenic components thereof that may be present in the sample. The formation of an immunological complex, if any, indicating the presence of the bacterial organism in the sample, is then detected and measured by suitable means. Such methods include, *inter alia*, homogeneous and heterogeneous binding immunoassays, such as radio-immunoassays (RIA), ELISA, immunofluorescence, immunohistochemistry, FACS, BIACORE and Western blot analyses.

[0104] Preferred assay techniques, especially for large-scale clinical screening of patient sera and blood and blood-derived products are ELISA and Western blot techniques. ELISA tests are particularly preferred. For use as reagents in these assays, the binding molecules or immunoconjugates of the invention are conveniently bonded to the inside surface of microtiter wells. The binding molecules or immunoconjugates of the invention may be directly bonded to the microtiter well. However, maximum binding of the binding molecules or immunoconjugates of the invention to the wells might be accomplished by pre-treating the wells with polylysine prior to the addition of the binding molecules or immunoconjugates of the invention. Furthermore, the binding molecules or immunoconjugates of the invention may be covalently attached by known means to the wells. Generally, the binding molecules or immunoconjugates are used between 0.01 to 100 µg/ml for coating, although higher as well as lower amounts may also be used. Samples are then added to the wells coated with the binding molecules or immunoconjugates of the invention.

[0105] Furthermore, binding molecules of the invention can be used to identify specific binding structures of a bacterial organism e.g. a *Staphylococcus*. The binding structures can be epitopes on proteins and/or polypeptides. They can be linear, but also structural and/or conformational. In one embodiment, the binding structures can be analyzed by means of PEPSCAN analysis (see *inter alia* WO 84/03564, WO 93/09872, Sloodstra et al., 1996). Alternatively, a random peptide library comprising peptides from a protein of a bacterial organism can be screened for peptides capable of binding to the binding molecules of the invention. The binding structures/peptides/epitopes found can be used as vaccines and for the diagnosis of bacterial infections. In case fragments other than proteins and/or polypeptides are bound by the binding molecules binding structures can be identified by

mass spectrometry, high performance liquid chromatography and nuclear magnetic resonance.

[0106] Also disclosed herein is a method of screening a binding molecule (or a functional fragment or variant thereof) for specific binding to the same epitope of a bacterial organism (Gram-positive and/or Gram-negative), *e.g.* *Staphylococcus*, as the epitope bound by a human binding molecule of the invention, wherein the method comprises the steps of (a) contacting a binding molecule to be screened, a binding molecule of the invention and a bacterial organism or fragment thereof, (b) measure if the binding molecule to be screened is capable of competing for specifically binding to the bacterial organism or fragment thereof with the binding molecule of the invention. In a further step it may be determined, if the screened binding molecules that are capable of competing for specifically binding to the bacterial organism or fragment thereof have killing activity, *e.g.* opsonic activity. A binding molecule that is capable of competing for specifically binding to the bacterial organism or a fragment thereof with the binding molecule of the invention is another part of the present invention. In the above-described screening method, "specifically binding to the same epitope" also contemplates specific binding to substantially or essentially the same epitope as the epitope bound by the a binding molecule of the invention. The capacity to block, or compete with, the binding of the binding molecules of the invention to the bacterial organism typically indicates that a binding molecule to be screened binds to an epitope or binding site on the bacterial organism that structurally overlaps with the binding site on the bacterial organism that is immunospecifically recognized by the binding molecules of the invention. Alternatively, this can indicate that a binding molecule to be screened binds to an epitope or binding site which is sufficiently proximal to the binding site immunospecifically recognized by the binding molecules of the invention to sterically or otherwise inhibit binding of the binding molecules of the invention to the bacterial organism.

[0107] In general, competitive inhibition is measured by means of an assay, wherein an antigen composition, *i.e.* a composition comprising a bacterial organism or fragments thereof, is admixed with reference binding molecules, *i. e.* the binding molecules of the invention, and binding molecules to be screened. Usually, the binding molecules to be screened are present in excess. Protocols based upon ELISAs and Western blotting are suitable for use in such simple competition studies. By using species or isotype secondary antibodies one will be able to detect only the bound reference binding molecules, the binding of which will be reduced by the presence of a binding molecule to be screened that recognizes substantially the same epitope. In conducting a binding molecule competition study between a reference binding molecule and any binding molecule to be screened (irrespective of species or isotype), one may first label the reference binding molecule with a detectable label, such as, *e.g.*, biotin, an enzymatic, a radioactive or other label to enable subsequent identification. Binding molecules identified by these competition assays ("competitive binding molecules" or "cross-reactive binding molecules") include, but are not limited to, antibodies, antibody fragments and other binding agents that bind to an epitope or binding site bound by the reference binding molecule, *i.e.* a binding molecule of the invention, as well as antibodies, antibody fragments and other binding agents that bind to an epitope or binding site sufficiently proximal to an epitope bound by the reference binding molecule for competitive binding between the binding molecules to be screened and the reference binding molecule to occur. Preferably, competitive binding molecules of the invention will, when present in excess, inhibit specific binding of a reference binding molecule to a selected target species by at least 10%, preferably by at least 25%, more preferably by at least 50%, and most preferably by at least 75%-90% or even greater. The identification of one or more competitive binding molecules that bind to about, substantially, essentially or at the same epitope as the binding molecules of the invention is a straightforward technical matter. As the identification of competitive binding molecules is determined in comparison to a reference binding molecule, *i. e.* a binding molecule of the invention, it will be understood that actually determining the epitope to which the reference binding molecule and the competitive binding molecule bind is not in any way required in order to identify a competitive binding molecule that binds to the same or substantially the same epitope as the reference binding molecule.

EXAMPLES

[0108] To illustrate the invention, the following examples are provided. The examples are not intended to limit the scope of the invention in any way.

Example 1

Constriction of scFv phage display libraries using RNA extracted from donors screened for opsonic activity

[0109] Samples of blood were taken from donors reporting a recent gram-positive bacterial infection as well as healthy adults between 25-50 years of age. Peripheral blood leukocytes were isolated by centrifugation and the blood serum was saved and

frozen at - 80°C. Donor serum was screened for opsonic activity using a FACS-based phagocytosis assay (Cantinieux *et al.*, 1989) and compared to a pool of normal healthy donor serum. Sera from donors having a higher phagocytic activity compared to normal serum were chosen to use for the generation of phage display libraries. Total RNA was prepared from the peripheral blood leukocytes of these donors using organic phase separation and subsequent ethanol precipitation. The obtained RNA was dissolved in RNase-free water and the concentration was determined by OD 260nm measurement. Thereafter, the RNA was diluted to a concentration of 100 ng/μl. Next, 1 μg of RNA was converted into cDNA as follows: To 10 μl total RNA, 13 μl DEPC-treated ultrapure water and 1 μl random hexamers (500 ng/μl) were added and the obtained mixture was heated at 65°C for 5 minutes and quickly cooled on wet-ice. Then, 8 μl 5X First-Strand buffer, 2 μl dNTP (10 mM each), 2 μl DTT (0.1 M), 2 μl RNase-inhibitor (40 U/μl) and 2 μl Superscript™III MMLV reverse transcriptase (200 U/μl) were added to the mixture, incubated at room temperature for 5 minutes and incubated for 1 hour at 50°C. The reaction was terminated by heat inactivation, *i.e.* by incubating the mixture for 15 minutes at 75°C. The obtained cDNA products were diluted to a final volume of 200 μl with DEPC-treated ultrapure water. The OD 260 nm of a 50 times diluted solution (in 10 mM Tris buffer) of the dilution of the obtained cDNA products was used to determine the cDNA concentration. For each donor 5 to 10 μl of the diluted cDNA products were used as template for PCR amplification of the immunoglobulin gamma heavy chain family and kappa or lambda light chain sequences using specific oligonucleotide primers (see Tables 1-7). In addition, for one donor PCR amplification of the immunoglobulin mu heavy chain family and kappa or lambda light chain sequences was carried out. PCR reaction mixtures contained, besides the diluted cDNA products, 25 pmol sense primer and 25 pmol anti-sense primer in a final volume of 50 μl of 20 mM Tris-HCl (pH 8.4), 50 mM KCl, 1.5 mM MgCl₂, 250 μM dNTPs and 1.25 units Taq polymerase. In a heated-lid thermal cycler having a temperature of 96°C, the mixtures obtained were quickly melted for 2 minutes, followed by 30 cycles of: 30 seconds at 96°C, 30 seconds at 55°C or 60°C and 60 seconds at 72°C. Finally, the samples were incubated 10 minutes at 72°C and refrigerated at 4°C until further use.

[0110] In a first round amplification, each of eighteen light chain variable region sense primers (twelve for the lambda light chain (see Table 1; the HuVL1A-Back, HuVL1B-Back and HuVL1C-Back sense primers were mixed to equimolarity before use, as well as the HuVL9-Back and HuVL10-Back sense primers) and six for the kappa light chain (see Table 2)) were combined with an anti-sense primer recognizing the C-kappa constant region called HuCK-FOR 5'-ACACTCTCCCTGTTGAAGCTCTT-3' (SEQ ID NO:37) or C-lambda constant region HuCL2-FOR 5'-TGAACATTCTGTAGGGGCCACTG-3' (SEQ ID NO:38) and HuCL7-FOR 5'-AGAGCATTCTGCAGGGGCCACTG-3' (SEQ ID NO:39) (the HuCL2-FOR and HuCL7-FOR anti-sense primers were mixed to equimolarity before use), yielding 15 products of about 650 base pairs. These products were purified on agarose gel and isolated from the gel using Qiagen gel-extraction columns. 1/10 of each of the isolated products was used in an identical PCR reaction as described above using eighteen sense primers, whereby each lambda light chain sense primer was combined with one of the three J-lambda-region specific anti-sense primers and each kappa light chain sense primer was combined with one of the five J-kappa-region specific anti-sense primers (see Table 3; the HuVL1A-Back-SAL, HuVL1B-Back-SAL and HuVL1C-Back-SAL sense primers were mixed to equimolarity before use, as well as the HuVL9-Back-SAL and HuVL10-Back-SAL sense primers). The sense primers used in the second amplification were the same primers as used in the first amplification, but extended with restriction sites (see Table 3) to enable directed cloning in the phage display vector PDV-C06 (SEQ ID NO:40). This resulted in 57 products of approximately 400 base pairs that were pooled as shown in Table 4 to maintain the natural distribution of the different J segments and light chain families within the library and not to over or under represent certain families. The pooled products were purified using Qiagen PCR purification columns. In the next step, 3 μg of pooled products and 100 μg PDV-C06 vector were digested with Sall and NotI and purified from gel. Thereafter, a ligation was performed overnight at 16°C as follows. To 500 ng PDV-C06 vector either 35, 70 or 140 ng pooled products were added in a total volume of 50 μl ligation mix containing 50 mM Tris-HCl (pH 7.5), 10 mM MgCl₂, 10 mM DTT, 1 mM ATP, 25 μg/ml BSA and 2.5 μl T4 DNA Ligase (400 U/μl). The ligation mixes were purified by phenol/chloroform extraction, followed by a chloroform extraction and ethanol precipitation, methods well known to the skilled artisan. The DNA obtained was dissolved in 50 μl 10 mM Tris-HCl pH 8.5 and per ligation mix 1 or 2 μl was electroporated into 40 μl of TG1 competent *E. coli* bacteria according to the manufacturer's protocol (Stratagene). Transformants were grown overnight at 37°C on 2TY agar supplemented with 50 μg/ml ampicillin and 4.5% glucose. Colonies were counted to determine the optimal vector to insert ratio. From the ligation mix with the optimal ratio, multiple 1 or 2 μl aliquots were electroporated as above and transformants were grown overnight at 37°C, typically yielding ~10⁷ colonies. A (sub)library of variable light chain regions was obtained by scraping the transformants from the agar plates. This (sub)library was directly used for plasmid DNA preparation using a Qiagen™ QIAfilter MAXI prep kit.

[0111] Heavy chain immunoglobulin sequences were amplified from the same cDNA preparations in a similar two round PCR procedure and identical reaction parameters as described above for the light chain regions with the proviso that the primers depicted in Tables 5 and 6 were used. The first amplification was performed using a set of eight sense directed primers (see Table 5; the HuVH1B/7A-Back and HuVH1C-Back sense primers were mixed to equimolarity before use) each combined with an IgG specific constant region anti-sense primer called HuClgG 5'-GTC CAC CTT GGT GTT GCT GGG CTT-3' (SEQ ID NO:41) yielding seven products of about 650 base pairs. For one donor an IgM specific constant region anti-sense primer called HuClgM 5'-TGG AAG AGG CAC GTT CTT TTC TTT-3' (SEQ ID NO:42) was used instead of primer HuClgG. The products were purified

on agarose gel and isolated from the gel using Qiagen gel-extraction columns. 1/10 of each of the isolated products was used in an identical PCR reaction as described above using eight sense primers, whereby each heavy chain sense primer was combined with one of the four JH-region specific anti-sense primers (see Table 6; the HuVH1B/7A-Back-Sfi and HuVH1C-Back-Sfi sense primers were mixed to equimolarity before use). The sense primers used in the second round were the same primers as used in the first amplification, but extended with restriction sites (see Table 6) to enable directed cloning in the light chain (sub)library vector. This resulted in 28 products of approximately 400 base pairs that were pooled as shown in Table 7 to maintain the natural distribution of the different J segments and heavy chain families within the library and not to over or under represent certain families. The pooled products were purified using Qiagen PCR purification columns. Next, 3 µg of purified products was digested with SfiI and XhoI and ligated in the light chain (sub)library vector, which was cut with the same restriction enzymes, using the same ligation procedure and volumes as described above for the light chain (sub)library. Ligation mix purification and subsequent transformation of the resulting definitive library was also performed as described above for the light chain (sub)library. All bacteria, typically $\sim 10^7$, were harvested in 2TY culture medium containing 50 µg/ml ampicillin and 4.5% glucose, mixed with glycerol to 15% (v/v) and frozen in 1.5 ml aliquots at -80°C . Rescue and selection of each library were performed as described below. The various libraries were named GPB-05-M01, GPB-05-G01, GPB-05-G02, GPB-05-G03, GPB-05-G04 and GPB-05-G05. Two other libraries, RAB-03-G01 and RAB-04-G01, were constructed using a method similar to the procedure above, as described previously in international patent application WO 2005/118644.

Example 2

Constriction of scFv phage display libraries using RNA extracted from memory B cells

[0112] Peripheral blood was collected from normal healthy donors, convalescent donors or vaccinated donors by venapuncture using EDTA anti-coagulation sample tubes. A blood sample (45 ml) was diluted twice with PBS and 30 ml aliquots were underlaid with 10 ml Ficoll-Hypaque (Pharmacia) and centrifuged at 900xg for 20 minutes at room temperature without breaks. The supernatant was removed carefully to just above the white layer containing the lymphocytic and thrombocytic fraction. Next, this layer was carefully removed (~ 10 ml), transferred to a fresh 50 ml tube and washed three times with 40 ml PBS and spun at 400xg for 10 minutes at room temperature to remove thrombocytes. The obtained pellet containing lymphocytes was resuspended in RPMI medium containing 2% FBS and the cell number was determined by cell counting. Approximately 1×10^8 lymphocytes were stained for fluorescent cell sorting using CD24, CD27 and surface IgM as markers for the isolation of switched and IgM memory B cells. A Becton Dickinson Digital Vantage apparatus set in Yield Mode was used for physical memory B cell sorting and isolation. Lymphocytes were gated as the small compact population from the FSC/SSC window. Memory B cells (CD24+/CD27+) were subsequently separated from naive B cells (CD24-/CD27-) and memory T cells (CD24-/CD27+). In a next step, IgM memory B cells (IgM+) were separated from switch memory B cells (IgM-) using IgM expression. In this step IgM memory B cells and switch memory B cells were sorted in separate sample tubes. 1×10^5 to 1×10^6 cells of each population were collected in DMEM/50% FBS and after completion of the sort they were each centrifuged at 400xg for 10 minutes. The sorted IgM memory B cells were then used as starting material for library construction according to the method described in Example 1, using primer HuCIgM in the first round amplification of heavy chain immunoglobulin sequences. The various libraries obtained were named MEM-05-M01, MEM-05-M02, MEM-05-M03, MEM-05-M04, MEM-05-M05, MEM-05-M06, MEM-05-M07, MEM-05-M08, MEM-05-M09 and MEM-05-M10.

Example 3

Selection of phages carrying single chain Fv fragments specifically binding to staphylococci

[0113] Antibody fragments were selected using antibody phage display libraries, general phage display technology and MAbstract® technology, essentially as described in US Patent Number 6,265,150 and in WO 98/15833. The antibody phage libraries used were screened donor libraries prepared as described in Example 1, IgM memory libraries prepared as described in Example 2 and a semi-synthetic scFv phage library (JK1994) which has been described in de Kruif *et al.*, 1995b. The methods and helper phages as described in WO 02/103012 were used in the present invention. For identifying phage antibodies recognizing staphylococci, phage selection experiments were performed using live bacteria in suspension. The clinical isolates used for selection and screening are described in Table 8. The isolates are different based on RFLP-typing.

[0114] Bacteria were grown overnight at 37°C on blood agar plates and scraped into RPMI buffer containing 1 mg/ml of Rabbit IgG and 1% BSA at a concentration of 5×10^9 bacteria/ml and incubated for 60 minutes at room temperature. An aliquot of a phage library (approximately 10^{13} cfu, amplified using CT helper phage (see WO 02/103012)) was blocked in blocking buffer (2% ELK in PBS) for 1-2 hours at room temperature. The blocked phage library was added to the blocked bacterial suspension making a total volume of 1.5 ml and incubated for 2 hours at room temperature in an end-over-end rotor (5 rpm). The suspension was centrifuged at 6800xg for 3 minutes at room temperature and the supernatant was discarded. Bacteria were washed five times with RPMI buffer containing 1% BSA and 0.05% v/v Tween-20, then five times with RPMI buffer containing 1% BSA to remove unbound phages. Bound phages were eluted from the antigen by incubation with 1 ml of 0.1 M triethylamine for 10 minutes at room temperature in an end-over-end rotor (5 rpm). The entire content of the tube was then mixed with 0.5 ml of 1 M Tris-HCl pH 7.5 to neutralize the pH. This mixture was used to infect 5 ml of an XL1-Blue *E.coli* culture that had been grown at 37°C to an OD 600nm of approximately 0.3. The phages were allowed to infect the XL1-Blue bacteria for 30 minutes at 37°C. Then, the mixture was centrifuged for 10 minutes at 3200*g at room temperature and the bacterial pellet was resuspended in 0.5 ml 2-trypton yeast extract (2TY) medium. The obtained bacterial suspension was divided over two 2TY agar plates supplemented with tetracyclin, ampicillin and glucose. After overnight incubation of the plates at 37°C, the colonies were scraped from the plates and used to prepare an enriched phage library, essentially as described by De Kruif et al. (1995a) and WO 02/103012. Briefly, scraped bacteria were used to inoculate 2TY medium containing ampicillin, tetracycline and glucose and grown at a temperature of 37°C to an OD 600nm of ~0.3. CT helper phages were added and allowed to infect the bacteria after which the medium was changed to 2TY containing ampicillin, tetracycline and kanamycin. Incubation was continued overnight at 30°C. The next day, the bacteria were removed from the 2TY medium by centrifugation after which the phages in the medium were precipitated using polyethylene glycol (PEG) 6000/NaCl. Finally, the phages were dissolved in 2 ml of PBS with 1% bovine serum albumin (BSA), filter-sterilized and used for the next round of selection.

[0115] Typically, two rounds of selections were performed before isolation of individual phage antibodies. Selection was carried out twice on the same strain of bacteria or different strains were used sequentially (see Table 8 for selection strains). After the second round of selection, individual *E.coli* colonies were used to prepare monoclonal phage antibodies. Essentially, individual colonies were grown to log-phase in 96 well plate format and infected with CT helper phages after which phage antibody production was allowed to proceed overnight. The produced phage antibodies were PEG/NaCl-precipitated and filter-sterilized and tested in ELISA and/or FACS for binding to *Staphylococcus* prepared as described *supra*.

Example 4

Validation of the staphylococci specific single-chain phage antibodies

[0116] Selected single-chain phage antibodies that were obtained in the screens described above were validated in FACS for specific staphylococcal binding activity, *i.e.* binding to one or more staphylococcal strain prepared as described *supra* but lacking binding to *Enterococcus* as measured by a FACS-based enterococcus binding assay. Phage antibodies were blocked with FACS buffer (20 mM HEPES buffer pH 7.5, 100 mM NaCl, 1% BSA) for 20 minutes on ice. For each staining 1×10^9 bacterial cells, scraped from blood agar plates and washed in FACS buffer, were added to each eppendorf tube. The bacteria were blocked with FACS buffer containing 15% human serum (Biowhittaker) for 30 minutes at room temperature. The bacteria were pelleted by centrifugation at 1700xg for 3 minutes at 4°C and resuspended with the blocked phage antibodies and incubated for 1.5 hours on ice. The bacteria were then washed with FACS buffer and sequentially incubated with murine biotinylated anti-M13 antibodies (RDI) followed by streptavidin-PE. The cells were fixed in buffered 4% formaldehyde and analysed on a FACS caliber. SC05-132 and SC05-133 (both selected from RAB-03-G01 on strain Cowan in suspension) showed staining on all clinical isolates tested indicating that they recognise a pan-staphylococcal target. SC02-430 (selected from JK1994 on strain Cowan in suspension) showed specific binding to the staphylococcal strain Cowan (see Table 9). In further selections the single-chain phage antibodies called SC06-166, SC06-171, SC06-176, SC06-187, SC06-193, SC06-249, SC06-273, SC06-389, SC06-403, SC06-406, SC06-410, SC06-446, SC06-450, SC06-452, SC06-453, SC06-464, SC06-471, SC06-516, SC06-517, SC06-526, SC06-528, SC06-531, SC06-533, SC06-536, SC06-537, SC06-538, SC06-540, SC06-544, SC06-566, SC06-625 were obtained. These antibodies bound at least one of the clinical isolates tested (see Table 9). SC06-166, SC06-171, SC06-176 and SC06-187 were selected from immune libraries, while the other phage antibodies were selected from IgM memory B cell libraries.

[0117] To test for non-specific reactivity against non-bacterial antigens an ELISA assay was used. The complex antigens 5% FBS, 2% ELK and 1% BSA were coated overnight to Maxisorp™ ELISA plates. Selected single-chain phage antibodies were incubated for 15 minutes in an equal volume of PBS containing 1% BSA to obtain blocked phage antibodies. The plates were

emptied, and the blocked single-chain phage antibodies were added to the wells. Incubation was allowed to proceed for two hours at room temperature, the plates were washed in PBS containing 0.1% v/v Tween-20 and bound phage antibodies were detected by means of OD 492nm measurement using an anti-M13 antibody conjugated to peroxidase. As a control, the procedure was performed simultaneously without single-chain phage antibody, with a negative control single-chain phage antibody directed against West Nile virus envelope protein (SC04-374). As shown in Table 10, the selected phage antibodies called SC02-430, SC05-132 and SC05-133, did not display any detectable binding to the negative control antigens FBS, ELK and BSA.

Example 5

Characterization of the staphylococci specific scFvs

[0118] From the selected specific single-chain phage antibody (scFv) clones plasmid DNA was obtained and nucleotide sequences were determined according to standard techniques. The nucleotide sequences of the scFvs (including restriction sites for cloning) called SC02-430, SC05-132, and SC05-133 are shown in SEQ ID NO:19, SEQ ID NO:21 and SEQ ID NO:23, respectively. The amino acid sequences of the scFvs called SC02-430, SC05-132 and SC05-133 are shown in SEQ ID NO:20, SEQ ID NO:22 and SEQ ID NO:24, respectively.

[0119] The VH and VL gene identity (see Tomlinson IM, Williams SC, Ignatovitch O, Corbett SJ, Winter G. VBASE Sequence Directory. Cambridge United Kingdom: MRC Centre for Protein Engineering (1997)) and the CDR sequences of the scFvs specifically binding staphylococci are depicted in Tables 11 and 12, respectively.

[0120] Similar to the single-chain phage antibodies disclosed above, the nucleotide and amino acid sequence, VL and VH gene identity and CDR sequences of the single-chain phage antibodies called SC06-166, SC06-171, SC06-176, SC06-187, SC06-193, SC06-249, SC06-273, SC06-389, SC06-403, SC06-406, SC06-410, SC06-446, SC06-450, SC06-452, SC06-453, SC06-464, SC06-471, SC06-516, SC06-517, SC06-526, SC06-528, SC06-531, SC06-533, SC06-536, SC06-537, SC06-538, SC06-540, SC06-544, SC06-566 and SC06-625 were determined (data not shown).

Example 6

Constriction of fully human immunoglobulin molecules (human monoclonal anti-staphylococci antibodies) from the selected anti-staphylococci single chain Fvs

[0121] The heavy and light chain variable region of SC02-430 was PCR-amplified using oligonucleotides to append restriction sites and/or sequences for expression in the IgG expression vectors pSyn-C03-HCγ1 (SEQ ID No:43) and pSyn-C04-Cλ (SEQ ID No:44). The heavy chain variable region of SC02-430 was cloned into the vector pSyn-C03-HCγ1; the light chain variable region of SC02-430 was cloned into the vector pSyn-C04-Cλ. The VL lambda gene was first amplified using the following oligonucleotides set; 5L-B (SEQ ID NO:45) and sy3L-A (SEQ ID NO:46) and the PCR product was cloned into vector pSyn-C04-Cλ. The nucleotide sequence of the construct was verified according to standard techniques known to the skilled artisan. The VH gene was first amplified using the following oligonucleotide set: 5H-F (SEQ ID NO:47) and sy3H-A (SEQ ID NO:48). Thereafter, the PCR product was cloned into vector pSyn-C03-HCγ1 and the nucleotide sequence was verified according to standard techniques known to the skilled person in the art.

[0122] Heavy and light chain variable regions of the scFv called SC05-132, SC05-133, SC06-166, SC06-171, SC06-176, SC06-187, SC06-193, SC06-249, SC06-273, SC06-389, SC06-403, SC06-406, SC06-410, SC06-446, SC06-450, SC06-452, SC06-453, SC06-464, SC06-471, SC06-516, SC06-517, SC06-526, SC06-528, SC06-531, SC06-533, SC06-536, SC06-537, SC06-538, SC06-540, SC06-544, SC06-566, SC06-625 were cloned directly by restriction digest for expression in the IgG expression vectors plg-C911-HCgamma1 (SEQ ID NO:49) and plg-C909-Ckappa (SEQ ID NO:50) or plg-C910-Clambda (SEQ ID NO:115). The heavy chain variable regions of the scFvs called SC05-132, SC05-133, SC06-166, SC06-171, SC06-176, SC06-187, SC06-193, SC06-249, SC06-273, SC06-389, SC06-403, SC06-406, SC06-410, SC06-446, SC06-450, SC06-452, SC06-453, SC06-464, SC06-471, SC06-516, SC06-517, SC06-526, SC06-528, SC06-531, SC06-533, SC06-536, SC06-537, SC06-538, SC06-540, SC06-544, SC06-566 and SC06-625 were cloned into the vector plg-C911-HCgamma1 by restriction digest using the enzymes SfiI and XhoI and the light chain variable regions of the scFvs called SC05-132, SC05-133, SC06-166, SC06-171, SC06-

176, SC06-187, SC06-193, SC06-249, SC06-273, SC06-389, SC06-403, SC06-406, SC06-410, SC06-446, SC06-450, SC06-452, SC06-453, SC06-464, SC06-471, SC06-516, SC06-517, SC06-526, SC06-528, SC06-531, SC06-533, SC06-536, SC06-537, SC06-538, SC06-540, SC06-544, SC06-566 and SC06-625 were cloned into the vector plg-C909-Ckappa or plg-C910-Clambda by restriction digest using the enzymes Sall and NotI. Thereafter the nucleotide sequences were verified according to standard techniques known to the person skilled in the art.

[0123] The resulting expression plasmids pgG102-430C03, pgG105-132C911, pgG105-133C911, pgG106-166C911, pgG106-171C911, pgG106-176C911, pgG106-187C911, pgG106-193C911, pgG106-249C911, pgG106-273C911, pgG106-389C911, pgG106-403C911, pgG106-406C911, pgG106-410C911, pgG106-446C911, pgG106-450C911, pgG106-452C911, pgG106-453C911, pgG106-464C911, pgG106-471C911, pgG106-516C911, pgG106-517C911, pgG106-526C911, pgG106-528C911, pgG106-531C911, pgG106-533C911, pgG106-536C911, pgG106-537C911, pgG106-538C911, pgG106-540C911, pgG106-544C911, pgG106-566C911, and pgG106-625C911 encoding the anti-staphylococci human IgG1 heavy chains and pSyn-C04-V12, pgG105-132C909, pgG105-133C909, pgG106-166C910, pgG106-171C910, pgG106-176C909, pgG106-187C909, pgG106-193C910, pgG106-249C910, pgG106-273C910, pgG106-389C910, pgG106-403C910, pgG106-406C910, pgG106-410C910, pgG106-446C910, pgG106-450C910, pgG106-452C909, pgG106-453C909, pgG106-464C910, pgG106-471C910, pgG106-516C909, pgG106-517C910, pgG106-526C910, pgG106-528C910, pgG106-531C910, pgG106-533C909, pgG106-536C909, pgG106-537C910, pgG106-538C910, pgG106-540C910, pgG106-544C910, pgG106-566C910, pgG106-625C910 encoding the anti-staphylococci human Ig light chains were transiently expressed in combination in 293T cells and supernatants containing human IgG1 antibodies were obtained. The nucleotide sequences of the heavy chains of the antibodies called CR2430, CR5132, CR5133, CR6166, CR6171, CR6176, CR6187, CR6193, CR6249, CR6273, CR6389, CR6403, CR6406, CR6410, CR6446, CR6450, CR6452, CR6453, CR6464, CR6471, CR6516, CR6517, CR6526, CR6528, CR6531, CR6533, CR6536, CR6537, CR6538, CR6540, CR6544, CR6566, and CR6625 are shown in SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:168, SEQ ID NO:170, SEQ ID NO:172 and SEQ ID NO:174, respectively. The amino acid sequences of the heavy chains of the antibodies called CR2430, CR5132, CR5133, CR6166, CR6171, CR6176, CR6187, CR6193, CR6249, CR6273, CR6389, CR6403, CR6406, CR6410, CR6446, CR6450, CR6452, CR6453, CR6464, CR6471, CR6516, CR6517, CR6526, CR6528, CR6531, CR6533, CR6536, CR6537, CR6538, CR6540, CR6544, CR6566, and CR6625 are shown in SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:165, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:171, SEQ ID NO:173 and SEQ ID NO:175, respectively. The nucleotide sequences of the light chain of antibodies CR2430, CR5132, CR5133, CR6166, CR6171, CR6176, CR6187, CR6193, CR6249, CR6273, CR6389, CR6403, CR6406, CR6410, CR6446, CR6450, CR6452, CR6453, CR6464, CR6471, CR6516, CR6517, CR6526, CR6528, CR6531, CR6533, CR6536, CR6537, CR6538, CR6540, CR6544, CR6566, and CR6625 are shown in SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:176, SEQ ID NO:178, SEQ ID NO:180, SEQ ID NO:182, SEQ ID NO:184, SEQ ID NO:186, SEQ ID NO:188, SEQ ID NO:190, SEQ ID NO:192, SEQ ID NO:194, SEQ ID NO:196, SEQ ID NO:198, SEQ ID NO:200, SEQ ID NO:202, SEQ ID NO:204, SEQ ID NO:206, SEQ ID NO:208, SEQ ID NO:210, SEQ ID NO:212, SEQ ID NO:214, SEQ ID NO:216, SEQ ID NO:218, SEQ ID NO:220, SEQ ID NO:222, SEQ ID NO:224, SEQ ID NO:226, SEQ ID NO:228, SEQ ID NO:230, SEQ ID NO:232 and SEQ ID NO:234, respectively. The amino acid sequences of the light chain of antibodies CR2430, CR5132, CR5133, CR6166, CR6171, CR6176, CR6187, CR6193, CR6249, CR6273, CR6389, CR6403, CR6406, CR6410, CR6446, CR6450, CR6452, CR6453, CR6464, CR6471, CR6516, CR6517, CR6526, CR6528, CR6531, CR6533, CR6536, CR6537, CR6538, CR6540, CR6544, CR6566, and CR6625 are shown in SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:177, SEQ ID NO:179, SEQ ID NO:181, SEQ ID NO:183, SEQ ID NO:185, SEQ ID NO:187, SEQ ID NO:189, SEQ ID NO:191, SEQ ID NO:193, SEQ ID NO:195, SEQ ID NO:197, SEQ ID NO:199, SEQ ID NO:201, SEQ ID NO:203, SEQ ID NO:205, SEQ ID NO:207, SEQ ID NO:209, SEQ ID NO:211, SEQ ID NO:213, SEQ ID NO:215, SEQ ID NO:217, SEQ ID NO:219, SEQ ID NO:221, SEQ ID NO:223, SEQ ID NO:225, SEQ ID NO:227, SEQ ID NO:229, SEQ ID NO:231, SEQ ID NO:233 and SEQ ID NO:235, respectively. A person skilled in the art can determine the variable regions of the heavy and light chains of the above antibodies and single chain phage antibodies by following Kabat et al. (1991) as described in Sequences of Proteins of Immunological Interest, US Dept. Health and Human Services, NIH, USA (fifth edition). A person skilled in the art can determine the CDR regions of the heavy and light chains of the above antibodies and single chain phage antibodies by following Kabat *et al.* (1991), Chothia and Lesk (1987) or a combination of both. Alternatively, the variable and CDR regions can be determined using the VBASE database, a database well known to persons skilled in the art of antibodies. Sequences of the antibodies of the invention can be compared with immunoglobulin sequences in the VBASE database (see Tomlinson IM, Williams SC, Ignatovitch O, Corbett SJ, Winter G. VBASE Sequence Directory. Cambridge United Kingdom: MRC Centre for Protein Engineering (1997)) <http://vbase.mrc-cpe.cam.ac.uk/>, MRC Centre for Protein Engineering) and on the basis thereof variable regions and CDR

regions can be determined. The variable regions of the some of the antibodies are given in Table 13. Human anti-staphylococci IgG1 antibodies were validated for their ability to bind to staphylococci by FACS essentially as described for scFvs (see Table 14). The negative control was an anti-West Nile virus antibody (CR4374). Alternatively, batches of greater than 1 mg of each antibody were produced and purified using standard procedures.

Example 7

In vitro opsonic phagocytic activity of staphylococcal specific IgGs as measured by FACS

[0124] The opsonic activity of anti-staphylococcal IgGs was measured in an opsonophagocytotic (OPA) assay using freshly differentiated HL-60 cells. During the OPA assay fluorescent bacteria were mixed with differentiated HL-60 cells and serially diluted IgGs. Bacteria were grown to stationary or to logarithmic (log) phase prior to labelling. To grow the bacteria to stationary phase different staphylococcal isolates were incubated overnight on sheep blood agar plates at 37°C. The bacteria were resuspended in 5 ml of bicarbonate buffer (0.1 M NaHCO₃, pH 8.0), harvested by centrifugation at 800xg for 10 minutes at room temperature and diluted until a concentration of 2.9x10⁹ bacteria/ml. Bacteria that were grown until logarithmic phase were first cultured overnight in LB medium at 37°C, then the culture was diluted 10 times and grown for an additional 3 hours in LB medium at 37°C. Bacteria were harvested by centrifugation at 800xg for 10 minutes and resuspended in bicarbonate buffer washed until a concentration of 2.9x10⁹ bacteria/ml. Fifty microliters of a 5,6-carboxyfluorescein, succinimidyl ester solution ((FAM-SE; Molecular Probes, Eugene, Oregon); 10 mg/ml in dimethyl sulfoxide (Fisher Scientific Co., Fair Lawn, N.J.)) was added to 1 ml of 2.9x10⁹ bacteria and the mixture was incubated for 1 hour at 37°C without shaking. The labeled bacteria were washed three times in 20 ml opsonophagocytosis buffer (Hanks balanced salt solution with Ca²⁺ and Mg²⁺ and 0.2% bovine serum albumin), until no free dye in the supernatant was observed. FAM-SE-labeled bacteria were resuspended in 8 ml OPA buffer and stored in aliquots of 500 µl at -20°C under protection from light.

[0125] HL-60 cells (human promyelocytic leukemia cells; ECACC NO 98070106) were grown in cell densities of 1-9x10⁵ cells/ml in RPMI 1640 medium containing 2 mM L-glutamine supplemented with 10% heat-inactivated fetal bovine serum (HyClone Laboratories, Logan, Utah) and penicillin/streptomycin. Cells between passage 6 and 35 were used for differentiation. The cells were differentiated into granulocytes by culturing in the same medium supplemented with 5x10⁻⁷ M all-trans-retinoic acid (Sigma), 6x10⁻¹² M vitamin-D3 (Sigma) and 30 ng/ml human recombinant G-CSF (R&D). HL-60 cells were harvested by centrifugation at 160xg for 10 minutes and washed twice in 15 ml of wash buffer (Hanks balanced salt solution, without Ca²⁺ and Mg²⁺, containing 0.2% bovine serum albumin). The cells were washed once in opsonophagocytosis buffer, resuspended in 4 ml opsonophagocytosis buffer and counted in a hemocytometer. The cell concentration was adjusted to 5x10⁶ cells/ml.

[0126] The anti-staphylococcal IgGs and a control IgG (CR4374) were serially diluted in opsonophagocytosis buffer in a total volume of 20 µl to obtain dilutions having an IgG concentration of 2.50 µg/ml, 1.20 µg/ml, 0.60 µg/ml, 0.30 µg/ml, 0.15 µg/ml, 0.075 µg/ml, 0.0375 µg/ml and 0.019 µg/ml. Opsonic activity of dilutions was measured in the OPA assay in a round bottom plate that was blocked with 1% BSA in PBS. As a control, the assay was performed with no IgG. A 15 µl aliquot of a bacterial suspension containing 5.4x10⁶ cells was added to each well of the plate. When a bacterial suspension from *S. aureus* strain Cowan or *S. epidermidis* was used, the IgG/bacterium suspension was first incubated for 30 minutes at 37°C while the plate was horizontally shaking (1300 rpm) in a Heidolph titramax 1000. Next, 15 µl of the differentiated HL-60 cells (total: 75x10³ cells) were added to each well of the plate and the plate was incubated while shaking at 37°C for 30-45 minutes. The final volume in the well was 50 µl. The reaction was stopped by adding 50 µl of wash buffer containing 4% v/v formaldehyde. The content in each well was resuspended and transferred to polystyrene disposable tubes for flow cytometric analysis. The samples were stored in the dark at 4°C until analysis. The tubes were vortexed for 3 seconds before sampling in the flow cytometer. To control the differentiation of the HL-60 cells the expression of the complement receptor CD11b was measured. Fc-receptors of differentiated and non-differentiated cells were first blocked with rabbit IgG for 15 minutes on ice and the cells were subsequently labelled with CD11bAPC (BD) for 15 minutes on ice. Cells were considered properly differentiated when the mean fluorescent intensity (MFI) analyzed was at least between 10- to 100-fold higher compared to that of non-differentiated cells. Samples were assayed with a FACSCalibur immunocytometry system (Becton Dickinson and Co., Paramus, N.J.) and were analyzed with CELLQuest software (version 1.2 for Apple system 7.1; Becton Dickinson). 7,000 gated HL-60 granulocytes were analyzed per tube. FAM-SE was excited at a wavelength of 488 nm and the FAM-SE fluorescence signal of gated viable HL-60 cells was measured for each antibody dilution. IgGs were defined as positive in the phagocytic assay when concentration dependent phagocytosis could be

observed greater or equal to two times that of the control IgG. IgGs CR2430, CR5132 and CR5133 demonstrated opsonic activity against *S. aureus* strain Cowan in both the log (see Figure 1) and stationary growth phase (see Figure 2). The three IgGs were more effective in enhancing phagocytic activity during the log phase of growth. IgGs CR5132 and CR5133 enhanced phagocytosis of *S. aureus* strain SA125 compared to the negative control antibody (see Figure 3) and antibody CR5133 significantly enhanced phagocytic activity of the differentiated HL60 cells against *S. epidermidis* strain SE131, when compared to the negative control antibody (see Figure 4).

Example 8

Breadth of staphylococci specific IgG1 binding activity

[0127] To determine the extent to which the targets of selected human anti-staphylococcal IgG1 antibodies were conserved on staphylococci and other gram positive bacteria FACS assays were carried out on an extended panel of clinical bacterial isolates essentially as described before for scFvs (see Table 15). From the assay was deduced that CR5132 and CR5133 bound to all strains tested. CR5140 did bind all strains tested with the exception of *S. hominis* KV111, *S. warneri* KV112, *S. warneri* KV114, *S. epidermidis* KV115, *S. haemolyticus* KV117, *S. warneri* vd65, *S. warneri* vd66, *S. warneri* vd732, *S. hominis* vd136, *S. hominis* vd139, and *S. hominis* K136. CR6171 did bind all strains tested with the exception of *S. epidermidis* KV110, *S. hominis* KV111, *S. warneri* KV112, *S. saprophyticus* KV113, *S. warneri* KV114, *S. haemolyticus* KV117, *S. hominis* KV118, *S. haemolyticus* K119, *S. warneri* vd65, *S. warneri* vd66, *S. warneri* vd732, *S. hominis* vd136, *S. hominis* vd139, and *S. hominis* K136. Finally, CR6453 did bind all strains tested with the exception of *S. hominis* vd136 and *S. hominis* K136.

[0128] In addition, using the same FACS based approach antibodies from the panel were demonstrated to bind to other gram-positive bacteria. The antibodies CR5132 and CR6453 were shown to bind *Listeria monocytogenes*, *Bacillus cereus* and *Streptococcus group A* and CR5132 also bound to *Propionibacterium spp.* The antibodies CR5133, CR5140 and CR6171 were shown to bind *Streptococcus group A* and CR5140 was also shown to bind *Enterococcus faecalis* (data not shown).

Example 9

In vitro opsonic phagocytic activity of staphylococcal specific IgGs measured by opsonophagocytic killing assay (OPKA)

[0129] To better determine the functional activity of the antibody panel an opsonophagocytic assay was conducted to quantify the killing activity of anti-staphylococcal human IgG1 against the *Staphylococcus aureus* strains 502, Mn8 and Newman and *Staphylococcus epidermidis* strain M187. Freshly drawn human blood (10 to 30 ml) was mixed with an equal volume of dextran-heparin buffer (4.5 g of dextran, Sigma Chemical, St. Louis; 28.4 mg of heparin sodium in 500 ml of distilled water), and the mixture was incubated at 37°C for 1 hour. The upper layer containing the leukocytes was collected by centrifugation, and hypotonic lysis of the remaining erythrocytes was accomplished by suspension of the cell pellet in 1% (w/v) NH_4Cl . The leukocyte population was subsequently washed in RPMI with 15% (v/v) fetal bovine serum. Trypan blue staining and counting in a hemocytometer were used to determine the concentration of live leukocytes, and the final leukocyte concentration was adjusted to 2×10^7 cells/ml. The phagocytosis assay was performed in duplicate with or without 100 μl of leukocyte suspension added to 100 μl of bacteria (concentration adjusted spectrophotometrically to 2×10^7 per ml and confirmed by viable counts), 100 μl of anti-staphylococcal human IgG1 diluted in RPMI, and 100 μl of baby rabbit complement. The reaction mixture was incubated on a rotor rack at 37°C for 90 minutes; samples were taken at time 0 and after 90 minutes, diluted in 1% Proteose Peptone (Difco Laboratories, Detroit, Mich.), and plated onto tryptic soy agar plates. The killing activity (%) of the antibodies was calculated as the mean number of CFU surviving in the sample containing leukocytes subtracted from the mean number of CFU surviving in the sample without leukocytes, divided by the latter and amplified by 100. The killing activity of the anti-staphylococcal human IgG1 was tested at two concentrations 1250 and 12.5 ng/ml (see Table 16).

[0130] The results show that antibodies CR5132, CR5133, CR6446, CR6453, and CR6566 have more than 20% killing activity against *S. epidermidis* strain M187, even at a low concentration of 12.5 ng/ml.

Example 10

IgG1 competition assay

[0131] To establish whether antibodies in the panel competed for binding to the same target a competition ELISA was developed. The *S. epidermidis* strain SE132 was streaked onto a blood agar plate and incubated overnight at 37°C. Colonies were scraped from the plate using 5 ml of 50 mM carbonate buffer (8 volumes of 0.2 M Na₂CO₃, 17 volumes of 0.2 M NaHCO₃ and 75 volumes of distilled water) and centrifuged for 3 minutes at 4000 rpm. The obtained pellet was resuspended in 500 µl of carbonate buffer, centrifuged again and the pellet was resuspended in 500 µl carbonate buffer. Cell density was determined by measuring OD₆₀₀ of a dilution series of the bacteria. The *S. epidermidis* strain was diluted to a density of 5x10⁹ cells/ml and 100 µl (5x10⁸ cells) per well was coated overnight at 4°C on Nunc-Immuno Maxisorp F96 plates. After incubation, the wells were washed three times with PBS and blocked for one hour at room temperature with 300 µl 2% (v/v) ELK in PBS per well. In separate tubes 25 µl of each scFv-phage maxiprep (produced as above) diluted to subsaturating levels (as determined by ELISA above) was mixed with 25 µl blocking buffer (4% (v/v) ELK/PBS) and 50 µl of IgG1 supernatant diluted to 10 µg/ml in PBS and incubated for 20 minutes on ice. After removing the blocking solution, 100 µl of the blocked phages and IgG1 mixture was added to each well and incubated for one hour at room temperature. The wells were washed three times with PBS/0.01% (v/v) Tween and once with PBS. After washing, 100 µl of anti-M13 HRP (1:5000 in 2% (v/v) ELK in PBS) was added per well and incubated for 60 minutes at room temperature. The wells were washed again and staining was visualized by adding 100 µl OPD-solution to each well. Reaction was stopped after 5-10 minutes by adding 50 µl 1 M H₂SO₄ to each well and OD measured at 492nm. The experiment was repeated twice with the entire panel of antibodies and a control IgG1 CR4374. The results showed that the antibodies fell into five distinct groups. Group A consisted of CR5132, CR5133, CR6187 and CR6453; Group B consisted of CR5140 and CR6171; Group C consisted of CR6176; Group D consisted of CR6526; and Group E consisted of the rest of the panel CR6166, CR6193, CR6249, CR6273, CR6403, CR6406, CR6410, CR6446, CR6450, CR6452, CR6464, CR6471, CR6516, CR6517, CR6528, CR6531, CR6533, CR6536, CR6537, CR6538, CR6540, CR6544, CR6566, CR6625. The binding activity and functional activity of the antibodies was consistent with the grouping.

Example 11**Target identification of IgG1 in group A**

[0132] To determine the binding target of the panel antibodies, representatives of each of the groups determined above (within each group the most potent antibody based on opsonic activity was chosen) was incubated with LTA extracted from *S. aureus* in a solid phase ELISA (see Table 17). A solution of 1 µg/ml lipoteichoic acid (Sigma) in PBS was coated on wells overnight at room temperature. Plates were washed once with PBS and blocked with 400 µl 2% (v/v) ELK in PBS. A serial dilution of each anti-staphylococcal IgG1 supernatant and negative control supernatant CR4374 and positive control anti-LTA murine mAb 12248 (Abcam) was incubated per well for one hour at room temperature. Wells were washed five times with PBS and 100 µl of anti-human HRP (1/2000) or antimouse HRP (1/2000) diluted in PBSE was added and incubated for one hour at room temperature. Wells were visualized and read as above. The results clearly demonstrate that CR5133 from group A binds strongly to LTA. The positive control murine monoclonal 12248 showed similar results. In contrast, none of the antibodies from the other groups nor the negative control antibody showed significant reactivity with LTA. Antibodies CR5132 and CR6453 from Group A were consistently shown to bind LTA, CR6187 however did not show binding reactivity to LTA (data not shown). This may be due to a lower affinity of CR6187 compared to the other antibodies in the group.

Example 12

In vitro opsonic phagocytic activity of staphylococcal specific IgGs against Staphylococcus epidermidis and Staphylococcus aureus grown under different culture conditions and measured by opsonophagocytic killing assay (OPKA)

[0133] To determine if the bacterial killing activity of the most potent and non-competitive opsonophagocytic anti-staphylococcal

IgG1 antibodies identified above is affected by different bacterial growth conditions, the opsonophagocytic assay described above was conducted against the *Staphylococcus aureus* strain Newman and *Staphylococcus epidermidis* strain RP62A grown in different media and under different conditions. LBA is immune serum taken from an infected patient and served as a positive control. The killing activity of the anti-staphylococcal human IgG1 was tested at five concentrations 10,000, 300, 10, 0.3, 0.01 ng/ml or -5, -6.5, -8, -9.5, -11 log [g/ml] against both staphylococcal strains either grown to mid logarithmic phase (Fig. 5A, B) or to static phase (Fig. 5G, H) or in medium consisting of 1% glucose (Fig. 5C, D) or 100% human plasma (Fig. 5E, F).

[0134] The results show that the antibodies CR5133, CR6166, CR6171, CR6176 and CR6526 have robust opsonophagocytic activity against the two staphylococcal strains under all the growth conditions tested. Importantly, they were significantly different from the negative control antibody CR3009, which showed little or no activity. This suggests that the targets of the antibody panel are stably expressed under a variety of bacterial growth conditions, a factor potentially important for therapeutic application where the target bacteria may be present in nutrient poor conditions.

Example 13

*In vivo protective activity of staphylococcal specific IgGs in a lethal *Staphylococcus aureus* challenge model*

[0135] A bacterial titration experiment in mice is carried out to determine the optimal inoculation dose to produce 80%-100% lethality. Animals are inoculated i.p. with *S. aureus* strains Mn8 at doses of 5×10^9 and 5×10^8 . Animals are observed for 5 days and survival is used as an endpoint. The dose that results in 0% survival after 5 days is chosen as the challenge dose for further experiments.

[0136] Using the dose determined above for the bacterial inoculum, a set of challenge experiments is conducted to assess the protective activity of the panel of Staphylococcal binding mAb (CR5133, CR6166, CR6171, CR6176 and CR6526) that have demonstrated in vitro opsonic phagocytic activity. For each experiment, purified mAb's (one isotype control IgG1 and 5 test IgG1) are injected i.p. (0.5-1 ml in PBS), at a dose of 15 mg/kg. 5 mAb are tested against *S. aureus* Mn8.

[0137] After 24 hours animals are inoculated i.p. with the *S. aureus* strain at the inoculation dose determined above. Immediately prior to inoculation, a small amount of blood (~50-100 µl) is collected (using the tail cut method) to measure circulating antibody levels. The blood is kept at room temperature between 30 min and 2 hours, to allow the blood to clot, then centrifuged at 4°C for 5 min. The serum is removed and stored at -20°C. A human IgG1 ELISA is performed on all blood samples prior to inoculation and after sacrifice. Animals with no measurable antibody in their blood prior to inoculation are excluded from further analysis.

[0138] Mice are observed daily for five days and sacrificed when showing signs of severe distress. Survival is scored in each group at the end of five days. To validate each experiment there must be less than 20% survival in the negative control IgG1 group. Further experiments are carried out in the model described above where the antibodies are titrated at half-log doses from 10 mg/kg to determine their protective potency *in vivo*.

Table 1: Human lambda chain variable region primers (sense).

Primer name	Primer nucleotide sequence	SEQ ID NO
HuVL1A-Back	5'-CAGTCTGTGCTGACT CAGCCACC-3'	SEQ ID NO:51
HuVL1B-Back	5'-CAGTCTGTGYTGACG CAGCCGCC-3'	SEQ ID NO:52
HuVL1C-Back	5'-CAGTCTGTCGTGACG CAGCCGCC-3'	SEQ ID NO:53
HuVL2B-Back	5'-CAGTCTGCCCTGACT CAGCC-3'	SEQ ID NO:54

Primer name	Primer nucleotide sequence	SEQ ID NO
HuVL3A-Back	5'-TCCTATGWGCTGACT CAGCCACC-3'	SEQ ID NO:55
HuVL3B-Back	5'-TCTTCTGAGCTGACT CAGGACCC-3'	SEQ ID NO:56
HuVL4B-Back	5'-CAGCYTGTGCTGACT CAATC-3'	SEQ ID NO:57
HuVL5-Back	5'-CAGGCTGTGCTGACT CAGCCGTC-3'	SEQ ID NO:58
HuVL6-Back	5'-AATTTTATGCTGACT CAGCCCCA-3'	SEQ ID NO:59
HuVL7/8-Back	5'-CAGRCTGTGGTGACY CAGGAGCC-3'	SEQ ID NO:60
HuVL9-Back	5'-CWGCCTGTGCTGACT CAGCCMCC-3'	SEQ ID NO:61
HuVL10-Back	5'-CAGGCAGGGCTGACT CAG-3'	SEQ ID NO:62

Table 2: Human kappa chain variable region primers (sense).

Primer name	Primer nucleotide sequence	SEQ ID NO
HuVK1B-Back	5'- GACATCCAGWTGACCC AGTCTCC-3'	SEQ ID NO:63
HuVK2-Back	5'-GATGTTGTGATGACT CAGTCTCC-3'	SEQ ID NO:64
HuVK2B2	5'-GATATTGTGATGACC CAGACTCC-3'	SEQ ID NO:65
HuVK3B-Back	5'-GAAATTGTGWTGACR CAGTCTCC-3'	SEQ ID NO:66
HuVK5-Back	5'-GAAACGACACTCACG CAGTCTCC-3'	SEQ ID NO:67

Primer name	Primer nucleotide sequence	SEQ ID NO
HuVK6-Back	5'-GAAATTGTGCTGACTC AGTCTCC-3'	SEQ ID NO:68

Table 3: Human kappa chain variable region primers extended with Sall restriction sites (sense), human kappa chain J-region primers extended with NotI restriction sites (anti-sense), human lambda chain variable region primers extended with Sall restriction sites (sense) and human lambda chain J-region primers extended with NotI restriction sites (anti-sense).

Primer name	Primer nucleotide sequence	SEQ ID NO
HuVK1B-Back-SAL	5'-TGAGCACACAGGTCG ACGGACATCCAGWTGACC CAGTCTCC-3'	SEQ ID NO:69
HuVK2-Back-SAL	5'-TGAGCACACAGGTCG ACGGATGTTGTGATGACT CAGTCTCC-3'	SEQ ID NO:70
HuVK2B2-SAL	5'-TGAGCACACAGGTCG ACGGATATTGTGATGACC CAGACTCC-3'	SEQ ID NO:71
HuVK3B-Back-SAL	5'-TGAGCACACAGGTCG ACGGAAATTGTGWTGACR CAGTCTCC-3'	SEQ ID NO:72
HuVK5-Back-SAL	5'-TGAGCACACAGGTCGACG GAAACGACACTCAGCAGTCT CC-3'	SEQ ID NO:73
HuVK6-Back-SAL	5'-TGAGCACACAGGTCG ACGGAAATTGTGCTGACT CAGTCTCC-3'	SEQ ID NO:74
HuJK1-FOR-NOT	5'-GAGTCATTCTCGACTTGC GGCCGCACGTTTGATTCCAC CTTGGTCCC-3'	SEQ ID NO:75
HuJK2-FOR-NOT	5'-GAGTCATICTCGACT TGCGGCCGCACGTTTGAT CTCCAGCTTGGTCCC-3'	SEQ ID NO:76
HuJK3-FOR-NOT	5'-GAGTCATTCTCGACTTGC GGCCGCACGTTTGATATCC/ TTTGGTCCC-3'	SEQ ID NO:77

Primer name	Primer nucleotide sequence	SEQ ID NO
HuJK4-FOR-NOT	5'-GAGTCATTCTCGACT TGCGGCCGACGTTTGAT CTCCACCTTGGTCCC-3'	SEQ ID NO:78
HuJK5-FOR-NOT	5'-GAGTCATTCTCGACTTGC GGCCGCACGTTTAATCTCCAG TCGTGTCCC-3'	SEQ ID NO:79
HuVL1A-Back-SAL	5'-TGAGCACACAGGTCGACG CAGTCTGTGCTGACTCAGCCA CC-3'	SEQ ID NO:80
HuVL1B-Back-SAL	5'-TGAGCACACAGGTCGACG CAGTCTGTGYTGACGCAGCCG CC-3'	SEQ ID NO:81
HuVL1C-Back-SAL	5'-TGAGCACACAGGTCGACG CAGTCTGTCGTGACGCAGCCG CC-3'	SEQ ID NO:82
HuVL2B-Back-SAL	5'-TGAGCACACAGGTCGACG CAGTCTGCCCTGACTCAGCC- 3'	SEQ ID NO:83
HuVL3A-Back-SAL	5'-TGAGCACACAGGTCGACG TCCTATGWGCTGACTCAGCCA CC-3'	SEQ ID NO:84
HuVL3B-Back-SAL	5'-TGAGCACACAGGTCGACG	SEQ ID NO:85
	TCTTCTGAGCTGACTCAGGAC CC-3'	
HuVL4B-Back-SAL	5'-TGAGCACACAGGTCGACG CAGCYTGTGCTGACTCAATC- 3'	SEQ ID NO:86
HuVL5-Back-SAL	5'-TGAGCACACAGGTCGACG CAGGCTGTGCTGACTCAGCCG TC-3'	SEQ ID NO:87

Primer name	Primer nucleotide sequence	SEQ ID NO
HuVL6-Back-SAL	5'-TGAGCACACAGGTCGACG AATTTTATGCTGACTCAGCCC CA-3'	SEQ ID NO:88
HuVL7/8-Back-SAL	5'-TGAGCACACAGGTCGACG CAGRCTGTGGTGACYCAGGAG CC-3'	SEQ ID NO:89
HuVL9-Back-SAL	5'-TGAGCACACAGGTCGACG CWGCCTGTGCTGACTCAGCCM CC-3'	SEQ ID NO:90
HuVL10-Back-SAL	5'-TGAGCACACAGGTCGACG CAGGCAGGGCTGACTCAG-3'	SEQ ID NO:91
HuJL1-FOR-NOT	5'-GAGTCATTCTCGACTTGC GGCCGCACCTAGGACGGTGAC CTTGGTCCC-3'	SEQ ID NO:92
HuJL2/3-FOR-NOT	5'-GAGTCATTCTCGACTTGC GGCCGCACCTAGGACGGTCAG CTTGGTCCC-3'	SEQ ID NO:93
HuJL7-FOR-NOT	5'-GAGTCATTCTCGACTTGC GGCCGCACCGAGGACGGTCAG CTGGGTGCC-3'	SEQ ID NO:94

Table 4: Percentage of the different light chain products in the final mixture, based on concentrations determined by agarose gel analysis.

Sense primer	Antisense primer	Product	Percentage
HuVL1A-Back-SAL + HuVL1B-Back-SAL + HuVL1C-Back-SAL	HuJL1-FOR-NOT	L1J1	4.20%
	HuJL2/3-FOR-NOT	L1J2	8.40%
	HuJL7-FOR-NOT	L1J3	1.40%
	HuJL1-FOR-NOT	L2J1	3.00%
HuVL2B-Back-SAL	HuJL2/3-FOR-NOT	L2J2	6.00%
	HuJL7-FOR-NOT	L2J3	1.00%
	HuJL1-FOR-NOT	L3J1	3.00%
HuVL3A-Back-SAL	HuJL2/3-FOR-NOT	L3J2	6.00%
	HuJL7-FOR-NOT	L3J3	1.00%
	HuJL1-FOR-NOT	L4J1	0.30%
HuVL3B-Back-SAL	HuJL2/3-FOR-NOT	L4J2	0.60%
	HuJL7-FOR-NOT	L4J3	0.10%
	HuJL1-FOR-NOT	L5J1	0.30%
HuVL4B-Back-SAL	HuJL2/3-FOR-NOT	L5J2	0.60%
	HuJL7-FOR-NOT	L5J3	0.10%

Sense primer	Antisense primer	Product	Percentage
	HuJL1-FOR-NOT	L6J1	0.30%
HuVL5-Back-SAL	HuJL2/3-FOR-NOT	L6J2	0.60%
	HuJL7-FOR-NOT	L6J3	0.10%
	HuJL1-FOR-NOT	L7J1	0.30%
HuVL6-Back-SAL	HuJL2/3-FOR-NOT	L7J2	0.60%
	HuJL7-FOR-NOT	L7J3	0.10%
	HuJL1-FOR-NOT	L8J1	0.30%
HuVL7/8-Back-SAL	HuJL2/3-FOR-NOT	L8J2	0.60%
	HuJL7-FOR-NOT	L8J3	0.10%
HuVL9-Back-SAL + HuVL10-Back-SAL	HuJL1-FOR-NOT	L9J1	0.30%
	HuJL2/3-FOR-NOT	L9J2	0.60%
	HuJL7-FOR-NOT	L9J3	0.10%
	HuJK1-FOR-NOT	K1J1	7.50%
	HuJK2-FOR-NOT	K1J2	7.50%
HuVK1B-Back-SAL	HuJK3-FOR-NOT	K1J3	3.00%
	HuJK4-FOR-NOT	K1J4	7.50%
	HuJK5-FOR-NOT	K1J5	4.50%
	HuJK1-FOR-NOT	K2J1	1.00%
	HuJK2-FOR-NOT	K2J2	1.00%
HuVK2-Back-SAL	HuJK3-FOR-NOT	K2J3	0.40%
	HuJK4-FOR-NOT	K2J4	1.00%
	HuJK5-FOR-NOT	K2J5	0.60%
	HuJK1-FOR-NOT	K3J1	0.25%
	HuJK2-FOR-NOT	K3J2	0.25%
HuVK2B2-SAL	HuJK3-FOR-NOT	K3J3	0.10%
	HuJK4-FOR-NOT	K3J4	0.25%
	HuJK5-FOR-NOT	K3J5	0.15%
	HuJK1-FOR-NOT	K4J1	4.75%
	HuJK2-FOR-NOT	K4J2	4.75%
HuVK3B-Back-SAL	HuJK3-FOR-NOT	K4J3	1.90%
	HuJK4-FOR-NOT	K4J4	4.75%
	HuJK5-FOR-NOT	K4J5	2.85%
	HuJK1-FOR-NOT	K5J1	0.25%
	HuJK2-FOR-NOT	K5J2	0.25%
HuVK5-Back-SAL	HuJK3-FOR-NOT	K5J3	0.10%
	HuJK4-FOR-NOT	K5J4	0.25%
	HuJK5-FOR-NOT	K5J5	0.15%
	HuJK1-FOR-NOT	K6J1	1.25%
	HuJK2-FOR-NOT	K6J2	1.25%
HuVK6-Back-SAL	HuJK3-FOR-NOT	K6J3	0.50%
	HuJK4-FOR-NOT	K6J4	1.25%
	HuJK5-FOR-NOT	K6J5	0.75%

Table 5: Human IgG heavy chain variable region primers (sense).

Primer name	Primer nucleotide sequence	SEQ ID NO
HuVH1B/7A-Back	5'-CAGRTGCAGCTGGTG CARTCTGG-3'	SEQ ID NO:95
HuVH1C-Back	5'-SAGGTCCAGCTGGTR CAGTCTGG-3'	SEQ ID NO:96
HuVH2B-Back	5'-CAGRTCACCTTGAAG GAGTCTGG-3'	SEQ ID NO:97
HuVH3A-Back	5'-GAGGTGCAGCTGGTG GAG-3'	SEQ ID NO:98
HuVH3C-Back	5'-GAGGTGCAGCTGGTG GAGWCYGG-3'	SEQ ID NO:99
HuVH4B-Back	5'-CAGGTGCAGCTACAG CAGTGGGG-3'	SEQ ID NO:100
HuVH4C-Back	5'-CAGSTGCAGCTGCAG GAGTCSGG-3'	SEQ ID NO:101
HuVH6A-Back	5'-CAGGTACAGCTGCAG CAGTCAGG-3'	SEQ ID NO:102

Table 6: Human IgG heavy chain variable region primers extended with SfiI/NcoI restriction sites (sense) and human IgG heavy chain J-region primers extended with XhoI/BstEI restriction sites (anti-sense).

Primer name	Primer nucleotide sequence	SEQ ID NO
HuVH1B/7A-Back-Sfi	5'-GTCCTCGCAACTGCG GCCCAGCCGGCCATGGCC CAGRTGCAGCTGGTGCAR TCTGG-3'	SEQ ID NO:103
HuVH1C-Back-Sfi	5'-GTCCTCGCAACTGCG GCCCAGCCGGCCATGGCC	SEQ ID NO:104
	SAGGTCCAGCTGGTRCAG TCTGG-3'	
HuVH2B-Back-Sfi	5'-GTCCTCGCAACTGCG GCCCAGCCGGCCATGGCC CAGRTCACCTTGAAGGAG TCTGG-3'	SEQ ID NO:105

Primer name	Primer nucleotide sequence	SEQ ID NO
HuVH3A-Back-Sfi	5'-GTCCTCGCAACTGCGGCC CAGCCGGCCATGGCCGAGGTG CAGCTGGTGGAG-3'	SEQ ID NO:106
HuVH3C-Back-Sfi	5'-GTCCTCGCAACTGCG GCCCAGCCGGCCATGGCC GAGGTGCAGCTGGTGGAG WCYGG-3'	SEQ ID NO:107
HuVH4B-Back-Sfi	5'-GTCCTCGCAACTGCG GCCCAGCCGGCCATGGCC CAGGTGCAGCTACAGCAG TGGGG-3'	SEQ ID NO:108
HuVH4C-Back-Sfi	5'-GTCCTCGCAACTGCGGCC CAGCCGGCCATGGCCAGSTG CAGCTGCAGGAGTCSGG-3'	SEQ ID NO:109
HuVH6A-Back-Sfi	5'-GTCCTCGCAACTGCG GCCCAGCCGGCCATGGCC CAGGTACAGCTGCAGCAG TCAGG-3'	SEQ ID NO:110
HuJH1/2-FOR-XhoIB	5'-GAGTCATTCTCGACTCGA GACRGTGACCAGGGTGCC-3'	SEQ ID NO:111
HuJH3-FOR-Xho	5'-GAGTCATTCTCGACT CGAGACGGTGACCATGT CCC-3'	SEQ ID NO:112
HuJH4/5-FOR-Xho	5'-GAGTCATTCTCGACT CGAGACGGTGACCAGGGT	SEQ ID NO:113
	TCC-3'	
HuJH6-FOR-Xho	5'-GAGTCATTCTCGACTCGA GACGGTGACCGTGGTCCC-3'	SEQ ID NO:114

Table 7: Percentage of the different heavy chain products in the final mixture.

Sense primer	Antisense primer	Product	Percentage
	HuJH1/2-FOR-XhoIB	H1J1	2.5%
HuVH1B/7A-Back-Sfi + HuVH1C-Back-Sfi	HuJH3-FOR-Xho	H1J2	2.5%
	HuJH4/5-FOR-Xho	H1J3	15.0%
	HuJH6-FOR-Xho	H1J4	5.0%

Sense primer	Antisense primer	Product	Percentage
HuVH2B-Back-Sfi	HuJH1/2-FOR-XhoIB	H2J1	0.2%
	HuJH3-FOR-Xho	H2J2	0.2%
	HuJH4/5-FOR-Xho	H2J3	1.2%
	HuJH6-FOR-Xho	H2J4	0.4%
HuVH3A-Back-Sfi	HuJH1/2-FOR-XhoIB	H3J1	2.5%
	HuJH3-FOR-Xho	H3J2	2.5%
	HuJH4/5-FOR-Xho	H3J3	15.0%
	HuJH6-FOR-Xho	H3J4	5.0%
HuVH3C-Back-Sfi	HuJH1/2-FOR-XhoIB	H4J1	2.5%
	HuJH3-FOR-Xho	H4J2	2.5%
	HuJH4/5-FOR-Xho	H4J3	15.0%
	HuJH6-FOR-Xho	H4J4	5.0%
HuVH4B-Back-Sfi	HuJH1/2-FOR-XhoIB	H5J1	0.2%
	HuJH3-FOR-Xho	H5J2	0.2%
	HuJH4/5-FOR-Xho	H5J3	1.2%
	HuJH6-FOR-Xho	H5J4	0.4%
HuVH4C-Back-Sfi	HuJH1/2-FOR-XhoIB	H6J1	2.0%
	HuJH3-FOR-Xho	H6J2	2.0%
	HuJH4/5-FOR-Xho	H6J3	12.0%
	HuJH6-FOR-Xho	H6J4	4.0%
HuVH6A-Back-Sfi	HuJH1/2-FOR-XhoIB	H7J1	0.1%
	HuJH3-FOR-Xho	H7J2	0.1%
	HuJH4/5-FOR-Xho	H7J3	0.6%
	HuJH6-FOR-Xho	H7J4	0.2%

Table 8: staphylococcal clinical isolates used for selection and screening of anti-staphylococcal single-chain (scFv) phage antibodies.

ID	Strain	Hospital Code	Site of Isolation
Cowan	<i>S. aureus</i>	NA	NA
SA099	<i>S. aureus</i>	D3	Anterior Nares
SA100	<i>S. aureus</i>	D8	Anterior Nares
SA101	<i>S. aureus</i>	D13	Anterior Nares
SA102	<i>S. aureus</i>	D15	Anterior Nares
SA103	<i>S. aureus</i>	D16	Anterior Nares
SA104	<i>S. aureus</i>	D17	Anterior Nares
SA105	<i>S. aureus</i>	D18	Anterior Nares
SA108	<i>S. aureus</i>	D20	Anterior Nares
SA109	<i>S. aureus</i>	D21	Anterior Nares
SA110	<i>S. aureus</i>	D23	Anterior Nares
SA111	<i>S. aureus</i>	D26	Anterior Nares
SA112	<i>S. aureus</i>	D34	Anterior Nares
SA113	<i>S. aureus</i>	D43	Anterior Nares
SA114	<i>S. aureus</i>	D44	Anterior Nares
SA115	<i>S. aureus</i>	Kv2	Renal Dialysis

ID	Strain	Hospital Code	Site of Isolation
SA116	<i>S. aureus</i>	Kv3	Renal Dialysis
SA117	<i>S. aureus</i>	Kv5	Blood
SA118	<i>S. aureus</i>	Kv6	Blood
SA119	<i>S. aureus</i>	Kv7	Blood
SA120	<i>S. aureus</i>	Kv8	Wound
SA121	<i>S. aureus</i>	Kv9	Wound
SA122	<i>S. aureus</i>	Kv11	Wound
SA123	<i>S. aureus</i>	Kv24	CSF
SA124	<i>S. aureus</i>	Kv25	CSF
SA125	<i>S. aureus</i>	Kv27	Lung Pleura
SA126	<i>S. aureus</i>	Kv28	Lung Pleura
SA127	<i>S. aureus</i>	Kv30	Pericardiac
SA128	<i>S. aureus</i>	Kv31	Joint
SA129	<i>S. aureus</i>	Kv32	Joint
SE130	<i>S. epidermidis</i>	1587/29	Blood
SE131	<i>S. epidermidis</i>	1688/35	Blood
SE132	<i>S. epidermidis</i>	1724/42	Blood
SE133	<i>S. epidermidis</i>	1587 (Kv110)	Unknown
SE134	<i>S. epidermidis</i>	V48 (Kv115)	Unknown
SE135	<i>S. epidermidis</i>	354 (Kv118)	Unknown
SE136	<i>S. epidermidis</i>	V16	Renal Dialysis
SE137	<i>S. epidermidis</i>	V29	Renal Dialysis
SE138	<i>S. epidermidis</i>	V33	Renal Dialysis
SE139	<i>S. epidermidis</i>	V65	Renal Dialysis
SE140	<i>S. epidermidis</i>	V75	Renal Dialysis

Table 9: Staphylococcal specific binding activity of single-chain (scFv) phage antibodies as measured by FACS.

Name phage antibody	Staphylococcal strains (% positive)								
	Cowan	SA102	SA103	SA120	SA124	SA125	SE130	SA131	SA132
SC02-430	89.0	ND	30.0	13.0	ND	ND	ND	ND	ND
SC05-132	21.9	ND	82.7	86.5	ND	84.2	ND	ND	ND
SC05-133	48.2	ND	77.9	83.4	ND	76.2	ND	ND	ND
sc06-166	31.2	51.4	48.1	ND	58.4	59.0	22.0	53.3	43.2
sc06-171	32.1	69.7	67.4	ND	71.7	71.2	5.0	39.3	29.2
sc06-176	30.1	11.7	30.1	ND	29.9	27.2	1.9	27.6	15.1
sc06-187	24.5	72.5	65.5	ND	67.8	63.8	36.6	31.4	43.7
sc06-193	12.0	27.7	37.2	ND	50.3	56.2	2.9	17.0	8.9
sc06-249	10.4	ND	ND	ND	ND	ND	ND	ND	7.6
sc06-273	5.1	10.1	33.2	ND	36.9	44.0	2.2	12.4	8.0
sc06-389	7.3	12.9	35.7	ND	46.4	44.2	3.0	14.4	2.3
sc06-403	6.3	8.8	7.7	ND	10.4	11.5	0.7	5.4	2.7
sc06-406	6.8	14.7	28.5	ND	36.7	48.3	5.3	14.4	8.0
sc06-410	13.3	ND	ND	ND	ND	ND	ND	ND	8.1
sc06-446	9.5	16.9	14.6	ND	14.3	26.8	1.0	7.3	2.0

Name phage antibody	Staphylococcal strains (% positive)								
	Cowan	SA102	SA103	SA120	SA124	SA125	SE130	SA131	SA132
sc06-450	46.7	61.1	58.4	ND	63.9	55.1	1.3	14.0	6.4
sc06-452	9.6	ND	ND	ND	ND	ND	1.2	18.5	2.5
sc06-453	41.0	26.2	33.6	ND	56.7	59.3	36.0	55.8	42.0
sc06-464	20.4	33.2	19.6	ND	45.2	47.2	6.2	25.7	7.2
sc06-471	2.1	53.5	46.0	ND	64.4	62.8	0.4	10.7	1.0
sc06-516	12.2	ND	ND	ND	ND	ND	3.7	22.3	10.0
sc06-517	26.5	21.6	17.7	ND	24.4	24.9	12.4	14.3	13.8
sc06-526	8.5	8.1	3.4	ND	15.7	16.3	3.6	6.7	6.3
sc06-528	29.9	19.6	10.1	ND	31.3	28.4	15.5	17.6	24.3
sc06-531	10.4	10.2	10.2	ND	15.6	12.0	0.8	5.3	1.7
sc06-533	15.7	3.9	8.6	ND	15.8	8.3	ND	6.0	0.8
sc06-536	14.5	9.8	12.6	ND	20.1	10.9	2.0	7.5	3.1
sc06-537	38.0	5.5	10.0	ND	9.2	22.4	2.6	23.5	8.3
sc06-538	14.3	6.2	9.6	ND	7.9	16.4	0.4	9.1	2.1
sc06-540	9.3	7.3	10.5	ND	22.7	23.4	0.6	6.4	1.7
sc06-544	22.6	8.5	12.1	ND	7.6	17.2	1.6	13.8	11.7
sc06-566	8.00	13.5	22.6	ND	37.1	39.4	1.0	13.4	1.7
sc06-625	9.00	8.00	15.4	ND	21.4	24.2	0.9	8.00	1.9
Neg. Ctrl	13.2	1.5	2.5	ND	5.8	20.8	0.9	1.4	0.5

ND not determined

Table 10: Non-specific binding activity of staphylococci reactive single-chain (scFv) phage antibodies measured by ELISA at 492nm.

Name phage antibody	Negative controls		
	ELISA (OD492nm)		
	BSA (1%)	FBS (5%)	ELK (2%)
SC02-430	0.04	0.04	0.05
SC05-132	0.04	0.04	0.04
SC05-133	0.04	0.04	0.04
No phage antibody	0.04	0.04	0.04
Negative control	0.04	0.06	0.16

Table 11: Data of the *Staphylococcus* specific single-chain Fvs.

Name scFv	SEQ ID NO of nucl. sequence	SEQ ID NO of amino acid sequence*	VH-locus	VL-locus
SC02-430	19	20 (Vh 1-118; V1 134-242)	VH4 (4-31)	VI 2 (2b2)
SC05-132	21	22 (Vh 1-118; VI 135-242)	VH3 (3-07)	Vkl (L12)
SC05-133	23	24 (Vh 1-120; VI 137-244)	VH3 (3-11)	Vklll (A27)

* between brackets the amino acids making up the heavy chain variable region (VH) and the light chain variable region (VL) is shown

Table 12: Data of the CDR regions of the *Staphylococcus* specific single-chain Fvs.

Name scFv	HCDR1 (SEQ ID NO:)	HCDR2 (SEQ ID NO:)	HCDR3 (SEQ ID NO:)	LCDR1 (SEQ ID NO:)	LCDR2 (SEQ ID NO:)	LCDR3 (SEQ ID NO:)
SC02-430	1	2	3	4	5	6
SC05-132	7	8	9	10	11	12
SC05-133	13	14	15	16	17	18

Table 13: Data of the *Staphylococcus* specific IgGs.

Name IgG	SEQ ID NO of nucl. sequence heavy chain	SEQ ID NO of amino acid sequence* heavy chain	SEQ ID NO of nucl. sequence light chain	SEQ ID NO of amino acid sequence* light chain
CR2430	25	26 (Vh 1-118)	31	32 (VI 1-109)
CR5132	27	28 (Vh 1-118)	33	34 (VI 1-110)
CR5133	29	30 (Vh 1-120)	35	36 (VI 1-110)

* between brackets the amino acids making up the heavy chain variable region (VH) and the light chain variable region (VL) is shown

Table 14: Staphylococcal specific binding activity of IgG1 molecules as measured by FACS.

Name phage antibody	Staphylococcal strains (MFI)								
	Cowan	SA102	SA103		SA124	SA125	SE130	SA131	SA132
CR2430	281.4	ND	ND		ND	ND	ND	ND	ND
CR5132	192.4	9.7	9.3		20.1	13.7	222.5	141.5	128.5
CR5133	285.8	ND	ND		ND	ND	229.9	203.3	252.6
Neg. Ctrl	3.6	3.2	3.0		3.3	3.5	2.5	3.1	2.7

ND not determined

Table 15: Staphylococcal binding activity of IgG1 antibodies as measured by FACS.

Strain	Isolation site/ resistance	Name	IgG1 binding activity (MFI)					
			Ctrl	CR5132	CR5133	CR5140	CR6171	C6453
<i>S. aureus</i>	CAPD/ND	KV01	4.05	1064	850	756	2	564
<i>S. aureus</i>	CAPD/ND	KV02	16.63	919	558	433	147	552
<i>S. aureus</i>	CAPD/ND	KV03	36.3	949	583	358	164	668
<i>S. aureus</i>	CAPD/ND	KV04	11.64	1123	629	546	197	752
<i>S. aureus</i>	Blood/ND	KV05	12.33	564	652	447	134.2	525
<i>S. aureus</i>	Blood/ND	KV06	10.41	634	526	386	142.2	439
<i>S. aureus</i>	Blood/ND	KV07	21.04	881	705	441	168.4	614
<i>S. aureus</i>	Wound/ND	KV09	23.83	754	483	305	134.7	515
<i>S. aureus</i>	Wound/ND	KV11	16.12	363	280	226	106.7	362
<i>S. aureus</i>	Wound/ND	KV12	27.55	571	381	224	127.4	457
<i>S. aureus</i>	Blood/ND	KV13	23.19	576	403	278	141.8	503
<i>S. aureus</i>	NA/ND	Newman	8.01	655	430	384	153.1	387
<i>S. aureus</i>	CAPD/ND	KV15	22.1	674	311	232	99.8	481
<i>S. aureus</i>	CAPD/ND	KV16	9.09	458	291	248	97.9	334
<i>S. aureus</i>	CAPD/ND	KV17	8.4	226	184.5	161.1	57.4	154.5
<i>S. aureus</i>	CAPD/ND	KV18	13.91	269	203	166.2	62.4	158.7
<i>S. aureus</i>	Blood/ND	KV19	2.66	190.9	194.6	203	44.6	83.3
<i>S. aureus</i>	Blood/ND	KV20	5.12	311	298	251	64.9	95
<i>S. aureus</i>	Blood/ND	KV21	3.67	353	266	290	73.9	140
<i>S. aureus</i>	Liquor/ND	KV24	4.28	320.2	242	223	69.9	102
<i>S. aureus</i>	Liquor/ND	KV25	3.37	269	219	188.5	53.3	105.5
<i>S. aureus</i>	Liquor/ND	KV26	10.03	217	183.7	162.9	38.6	86.4
<i>S. aureus</i>	Pleura/ND	KV27	4.03	348	235	239	52.9	129.4
<i>S. aureus</i>	Pleura/ND	KV28	6.98	217.4	184.6	203	46.7	74.1
<i>S. aureus</i>	Pleura/ND	KV29	2.99	183.4	182.6	147.9	38.5	110.2
<i>S. aureus</i>	Pericard/ND	KV30	3.55	357	358	372	77.7	152.1

Strain	Isolation site/ resistance	Name	IgG1 binding activity (MFI)					
			Ctrl	CR5132	CR5133	CR5140	CR6171	C6453
<i>S. aureus</i>	Joint/ND	KV31	4.89	200	192.3	178.7	38.1	106.5
<i>S. aureus</i>	Joint/ND	KV33	5.88	222	232	177	58.5	174.4
<i>S. aureus</i>	Wound/ND	KV34	7.45	286	199	160.8	59.6	183.5
<i>S. aureus</i>	Wound/ND	KV35	4.02	237	213	232	70.2	190.9
<i>S. aureus</i>	Wound/ND	KV36	3.44	285	247	229	76.4	218
<i>S. aureus</i>	Wound/ND	KV37	4.05	217	215	212	42.6	125.5
<i>S. aureus</i>	ND/MRSA	KV38	6.1	920	642	192.3	20.4	683
<i>S. aureus</i>	ND/MRSA	KV39	6.06	953	657	615	173	604
<i>S. aureus</i>	ND/MRSA	KV41	6.8	1038	854	732	226	739
<i>S. aureus</i>	ND/MRSA	KV42	12.41	1340	950	678	221	973
<i>S. aureus</i>	ND/MRSA	KV43	5.55	1084	711	480	129.6	772
<i>S. aureus</i>	Enterotoxin-/ND	KV46	18.38	1144	607	247	79	776
<i>S. aureus</i>	enterotoxin-/ND	KV47	8.58	809	513	353	102.1	436
<i>S. aureus</i>	Blood pediatric /ND	KV48	5.29	306	271	210	34.5	153
<i>S. aureus</i>	Blood pediatric /ND	KV49	6.53	747	562	522	99.7	388
<i>S. aureus</i>	Blood pediatric /ND	KV50	15.86	939	539	397	117.8	864
<i>S. aureus</i>	Blood pediatric /ND	KV51	10.25	818	680	510	111.9	410
<i>S. aureus</i>	NA/ND	MW2	9.15	1080	1021	774	210	818
<i>S. aureus</i>	NA/ND	COL	19.62	471	542	192	61.7	339
<i>S.epidermi-dis</i>	NA/ND	KV110	9.01	438	1221	499	7.04	1210
<i>S.homilis</i>	NA/ND	KV111	4.57	16.91	39.1	4.11	4.01	13.43
<i>S.warneri</i>	NA/ND	KV112	2.95	126.4	11.7	5.44	4.39	105.6
<i>S.saprof.</i>	NA/ND	KV113	6.35	186.2	17.34	136.6	9.16	118.8
<i>S.warneri</i>	NA/ND	KV114	8.67	292	303	8.63	9.17	113.4
<i>S.epidermi-dis</i>	NA/ND	KV115	12.58	886	1577	11.76	90.2	369
<i>S.haemolyti-cus</i>	NA/ND	KV117	7.23	111.8	79.5	9.89	6.44	79.9
<i>S.hominis</i>	NA/ND	KV118	11	1334	2085	97.8	9.02	1750
<i>S.haemolyti-cus</i>	NA/ND	K119	16.71	816	888	103.9	11.71	371
<i>S.warneri</i>	NA/ND	vd65	8.24	419	192.2	5.08	4.78	73.4
<i>S.warneri</i>	NA/ND	vd66	5.77	237	104.9	6.23	5.57	80.5
<i>S.warneri</i>	NA/ND	vd732	7.82	285	289	7.62	4.32	100.6
<i>S.warneri</i>	NA/ND	K706	4.21	214	225	14.62	10.3	68.7
<i>S.homilis</i>	NA/ND	vd136	4.54	25.4	815	7.37	4.13	6.4
<i>S.homilis</i>	NA/ND	vd139	5.64	90.3	211	5.47	4.4	133.7
<i>S.homilis</i>	NA/ND	K136	6.48	25.3	842	10.57	6.83	6.02

Table 16: Staphylococcal killing activity of IgG1 antibodies as measured by OPKA.

Strain	Mean staphylococcal killing activity (%)							
	502		Mn8		Newman		M187	
[ng/ml]	1250	12.5	1250	12.5	1250	12.5	1250	12.5
IgG1 antibody								
CR5132	83.9	43.2	85.0	37.3	70.4	47.5	80.9	64.0

Strain	Mean staphylococcal killing activity (%)							
	502		Mn8		Newman		M187	
CR5133	92.1	62.5	84.5	46.4	72.4	53.1	78.1	54.9
CR6166	71.6	35.1	52.1	5.5	64.8	35.1	19.3	3.3
CR6171	81.9	40.1	88.8	52.7	62.8	39.9	29.0	14.7
CR6176	78.4	38.2	70.7	31.9	74.3	55.8	31.9	11.0
CR6187	78.1	47.1	70.3	39.0	47.3	24.7	5.9	3.7
CR6193	61.0	37.6	81.1	44.1	61.5	28.5	6.0	-0.8
CR6249	82.2	30.3	90.4	46.5	51.6	26.4	4.0	1.2
CR6273	91.5	58.2	64.0	9.1	58.8	39.9	14.8	4.7
C6403	85.4	35.9	62.1	21.7	59.8	35.6	22.7	7.6
CR6406	84.0	51.3	78.5	35.8	58.0	26.1	30.3	14.1
C6410	81.9	46.9	56.6	24.4	54.1	27.6	48.6	18.4
CR6446	69.5	41.3	54.6	33.6	64.1	41.2	59.1	48.6
CR6450	76.3	21.9	67.0	28.4	60.6	35.4	2.0	-0.7
CR6452	83.9	30.6	91.6	41.3	57.5	36.0	7.9	2.6
C6453	85.9	46.0	67.0	21.0	74.1	49.7	83.2	57.5
CR6464	85.9	36.7	55.5	11.4	57.2	30.7	6.8	1.4
CR6471	96.0	68.2	44.2	7.1	62.6	34.7	8.0	0.0
CR6516	85.9	49.4	68.1	36.1	59.9	23.2	8.5	3.9
CR6517	79.4	36.1	59.8	18.4	54.8	21.5	5.8	5.1
CR6526	88.8	55.3	51.1	16.7	56.5	23.7	35.2	9.4
CR6528	89.6	47.0	49.0	16.4	55.7	27.0	6.4	1.8
CR6531	77.5	35.6	61.2	37.5	62.1	23.0	7.9	-0.7
CR6533	73.6	38.4	53.6	28.9	67.2	37.8	7.1	3.3
CR6536	91.1	59.6	46.3	17.5	69.1	48.3	4.6	-1.4
CR6537	70.3	28.9	69.1	21.5	60.4	23.3	2.5	3.9
CR6538	64.9	22.6	63.9	15.2	66.3	35.2	3.3	2.0
CR6540	92.6	53.0	63.9	16.4	61.1	38.2	8.9	4.4
CR6544	79.8	28.8	59.3	22.5	62.3	25.4	3.2	2.0
CR6566	20.9	14.2	21.3	8.7	6.3	-1.6	54.3	30.4
CR6625	20.2	9.7	8.6	-0.8	51.0	23.3	43.8	19.1
Neg. Ctrl	ND	ND	ND	ND	4.0	ND	4.5	0.0

Table 17: LTA binding activity of IgG1 antibodies as measured by ELISA.

IgG1	ELISA binding to LTA (OD492nm)						
	10	3	1	0.3	0.1	0.03	0.01
CR5133	3.3	2.58	2.093	1.429	0.631	0.356	0.171
CR6166	0.052	0.051	0.051	0.049	0.054	0.052	0.049
CR6171	0.133	0.127	0.121	0.116	0.091	0.073	0.065
CR6176	0.048	0.053	0.05	0.046	0.046	0.062	0.111
CR6526	0.049	0.053	0.05	0.049	0.048	0.053	0.052
C4374	0.093	0.099	0.084	0.073	0.07	0.07	0.069
12248	2.574	2.297	2.054	1.457	0.799	0.402	0.26
PBS	0.113	0.124	0.098	0.094	0.09	0.108	0.094

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SEQUENCE LISTING**[0140]**

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Throsby, Mark

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Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370                375                380

aac gcc cag ccc gag aac aac tac aag acc acc ccc cct gtg ctg gac      1200
Asn Gly Cln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                390                395                400

agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac aag agc      1248
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
405                410                415

cgg tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg cac gag gcc      1296
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420                425                430

ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc ggc aag      1344
Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435                440                445

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<210> 26

<211> 448

<212> PRT

<213> Homo sapiens

<400> 26

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1          5          10          15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20          25          30

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Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Ser Ser
 50 55 60
 Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Lys Thr Val Met Asn Ser Phe Phe Asp Trp Gly Gln Gly Thr
 100 105 110
 Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
 115 120 125
 Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
 130 135 140
 Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
 145 150 155 160
 Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
 165 170 175
 Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
 180 185 190
 Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
 195 200 205
 Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
 210 215 220
 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 225 230 235 240
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 260 265 270
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285
 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 290 295 300
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 325 330 335
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350
 Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 370 375 380
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 385 390 395 400
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 405 410 415
 Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430
 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 435 440 445

<210> 27

<211> 1344

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1344)

<223>

<400> 27

gag gtg ctg gag tct ggg gga ggc ttg gtc caa ccg ggg ggg tcc ctg Glu Val Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu 1 5 10 15	48
aga ctg tcc tgt tca gac tct gga ttc tcc ttt aat aac tat tgg atg Arg Leu Ser Cys Ser Asp Ser Gly Phe Ser Phe Asn Asn Tyr Trp Met 20 25 30	96
acc tgg gtc cgc cag gct ccg ggg aag ggg ctg gag tgg gtg gcc aac Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Asn 35 40 45	144
ata aat cga gat gga agt gac aag tac cat gta gac tct gtg gag ggc Ile Asn Arg Asp Gly Ser Asp Lys Tyr His Val Asp Ser Val Glu Gly 50 55 60	192
cga ttc acc atc tcc aga gac aac tcc aag aac tca cta tac ctg caa Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr Leu Gln 65 70 75 80	240
atg aac aac ctg aga gcc gac gac gcg gcg gta tat ttt tgt gcg aga Met Asn Asn Leu Arg Ala Asp Asp Ala Ala Val Tyr Phe Cys Ala Arg 85 90 95	288
ggc ggc cgg act act agc tgg tat tgg aga aac tgg gcc cag gga acc Gly Gly Arg Thr Thr Ser Trp Tyr Trp Arg Asn Trp Gly Gln Gly Thr 100 105 110	336
ctg gtc acc gtc tgg agt gct agc acc aag ggc ccc agc gtg ttc ccc Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro 115 120 125	384
ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc gcc ctg ggc Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly 130 135 140	432
tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc tgg aac Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn 145 150 155 160	480
agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc gtg ctg cag Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln 165 170 175	528
agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg ccc agc agc Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser 180 185 190	576
agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac aag ccc agc Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser 195 200 205	624
aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac aag acc Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr 210 215 220	672
cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg gcc gga ccc tcc His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Gly Gly Pro Ser 225 230 235 240	720
gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc agc cgg Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg 245 250 255	768
acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag gac ccc Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro 260 265 270	816
gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg cac aac gcc Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala 275 280 285	864
aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg gtg gtg Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val 290 295 300	912
agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac gcc aag gag tac Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr 305 310 315 320	960
aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag aag acc Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr 325 330 335	1008
atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg tac acc ctg Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu 340 345 350	1056
ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc acc tgt Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys 355 360 365	1104
ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag tgg gag agc	1152

```

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370                               375                               380

aac ggc caq ccc gag aac aac tac aag acc acc ccc cct gtg ctg gac 1200
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                               390                               395                               400

agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac aag agc 1248
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
405                               410                               415

cgg tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg cac gag gcc 1296
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420                               425                               430

ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc ggc aag 1344
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435                               440                               445

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<210> 28

<211> 448

<212> PRT

<213> Homo sapiens

<400> 28

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Glu Val Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
1                               5                               10                               15

Arg Leu Ser Cys Ser Asp Ser Gly Phe Ser Phe Asn Asn Tyr Trp Met
20                               25                               30

Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Asn
35                               40                               45

Ile Asn Arg Asp Gly Ser Asp Lys Tyr His Val Asp Ser Val Glu Gly
50                               55                               60

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser Leu Tyr Leu Gln
65                               70                               75                               80

Met Asn Asn Leu Arg Ala Asp Asp Ala Ala Val Tyr Phe Cys Ala Arg
85                               90                               95

Gly Gly Arg Thr Thr Ser Trp Tyr Trp Arg Asn Trp Gly Gln Gly Thr
100                              105                              110

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

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130                              135                              140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                              150                              155                              160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165                              170                              175

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Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195 200 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
210 215 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225 230 235 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
245 250 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
260 265 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
290 295 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305 310 315 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340 345 350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser Leu Thr Cys
355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
405 410 415

Arg Trp Cln Cln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430

Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

- <210> 29
- <211> 1350
- <212> DNA
- <213> Homo sapiens
- <220>
- <221> CDS
- <222> (1)..(1350)
- <223>
- <400> 29

gag gtg cag ctg gtg gag act ggg gga ggc ttg gtc aag cct gga ggg Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Lys Pro Gly Gly 1 5 10 15	48
tcc ctg aga ctc tcc tgc tca gcc tct aga ttc agc ttc agg gac tac Ser Leu Arg Leu Ser Cys Ser Ala Ser Arg Phe Ser Phe Arg Asp Tyr 20 25 30	96
tac atg acg tgg atc cgc cag gct cca ggg aag ggg ccg gaa tgg gtt Tyr Met Thr Trp Ile Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val 35 40 45	144
tca cac ata agt ggc agt ggc agt acg att tac tac gca gac tct gtg Ser His Ile Ser Gly Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val 50 55 60	192
agg ggc cga ttc acc atc tcc agg gac aac gcc aag agc tcc ttg tat Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser Ser Leu Tyr 65 70 75 80	240
ctg caa atg gat agc cta cag gcc gac gac acg gcc gta tat tac tgt Leu Gln Met Asp Ser Leu Gln Ala Asp Asp Thr Ala Val Tyr Tyr Cys 85 90 95	288
gcg aga ggg ggt cgc gcc acc agt tac tac tgg gtc cac tgg ggc ccg Ala Arg Gly Gly Arg Ala Thr Ser Tyr Tyr Trp Val His Trp Gly Pro 100 105 110	336
gga acc ctg gtc acc gtc tgg agt gct agc acc aag ggc ccc agc gtg Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val 115 120 125	384
ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc gcc Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala 130 135 140	432
ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser 145 150 155 160	480
tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc gtg Trp Asn Ser Ser Gly Ala Leu Thr Ser Ser Gly Val His Thr Phe Pro Ala Val 165 170 175	528
ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg ccc Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro 180 185 190	576
agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac aag Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys 195 200 205	624
ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp 210 215 220	672

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aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc gga      720
lys thr his thr cys pro pro cys pro ala pro glu leu leu gly gly
225          230          235          240

ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc      768
pro ser val phe leu phe pro pro lys pro lys asp thr leu met ile
          245          250          255

agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag      816
ser arg thr pro glu val thr cys val val val asp val ser his glu
260          265          270

gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg cac      864
asp pro glu val lys phe asn trp tyr val asp gly val glu val his
275          280          285

aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg      912
asn ala lys thr lys pro arg glu glu gln tyr asn ser thr tyr arg
290          295          300

gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc aag      960
val val ser val leu thr val leu his gln asp trp leu asn gly lys
305          310          315          320

gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag      1008
glu tyr lys cys lys val ser asn lys ala leu pro ala pro ile glu
          325          330          335

aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg tac      1056
lys thr ile ser lys ala lys gly gln pro arg glu pro gln val tyr
340          345          350

acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc      1104
thr leu pro pro ser arg glu glu met thr lys asn gln val ser leu
355          360          365

acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag tgg      1152
thr cys leu val lys gly phe tyr pro ser asp ile ala val glu trp
370          375          380

gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct gtg      1200
glu ser asn gly gln pro glu asn asn tyr lys thr thr pro pro val
385          390          395          400

ctg gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac      1248
leu asp ser asp gly ser phe phe leu tyr ser lys leu thr val asp
405          410          415

aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg cac      1296
lys ser arg trp gln gln gly asn val phe ser cys ser val met his
420          425          430

gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc      1344
glu ala leu his asn his tyr thr gln lys ser leu ser leu ser pro
435          440          445

ggc aag
gly lys
450

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<210> 30

<211> 450

<212> PRT

<213> Homo sapiens

<400> 30

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Lys Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ser Ala Ser Arg Phe Ser Phe Arg Asp Tyr
 20 25 30
 Tyr Met Thr Trp Ile Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Ser His Ile Ser Gly Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
 50 55 60
 Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser Ser Leu Tyr
 65 70 75 80
 Leu Gln Met Asp Ser Leu Gln Ala Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Gly Gly Arg Ala Thr Ser Tyr Tyr Trp Val His Trp Gly Pro
 100 105 110
 Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125
 Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140
 Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160
 Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175
 Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190
 Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205
 Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
 210 215 220
 Lys Thr His Thr Cys Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
 225 230 235 240
 Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 245 250 255
 Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
 260 265 270
 Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285
 Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
 290 295 300
 Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320
 Glu Thr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
 325 330 335
 Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350
 Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
 355 360 365
 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380
 Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400
 Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 405 410 415
 Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430
 Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
 435 440 445
 Gly Lys
 450

<210> 31

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 31

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cag tcc gcc ctg acc cag ccc cgc tca gtg tct ggg tct cct gga cag      48
Gln Ser Ala Leu Thr Gln Pro Arg Ser Val Ser Gly Ser Pro Gly Gln
1      5      10      15

tcg atc acc atc tcc tgc act gga acc agc agt gat gtt ggg agt tat      96
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ser Tyr
      20      25      30

aac ctt gtc tcc tgg tac caa cag cac cca ggc aaa gcc ccc aaa ctc      144
Asn Leu Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
      35      40      45

atg att tat gag gtc agt aag cgg ccc tca ggg gtt tct aat cgc ttc      192

Met Ile Tyr Glu Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50      55      60

tct ggc tcc aag tct ggc aac acg gcc tcc ctg aca atc tct ggg ctc      240
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65      70      75      80

cag gct gag gac gag gct gat tat tac tgc tgc tca tat gca ggt agt      288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr Ala Gly Ser
      85      90      95

agc tgg gtg ttc gga act gcc acc aag gtg acc gtg ctg aag ctt acc      336
Ser Trp Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Lys Leu Thr
100      105      110

gtg ctg ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc      384
Val Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115      120      125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc      432
Ser Ser Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130      135      140

agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145      150      155      160

agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Cln Ser
165      170      175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180      185      190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc      624
Trp Lys Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Glu Gly Ser
195      200      205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210      215      220

```

<210> 32

<211> 220

<212> PRT

<213> Homo sapiens

<400> 32

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Gln Ser Ala Leu Thr Gln Pro Arg Ser Val Ser Gly Ser Pro Gly Gln
1      5      10      15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ser Tyr
20      25      30

Asn Leu Val Ser Trp Tyr Gln Cln His Pro Gly Lys Ala Pro Lys Leu
35      40      45

```

```

Met Ile Tyr Glu Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50                      55                      60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65                      70                      75                      80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr Ala Gly Ser
      85                      90                      95

Ser Trp Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Lys Leu Thr
 100                      105                      110

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

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

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
 145                      150                      155                      160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
      165                      170                      175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
 180                      185                      190

Trp Lys Ser Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
 195                      200                      205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
 210                      215                      220

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<210> 33

<211> 645

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(645)

<223>

<400> 33

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tcg acg gac atc cag atg acc cag tct cct tcc acc ctg tct gca tct      48
Ser Thr Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser
1      5                      10                      15

gta gga gac aga gtc acc atc act tgc cgg gcc agt cag agt att agt      96
Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser
20     25                      30

agc tgg ttg gcc tgg tat cag cag aaa cca ggg aaa gcc cct aag ctc     144

```

```

Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
35          40          45

ctg atc tat aag ggc tct agt tta gaa agt ggg gtc cca tca agg ttc    192
Leu Ile Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe
50          55          60

agc ggc agt gga tct ggg aca gaa ttc act ctc acc atc agc agc ctg    240
Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu
65          70          75          80

cag cct gat gat ttt gca act tat tac tgc caa cag tat aat agt tac    288
Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr
85          90          95

ccc ctc act ttc ggc gga ggg acc aag ctg gag atc aaa cgt gcg gcc    336
Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Ala
100         105         110

gca ccc agc gtg ttc atc ttc ccc ccc tcc gac gag cag ctg aag agc    384
Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115         120         125

ggc acc gcc agc gtg gtg tgc ctg ctg aac aac ttc tac ccc cgg gag    432
Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130         135         140

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Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145         150         155         160

cag gag agc gtg acc gag cag gac agc aag gac tcc acc tac agc ctg    528
Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165         170         175

agc agc acc ctc acc ctg agc aag gcc gac tac gag aag cac aag gtg    576
Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180         185         190

tac gcc tgc gag gtg acc cac caq gcc ctg agc agc ccc gtg acc aag    624
Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
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Ser Phe Asn Arg Gly Glu Cys
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Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
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Leu Ile Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe
50          55          60

Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu
65          70          75          80

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

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
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Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145         150         155         160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165         170         175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
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Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
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ggc tac tta ggc tgg tac caa cag aaa cct ggc cag gct ccc agg ctc      144
Gly Tyr Leu Gly Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu
35          40          45

ctc atc tat ggt gca tcc agc agg gcc act ggc atc cca gac agg ttc      192
Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe
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agt ggc agt ggg tct ggg aca gac ttc act ctc acc atc agc cgg ctg      240
Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu
65          70          75          80

gag cct gaa gat ttt gca gtg tat tac tgt cag cag tat ggt agc tca      288
Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser
85          90          95

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Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Ala
100         105         110

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Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
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ggc acc gcc agc gtg gtg tgc ctg ctg aac aac ttc tac ccc cgg gag      432
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gcc aag gtg cag tgg aag gtg gac aac gcc ctg cag agc ggc aac agc      480
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cag gag agc gtg acc gag cag gac agc aag gac tcc acc tac agc ctg      528
Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
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Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180         185         190

tac gcc tgc gag gtg acc cac cag gcc ctg agc agc ccc gtg acc aag      624
Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
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<210> 36

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Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Ala
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Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
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Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
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<210> 116

<211> 1353

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1353)

<223>

<400> 116

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tgg atc ggc tgg gtg cgc cag atg ccc ggg aaa ggc ctg gag tgg atg Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met 35 40 45	144
ggg atc atc tat cct ggt gac tct gat acc aga tac agc ccg tcc ttc Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe 50 55 60	192
caa ggc cag gtc acc atc tca gcc gac aag tcc atc agc acc gcc tac Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr 65 70 75 80	240
ctg cag tgg agc agc ctg aag gcc tgc gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95	288
gcg aga cgc gct agt ata gtg gga gct acc cac ttt gac tac tgg ggc Ala Arg Arg Ala Ser Ile Val Gly Ala Thr His Phe Asp Tyr Trp Gly 100 105 110	336
cag gga acc ctg gtc acc gtc tgc agt gct agc acc aag ggc ccc agc Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 115 120 125	384
gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala 130 135 140	432
gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 145 150 155 160	480
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aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220	672
gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240	720
gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255 260	768

245	250	255	
atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 270			816
gag gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285			864
cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr 290 295 300			912
cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc Arg Val Val Ser Val Leu Thr Val Val Leu His Cln Asp Trp Leu Asn Gly 305 310 315 320			960
aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335			1008
gag aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg Glu Lys Thr Ile Ser Lys Ala Lys Cln Cln Pro Arg Glu Pro Cln Val 340 345 350			1056
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser 355 360 365			1104
ctc acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380			1152
tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc ccc cct Trp Glu Ser Asn Cln Cln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400			1200
gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415			1248
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cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445			1344
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<210> 117

<211> 451

<212> PRT

<213> Homo sapiens

<400> 117

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 Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
 35 40 45
 Gly Ile Ile Tyr Pro Cys Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
 50 55 60
 Gln Gly Cln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Leu Cln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
 85 90 95
 Ala Arg Arg Ala Ser Ile Val Gly Ala Thr His Phe Asp Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140
 Ala Leu Cys Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Cys Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Cln Ser Ser Cys Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Cys Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Cln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Cys Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415
 Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420 425 430
 His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435 440 445
 Pro Gly Lys
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<210> 118

<211> 1353

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1353)

<223>

<400> 118

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ggc atg cac tgg gtc cgc cag gct gca ggc aag ggg ctg gag tgg gtg Gly Met His Trp Val Arg Gln Ala Ala Gly Lys Gly Leu Glu Trp Val 35 40 45	144
gca ttt ata tgg cct cat gga gta aat agg ttt tat gca gac tca atg Ala Phe Ile Trp Pro His Gly Val Asn Arg Phe Tyr Ala Asp Ser Met 50 55 60	192
gag ggc cga ttc acc atc tcc aga gac gat tcc aag aat atg ttg tat Glu Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Met Leu Tyr 65 70 75 80	240
cta gaa atg aat aat ctg aga acc gaa gac acg gct cta tat tac tgt Leu Glu Met Asn Asn Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys 85 90 95	288
aca aga gat caa gac tat gtc ccg aga aag tac ttc gat ctt tgg ggc Thr Arg Asp Gln Asp Tyr Val Pro Arg Lys Tyr Phe Asp Leu Trp Gly 100 105 110	336
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aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 1008	

325	330	335	
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Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val			
340	345	350	
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc			1104
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser			
355	360	365	
ctc acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag			1152
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu			
370	375	380	
tgg gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct			1200
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro			
385	390	395	400
gtg ctg gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg			1248
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val			
405	410	415	
gac aag agc cgg tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg			1296
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met			
420	425	430	
cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc			1344
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser			
435	440	445	
ccc ggc aag			1353
Pro Gly Lys			
450			

<210> 119

<211> 451

<212> PRT

<213> Homo sapiens

<400> 119

Glu Val Cln Leu Val Cln Thr Gly Gly Val Ala Val Cln Pro Gly Arg			
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Gly Met His Trp Val Arg Gln Ala Ala Gly Lys Gly Leu Glu Trp Val			
35	40	45	
Ala Phe Ile Trp Pro His Gly Val Asn Arg Phe Tyr Ala Asp Ser Met			
50	55	60	
Glu Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Met Leu Tyr			
65	70	75	80
Leu Glu Met Asn Asn Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys			
85	90	95	

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Thr Arg Asp Gln Asp Tyr Val Pro Arg Lys Tyr Phe Asp Leu Trp Gly
100                               105               110

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

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130                               135               140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                               150               155               160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165                               170               175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180                               185               190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195                               200               205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210                               215               220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225                               230               235               240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245                               250               255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260                               265               270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275                               280               285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290                               295               300

Arg Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu Asn Gly
305                               310               315               320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325                               330               335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340                               345               350

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

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370                               375               380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                               390               395               400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405                               410               415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420                               425               430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435                               440               445

Pro Gly Lys
450

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<210> 120

<211> 1377

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1377)

<223>

<400> 120

cag gtg cag ctg cag gag tgg ggc cgg aga ctg gtg aag cct tgg gag Cln Val Cln Leu Gln Glu Ser Gly Pro Arg Leu Val Lys Pro Ser Glu 1 5 10 15	48
acc ctg tcc ctc act tgc aat gtc tct gat gac tcc atc acg agt tat Thr Leu Ser Leu Thr Cys Asn Val Ser Asp Asp Ser Ile Thr Ser Tyr 20 25 30	96
ggg tac tat tgg ggc tgg atc cgc cag ccc cca ggg gag gca ctg gag Gly Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Glu Ala Leu Glu 35 40 45	144
tgg att ggc aat gtc ttt tac agt ggc atg gct tat tac aac cgg tcc Trp Ile Gly Asn Val Phe Tyr Ser Gly Met Ala Tyr Tyr Asn Pro Ser 50 55 60	192
ctc aag agt cga gtc acc ata tta ata gac aca tgg aag aaa cag ttt Leu Lys Ser Arg Val Thr Ile Leu Ile Asp Thr Ser Lys Lys Gln Phe 65 70 75 80	240
tcc ctg aga ctc aac tcc gtg acc gcc gcg gac acg gcc att tat tac Ser Leu Arg Leu Asn Ser Val Thr Ala Ala Asp Thr Ala Ile Tyr Tyr 85 90 95	288
tgt gcg aga gtg ccc ttt ctg atg ttt aga gtg aaa att gta cag ggg Cys Ala Arg Val Pro Phe Leu Met Phe Arg Val Lys Ile Val Gln Gly 100 105 110	336
acg ggt gct ttt gat atc tgg ggc caa ggg aca atg gtc acc gtc tgg Thr Cln Ala Phe Asp Ile Trp Gly Cln Cln Thr Met Val Thr Val Ser 115 120 125	384
agt gct agc acc aag ggc ccc agc gtg ttc ccc ctg gcc ccc agc agc Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser 130 135 140	432
aag agc acc agc ggc ggc aca gcc gcc ctg ggc tgc ctg gtg aag gac Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp 145 150 155 160	480
tac ttc ccc gag ccc gtg acc gtg agc tgg aac agc gcc gcc ttg acc Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr 165 170 175	528
agc ggc gtg cac acc ttc ccc gcc gtg ctg cag agc agc gcc ctg tac Ser Gly Val His Thr Phe Pro Ala Val Leu Cln Ser Ser Gly Leu Tyr 180 185 190	576
agc ctg agc agc gtg gtg acc gtg ccc agc agc agc ctg gcc acc cag Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln 195 200 205	624
acc tac atc tgc aac gtg aac cac aag ccc agc aac acc aag gtg gac Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp 210 215 220	672
aaa cgc gtg gag ccc aag agc tgc gac aag acc cac acc tgc ccc ccc Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro 225 230 235 240	720
tgc cct gcc ccc gag ctg ctg ggc gga ccc tcc gtg ttc ctg ttc ccc Cys Pro Ala Pro Glu Leu Leu Cln Gly Cln Pro Ser Val Phe Leu Phe Pro 245 250 255	768
ccc aag ccc aag gac acc ctc atg atc agc cgg acc ccc gag gtg acc Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr 260 265 270	816
tgc gtg gtg gtg gac gtg agc cac gag gac ccc gag gtg aag ttc aac Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn 275 280 285	864
tgg tac gtg gac ggc gtg gag gtg cac aac gcc aag acc aag ccc cgg Trp Tyr Val Asp Cln Val Glu Val His Asn Ala Lys Thr Lys Pro Arg 290 295 300	912
gag gag cag tac aac agc acc tac cgg gtg gtg agc gtg ctc acc gtg Glu Glu Cln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val 305 310 315 320	960
ctg cac cag gac tgg ctg aac gcc aag gag tac aag tgc aag gtg agc Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser 325 330 335	1008
aac aag gcc ctg cct gcc ccc atc gag aag acc atc agc aag gcc aag Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys 340 345 350	1056
ggc cag ccc cgg gag ccc cag gtg tac acc ctg ccc ccc agc cgg gag Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu 355 360 365	1104
gag atg acc aag aac cag gtg tcc ctc acc tgt ctg gtg aag gcc ttc Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe 370 375 380	1152
tac ccc agc gac atc gcc gtg gag tgg gag agc aac gcc cag ccc gag Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu 1200	

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385          390          395          400
aac aac tac aag acc acc ccc cct gtg ctg gac agc gac ggc agc ttc 1248
Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
          405          410          415

ttc ctg tac agc aag ctc acc gtg gac aag agc cgg tgg cag cag ggc 1296
Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
          420          425          430

aac gtg ttc agc tgc agc gtg atg cac gag gcc ctg cac aac cac tac 1344
Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
          435          440          445

acc cag aag agc ctg agc ctg agc ccc ggc aag 1377
Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
          450          455

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<210> 121

<211> 459

<212> PRT

<213> Homo sapiens

<400> 121

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Gln Val Gln Leu Gln Glu Ser Cly Pro Arg Leu Val Lys Pro Ser Glu
1          5          10          15

Thr Leu Ser Leu Thr Cys Asn Val Ser Asp Asp Ser Ile Thr Ser Tyr
          20          25          30

Gly Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Glu Ala Leu Glu
          35          40          45

Trp Ile Gly Asn Val Phe Tyr Ser Gly Met Ala Tyr Tyr Asn Pro Ser
          50          55          60

Leu Lys Ser Arg Val Thr Ile Leu Ile Asp Thr Ser Lys Lys Gln Phe
          65          70          75          80

Ser Leu Arg Leu Asn Ser Val Thr Ala Ala Asp Thr Ala Ile Tyr Tyr
          85          90          95

Cys Ala Arg Val Pro Phe Leu Met Phe Arg Val Lys Ile Val Gln Gly
          100          105          110

Thr Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
          115          120          125

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Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
130 135 140

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
145 150 155 160

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
165 170 175

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
180 185 190

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
195 200 205

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
210 215 220

Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
225 230 235 240

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
245 250 255

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
260 265 270

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
275 280 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
290 295 300

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
305 310 315 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
325 330 335

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
340 345 350

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
355 360 365

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
370 375 380

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
385 390 395 400

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
405 410 415

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
420 425 430

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
435 440 445

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 122

<211> 1350

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1350)

<223>

<400> 122

gag gtg cag ctg gtg gag tct ggg gga gac ttg gta cag ccg ggg ggg Glu Val Gln Leu Val Clu Ser Gly Gly Asp Leu Val Gln Pro Gly Gly 1 5 10 15	48
tcc ctg cga ctc tcc tgt gta ggc tct gga ttc acc ttt ggc cgc tat Ser Leu Arg Leu Ser Cys Val Gly Ser Gly Phe Thr Phe Gly Arg Tyr 20 25 30	96
gcc atg agt tgg gtc cgc cag gct cca ggg aag ggg ctg gag tgg gtc Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45	144
gcg tct att aac aat aat gga aat cca tac tac gca gac tcc gtg aag Ala Ser Ile Asn Asn Asn Gly Asn Pro Tyr Tyr Ala Asp Ser Val Lys 50 55 60	192
ggc cga ttc acc atc tcc gca gac aat tcc aag agc aca gtt tat ctg Gly Arg Phe Thr Ile Ser Ala Asp Asn Ser Lys Ser Thr Val Tyr Leu 65 70 75 80	240
caa atg aat agc ctg aqa gcc gaa gac acg gcc atg tat tac tgt gcg Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Tyr Cys Ala 85 90 95	288
aaa gac cac tat agc agt ggc tgg ccc gcg ttt gac cac tgg ggc cag Lys Asp His Tyr Ser Ser Gly Trp Pro Ala Phe Asp His Trp Gly Gln 100 105 110	336
gga acc ctg gtc acc gtc tgg agt gct agc acc aag ggc ccc agc gtg Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val 115 120 125	384
ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc gcc Phe Pro Leu Ala Pro Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala 130 135 140	432
ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Clu Pro Val Thr Val Ser 145 150 155 160	480
tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc gtg Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val 165 170 175	528
ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg ccc Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro 180 185 190	576
agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac aag Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys 195 200 205	624
ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp 210 215 220	672
aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc gga Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly 225 230 235 240	720
ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile 245 250 255	768
agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Clu 260 265 270	816
gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg cac Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His 275 280 285	864
aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg 290 295 300	912
gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc aag Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys 305 310 315 320	960
gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu 325 330 335	1008

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aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg tac 1056
lys thr ile ser lys ala lys gly gln pro arg glu pro gln val tyr
340 345 350

acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc 1104
thr leu pro pro ser arg glu glu met thr lys asn cln val ser leu
355 360 365

acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag tgg 1152
thr cys leu val lys gly phe tyr pro ser asp ile ala val glu trp
370 375 380

gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct gtg 1200
glu ser asn gly cln pro glu asn asn tyr lys thr thr pro pro val
385 390 395 400

ctg gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac 1248
leu asp ser asp gly ser phe phe leu tyr ser lys leu thr val asp
405 410 415

aag agc cgg tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg cac 1296
lys ser arg trp cln cln gly asn val phe ser cys ser val met his
420 425 430

gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc 1344
glu ala leu his asn his tyr thr gln lys ser leu ser leu ser pro
435 440 445

ggc aag 1350
gly lys
450

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<210> 123

<211> 450

<212> PRT

<213> Homo sapiens

<400> 123

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Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Val Gly Ser Gly Phe Thr Phe Gly Arg Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Ile Asn Asn Asn Gly Asn Pro Tyr Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Ala Asp Asn Ser Lys Ser Thr Val Tyr Leu
65 70 75 80

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Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

Lys Asp His Tyr Ser Ser Gly Trp Pro Ala Phe Asp His Trp Gly Gln
100 105 110

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

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Ileu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 124

<211> 1344

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1344)

<223>

<400> 124

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tct ctg aag atc tcc tgt aag ggt tct gga tac agc ttt acc agc tac Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr 20 25 30	96
tgg atc ggc tgg gtg cgc cag atg ccc ggg aaa ggc ctg gag tgg atg Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met 35 40 45	144
ggg atc atc tat cct ggt gac tct gat acc aga tac agc cgg tcc ttc Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe 50 55 60	192
caa ggc cag gtc acc atc tca gcc gac aag tcc atc agc acc gcc tac Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr 65 70 75 80	240
ctg cag tgg agc agc ctg aag gcc tgg gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95	288
gcg agg tac agt aac tcc caa ggt atg gac gtc tgg ggc caa ggg acc Ala Arg Tyr Ser Asn Ser Gln Gly Met Asp Val Trp Gly Gln Gly Thr 100 105 110	336
acg gtc acc gtc tgg agt gct agc acc aag ggc ccc agc gtg ttc ccc Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro 115 120 125	384
ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc gcc ctg ggc Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly 130 135 140	432
tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc tgg aac Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn 145 150 155 160	480
agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc gtg ctg cag Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln 165 170 175	528
agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg ccc agc agc Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser 180 185 190	576
agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac aag ccc agc Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser 195 200 205	624
aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac aag acc Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr 210 215 220	672
cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc gga ccc tcc His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser 225 230 235 240	720
gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc agc cgg Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg 245 250 255	768
acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag gac ccc Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro 260 265 270	816
gag gtg aag ttc aac tgg tac gtg gac gcc gtg gag gtg cac aac gcc Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala 275 280 285 290	864

275	280	285	
aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg gtg gtg lys thr lys pro arg glu glu gln tyr asn ser thr tyr arg val val 290 295 300			912
agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc aag gag tac ser val leu thr val leu his gln asp trp leu asn gly lys glu tyr 305 310 315 320			960
aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag aag acc lys cys lys val ser asn lys ala leu pro ala pro ile glu lys thr 325 330 335			1008
atc agc aag gcc aag gcc cag ccc cgg gag ccc cag gtg tac acc ctg ile ser lys ala lys gly gln pro arg glu pro gln val tyr thr leu 340 345 350			1056
ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc acc tgt pro pro ser arg glu glu met thr lys asn gln val ser leu thr cys 355 360 365			1104
ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag tgg gag agc leu val lys gly phe tyr pro ser asp ile ala val glu trp glu ser 370 375 380			1152
aac gcc cag ccc gag aac aac tac aag acc acc ccc cct gtg ctg gac asn gly gln pro glu asn asn tyr lys thr thr pro pro val leu asp 385 390 395 400			1200
agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg gac aag agc ser asp gly ser phe phe leu tyr ser lys leu thr val asp lys ser 405 410 415			1248
cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg cac gag gcc arg trp gln gln gly asn val phe ser cys ser val met his glu ala 420 425 430			1296
ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc gcc aag leu his asn his tyr thr gln lys ser leu ser leu ser pro gly lys 435 440 445			1344

<210> 125

<211> 448

<212> PRT

<213> Homo sapiens

<400> 125

Glu Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
 35 40 45
 Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
 50 55 60
 Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
 85 90 95
 Ala Arg Tyr Ser Asn Ser Gln Gly Met Asp Val Trp Cys Gln Gly Thr
 100 105 110
 Thr Val Thr Val Ser Ser Ala Ser Thr Lys Cys Pro Ser Val Phe Pro
 115 120 125
 Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
 130 135 140
 Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
 145 150 155 160
 Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
 165 170 175
 Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
 180 185 190
 Ser Leu Cys Thr Cln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
 195 200 205
 Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
 210 215 220
 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 225 230 235 240
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 260 265 270
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285
 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 290 295 300
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 325 330 335
 Ile Ser Lys Ala Lys Cys Cln Pro Arg Glu Pro Cln Val Tyr Thr Leu
 340 345 350
 Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365
 Leu Val Lys Cys Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Cln Ser
 370 375 380
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 385 390 395 400
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 405 410 415
 Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430
 Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser Pro Cys Lys
 435 440 445

<210> 126

<211> 1356

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1356)

<223>

<400> 126

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cag gtc cag ctg gta cag tct gga gca gag gtg aaa aag ccg ggg gag      48

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1      5      10      15

tct ctg aag atc tcc tgt aag ggt tct aga tac agc tct acc agc tac      96
Ser Leu Lys Ile Ser Cys Lys Gly Ser Arg Tyr Ser Ser Thr Ser Tyr
20     25     30

tgg atc ggc tgg gtg cgc cag atg ccc ggg gaa ggc ctg gag tgg atg     144
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Glu Gly Leu Glu Trp Met
35     40     45

ggg atc atc tat cct ggt gac tct gat acc aga tac agc ccg tcc ttc     192
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50     55     60

caa ggc cag gtc acc atc tca gcc gac aag tcc atc agc acc gcc tac     240
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65     70     75     80

ctg cag tgg agt agc ctg aag gcc tgg gac agc gcc tta tat tac tgt     288
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Ser Ala Leu Tyr Tyr Cys
85     90     95

ggc aga ggg gcc gtg gct gga acg gtc ggc aat ggt ttt gat gtc tgg     336
Ala Arg Gly Ala Val Ala Gly Thr Val Gly Asn Gly Phe Asp Val Trp
100    105    110

ggc caa ggg aca atg gtc acc gtc tgg agt gct agc acc aag ggc ccc     384
Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
115    120    125

agc gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc gcc aca     432
Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
130    135    140

gcc gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc     480
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145    150    155    160

gtg agc tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc     528
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
165    170    175

gcc gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc     576
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180    185    190

gtg ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac     624
Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
195    200    205

cac aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc     672
His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser
210    215    220

tgc gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg     720
Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
225    230    235    240

ggc gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctg     768
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245    250    255

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atg atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser 260 265 270	816
cac gag gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag His Glu Asp Pro Clu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu 275 280 285	864
gtg cac aac gcc aag acc aag ccc cgg gag gag caq tac aac agc acc Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr 290 295 300	912
tac cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn 305 310 315 320	960
ggc aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro 325 330 335	1008
atc gag aag acc atc agc aag gcc aag ggc caq ccc cgg gag ccc caq Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln 340 345 350	1056
gtg tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val 355 360 365	1104
tcc ctc acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val 370 375 380	1152
gag tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc ccc Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro 385 390 395 400	1200
cct gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr 405 410 415	1248
gtg gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val 420 425 430	1296
atg cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu 435 440 445	1344
agc ccc gcc aag Ser Pro Gly Lys 450	1356

<210> 127

<211> 452

<212> PRT

<213> Homo sapiens

<400> 127

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

[illegible]

<210> 128

<211> 1353

<212> DNA

<213> Homo sapiens

 $\langle 220 \rangle$

<221> CDS

<222> (1)..(1353)

<223>

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<400> 128
gag gtg cag ctg gtg gag act gga gca gag gtg aaa aag ccc ggg gag 48
Glu Val Gln Leu Val Glu Thr Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

tct ctg aag atc tcc tgt aag ggt tct gga tac agc ttt acc agc tac 96
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

tgg atc ggc tgg gtg cgc cag atg ccc ggg aaa ggc ctg gag tgg gtg 144
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

ggg atc atc tat cct ggt gac tct gat acc aga tac agc cag tcc ttc 192
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

caa ggc cag gtc acc atc tca gcc gac aag tcc atc agc acc gcc tac 240
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

ctg cag tgg agc agc ctg aag gcc tcg gac acc gcc atg tat tac tgt 288
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

ggc aga cgc cgt ggt tct acc agc tcc acg gac ttt gac tac tgg ggc 336
Ala Arg Arg Arg Gly Ser Thr Ser Ser Thr Asp Phe Asp Tyr Trp Gly
100 105 110

cag gga acc ctg gtc acc gtc tcg agt gct agc acc aag ggc ccc agc 384
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc 432
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg 480
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

agc tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc 528
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg 576
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac 624
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His

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195	200	205	
aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc lys pro ser asn thr lys val asp lys arg val glu pro lys ser cys 210 215 220			672
gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc asp lys thr his thr cys pro pro cys pro ala pro glu leu leu cly 225 230 235 240			720
gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg gly pro ser val phe leu phe pro pro lys pro lys asp thr leu met 245 250 255			768
atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac ile ser arg thr pro glu val thr cys val val val asp val ser his 260 265 270			816
gag gac ccc gag gtg aag ttc aac tgg tac gtg gac gcc gtg gag gtg glu asp pro glu val lys phe asn trp tyr val asp gly val glu val 275 280 285			864
cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac his asn ala lys thr lys pro arg glu glu gln tyr asn ser thr tyr 290 295 300			912
cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac gcc arg val val ser val leu thr val leu his gln asp trp leu asn gly 305 310 315 320			960
aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc lys glu tyr lys cys lys val ser asn lys ala leu pro ala pro ile 325 330 335			1008
gag aag acc atc agc aag gcc aag gcc cag ccc cgg gag ccc cag gtg glu lys thr ile ser lys ala lys gly cln pro arg glu pro cln val 340 345 350			1056
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc tyr thr leu pro pro ser arg glu glu met thr lys asn gln val ser 355 360 365			1104
ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag leu thr cys leu val lys gly phe tyr pro ser asp ile ala val glu 370 375 380			1152
tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc ccc cct trp glu ser asn cly cln pro cly asn asn tyr lys thr thr pro pro 385 390 395 400			1200
gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg val leu asp ser asp gly ser phe phe leu tyr ser lys leu thr val 405 410 415			1248
gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg asp lys ser arg trp cln gln gly asn val phe ser cys ser val met 420 425 430			1296
cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc his glu ala leu his asn his tyr thr gln lys ser leu ser leu ser 435 440 445			1344
ccc gcc aag			1353
Pro Gly Lys 450			

<210> 129

<211> 451

<212> PRT

<213> Homo sapiens

<400> 129

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

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

<210> 130

<211> 1353

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1353)

<223>

<400> 130

cag gtc cag ctg gta cag tct gga gca gag gtg aaa aag ccc ggg gag Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu 1 5 10 15	48
tct ctg aag atc tcc tgt aag ggt tct gga tac agc ttt agt aca tac Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Ser Thr Tyr 20 25 30	96
tgg atc ggc tgg gtg cgc cag atg ccc ggg aaa ggc ctg gag tgg atg Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met 35 40 45	144
ggg atc att tat cct ggt gac tct gat acc agg tac agc ccc tcc ttc Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe 50 55 60	192
caa ggc cag gtc acc atc tca gcc gac aag tcc atc agc acc gcc cac Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala His 65 70 75 80	240
ctg cag tgg agc agc ctg aag gcc tcg gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95	288
ggc agg cca gga ccc cgt gga tac aac cat ggc ttt gac tac tgg ggc Ala Arg Pro Gly Pro Arg Gly Tyr Asn His Gly Phe Asp Tyr Trp Gly 100 105 110	336
cag gga acc ctg gtc acc gtc tcg agt gct agc acc aag ggc ccc agc Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 115 120 125	384
gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc gcc aca gcc Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala 130 135 140	432
gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 145 150 155 160	480
agc tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc Ser Trp Asn Ser Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 165 170 175	528
gtg ctg cag agc agc gcc ctg tac agc ctg agc agc gtg gtg acc gtg Val Leu Gln Ser Ser Cys Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 185 190	576
ccc agc agc agc ctg gcc acc cag acc tac atc tgc aac gtg aac cac Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His 195 200 205	624
aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220	672
gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg gcc Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240	720
gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255	768
atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 270	816
gag gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285	864
cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr 290 295 300	912
cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac gcc Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 305 310 315 320	960
aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335	1008
gag aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350	1056
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser 355 360 365	1104
ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380	1152
tgg gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400	1200

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gtg ctg gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg      1248
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
      405                        410                        415

gac aag agc cgg tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg      1296
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
      420                        425                        430

cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc      1344
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
      435                        440                        445

ccc ggc aag
Pro Gly Lys
      450

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<210> 131

<211> 451

<212> PRT

<213> Homo sapiens

<400> 131

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1          5          10          15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Ser Thr Tyr
20          25          30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35          40          45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50          55          60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala His
65          70          75          80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85          90          95

Ala Arg Pro Gly Pro Arg Gly Tyr Asn His Gly Phe Asp Tyr Trp Gly
100         105         110

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

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala

```

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

<210> 132

<211> 1347

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1347)

<223>

<400> 132

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tct ctg aag atc tcc tgt aag ggt tct gga tac acc ttt gcc agc tat Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Ala Ser Tyr 20 25 30	96
tgg gtc gcc tgg gtg cgc cag atg ccc ggg aaa ggc ctg gag tgg atg Trp Val Ala Trp Val Asn Gln Met Pro Gly Lys Gly Leu Glu Trp Met 35 40 45	144
ggg atc atc tat cct ggt gac tct gat acc aga tac agc cgg tcc ttc Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe 50 55 60	192
caa ggc cag gtc acc gtc tca gcc gac aag tcc atc agc acc gcc tac Gln Gly Gln Val Thr Val Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr 65 70 75 80	240
ctg cag tgg agc agc ctg aag gcc tgg gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95	288
gcg aga tgg tgg ggc agc ttg cat gct ttt gat atc tgg gcc caa ggg Ala Asn Trp Trp Gly Ser Leu His Ala Phe Asp Ile Trp Gly Gln Gly 100 105 110	336
aca atg gtc acc gtc tgg agt gct agc acc aag ggc ccc agc gtg ttc Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe 115 120 125	384
ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc gcc ctg Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu 130 135 140	432
ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc tgg Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp 145 150 155 160	480
aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc gtg ctg Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu 165 170 175	528
cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg ccc agc Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser 180 185 190	576
agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac aag ccc Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro 195 200 205	624
agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac aag Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys 210 215 220	672
acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc gga ccc Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro 225 230 235 240	720
tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc agc Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser 245 250 255	768
cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag gac Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp 260 265 270	816
ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg cac aac Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn 275 280 285	864
gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg gtg Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val 290 295 300	912
gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc aag gag Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu 305 310 315 320	960
tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag aag Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys 325 330 335	1008
acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg tac acc	1056

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Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350
ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc acc 1104
Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365
tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag tgg gag 1152
Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380
agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct gtg ctg 1200
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400
gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac aag 1248
Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415
agc cgg tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg cac gag 1296
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430
gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc ggc 1344
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445
aag 1347
Lys

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<210> 133

<211> 449

<212> PRT

<213> Homo sapiens

<400> 133

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

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Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Trp Trp Gly Ser Leu His Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Cln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

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

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 134

<211> 1359

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1359)

<223>

<400> 134

gag gtg cag ctg gtg gag acc gga gca gag gtg caa aag ccc ggg gag Glu Val Gln Leu Val Glu Thr Gly Ala Glu Val Gln Lys Pro Gly Glu 1 5 10 15	48
tct ctg aag atc tcc tgt aag ggt tct gga tac acc ttt acc aac tac Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Asn Tyr 20 25 30	96
tgg atc gcc tgg gtg cgc cag aag ccc ggg aaa ggc ctg gag tgg atg Trp Ile Ala Trp Val Arg Gln Lys Pro Gly Lys Gly Leu Glu Trp Met 35 40 45	144
ggg atc atc tat cct ggt gac tct gat acc aga tac agc cgg tcc ttc Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe 50 55 60	192
caa ggc cag gtc acc atc tca gcc gac aag tcc atc agc acc gcc tac Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr 65 70 75 80	240
ctg cag tgg agc agc ctg aag gcc tgg gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95	288
gcg aga cga tat tgt act act acc agc tgc agt gct ggg ttc gac ccc Ala Arg Arg Tyr Cys Thr Thr Thr Ser Cys Ser Ala Gly Phe Asp Pro 100 105 110	336
tgg gcc cag gga acc ctg gtc acc gtc tgg agt gct agc acc aag gcc Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly 115 120 125	384
ccc agc gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc gcc gcc Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly 130 135 140	432
aca gcc gcc ctg gcc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val 145 150 155 160	480
acc gtg agc tgg aac agc gcc gcc ttg acc agc gcc gtg cac acc ttc Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe 165 170 175	528
ccc gcc gtg ctg cag agc agc gcc ctg tac agc ctg agc agc gtg gtg Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val 180 185 190	576
acc gtg ccc agc agc agc ctg gcc acc cag acc tac atc tgc aac gtg Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val 195 200 205	624
aac cac aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys 210 215 220	672
agc tgc gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 225 230 235 240	720
ctg gcc gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr 245 250 255	768
ctc atg atc agc cgg acc ccc caa gtg acc tgc gtg gtg gtg gac gtg Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val 260 265 270	816
agc cac gag gac ccc gag gtg aag ttc aac tgg tac gtg gac gcc gtg Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val 275 280 285	864

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gag gtg cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc      912
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290                295                300

acc tac cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg      960
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305                310                315                320

aac gcc aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc      1008
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325                330                335

ccc atc gag aag acc atc agc aag gcc aag gcc cag ccc cgg gag ccc      1056
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340                345                350

cag gtg tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag      1104
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355                360                365

gtg tcc ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc      1152
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370                375                380

gtg gag tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc      1200
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385                390                395                400

ccc cct gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc      1248
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405                410                415

acc gtg gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc      1296
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420                425                430

gtg atg cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc      1344
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435                440                445

ctg agc ccc gcc aag                                          1359
Leu Ser Pro Gly Lys
450

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<210> 135

<211> 453

<212> PRT

<213> Homo sapiens

<400> 135

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Glu Val Gln Leu Val Glu Thr Gly Ala Glu Val Gln Lys Pro Gly Glu
1          5          10          15

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Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Asn Tyr

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Cln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

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

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser
435 440 445

Ileu Ser Pro Gly Lys
450

<210> 136

<211> 1350

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1350)

<223>

<400> 136

gag gtg cag ctg gtg gag tct ggg gca gag gtg aaa aag ccg ggg gag Glu Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Glu 1 5 10 15	48
tct ctg aag atc tcc tgt aag ggt tct gga tac agc ttt acc aag tac Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Lys Tyr 20 25 30	96
tgg atc ggc tgg gtg cgc cag aag ccc ggg aaa ggc ctg gag tgg atg Trp Ile Gly Trp Val Arg Gln Lys Pro Gly Lys Gly Leu Glu Trp Met 35 40 45	144
ggg atc atc tat cct ggt gac tct gat acc aga tac agc ccg tcc ttc Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe 50 55 60	192
caa ggc cag gtc acc atc tca acc gac aag tcc atc agc acc gcc tac Gln Gly Gln Val Thr Ile Ser Thr Asp Lys Ser Ile Ser Thr Ala Tyr 65 70 75 80	240
ctg cag tgg agc agc ctg aag gcc tcg gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95	288
gcg aga ctg ggg ggg ggg ata gca gca gca ttt gac tac tgg ggc cag Ala Arg Leu Gly Gly Gly Ile Ala Ala Ala Phe Asp Tyr Trp Gly Gln 100 105 110	336
gga acc ctg gtc acc gtc tcg agt gct agc acc aag ggc ccc agc gtg Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val 115 120 125	384
ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc gcc Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala 130 135 140	432
ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser 145 150 155 160	480
tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc gtg Trp Asn Ser Ser Gly Ala Leu Thr Ser Ser Gly Val His Thr Phe Pro Ala Val 165 170 175	528
ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg ccc Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro 180 185 190	576
agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac aag Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys 195 200 205	624
ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp 210 215 220	672

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aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc gga 720
lys thr his thr cys pro pro cys pro ala pro glu leu leu gly gly
225 230 235 240

ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc 768
pro ser val phe leu phe pro pro lys pro lys asp thr leu met ile
245 250 255

agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag 816
ser arg thr pro glu val thr cys val val val asp val ser his glu
260 265 270

gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg cac 864
asp pro glu val lys phe asn trp tyr val asp gly val glu val his
275 280 285

aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg 912
asn ala lys thr lys pro arg glu glu gln tyr asn ser thr tyr arg
290 295 300

gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc aag 960
val val ser val leu thr val leu his gln asp trp leu asn gly lys
305 310 315 320

gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag 1008
glu tyr lys cys lys val ser asn lys ala leu pro ala pro ile glu
325 330 335

aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg tac 1056
lys thr ile ser lys ala lys gly gln pro arg glu pro gln val tyr
340 345 350

acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc 1104
thr leu pro pro ser arg glu glu met thr lys asn gln val ser leu
355 360 365

acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag tgg 1152
thr cys leu val lys gly phe tyr pro ser asp ile ala val glu trp
370 375 380

gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct gtg 1200
glu ser asn gly gln pro glu asn asn tyr lys thr thr pro pro val
385 390 395 400

ctg gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac 1248
leu asp ser asp gly ser phe phe leu tyr ser lys leu thr val asp
405 410 415

aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg cac 1296
lys ser arg trp gln gln gly asn val phe ser cys ser val met his
420 425 430

gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc 1344
glu ala leu his asn his tyr thr gln lys ser leu ser leu ser pro
435 440 445

ggc aag 1350
gly lys
450

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<210> 137

<211> 450

<212> PRT

<213> Homo sapiens

<400> 137

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

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

<210> 138

<211> 1350

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1350)

<223>

<400> 138

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

165	170	175	
ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg ccc Leu Gln Ser Ser Cln Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro 180 185 190			576
agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac aag Ser Ser Ser Leu Cln Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys 195 200 205			624
ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp 210 215 220			672
aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc gga Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly 225 230 235 240			720
ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile 245 250 255			768
agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu 260 265 270			816
gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg cac Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His 275 280 285			864
aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg Asn Ala Lys Thr Lys Pro Arg Cln Cln Tyr Asn Ser Thr Tyr Arg 290 295 300			912
gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc aag Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu Asn Cln Lys 305 310 315 320			960
gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu 325 330 335			1008
aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg tac Lys Thr Ile Ser Lys Ala Lys Gly Cln Pro Arg Glu Pro Gln Val Tyr 340 345 350			1056
acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc Thr Leu Pro Pro Ser Arg Cln Glu Met Thr Lys Asn Cln Val Ser Leu 355 360 365			1104
acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag tgg Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp 370 375 380			1152
gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct gtg Glu Ser Asn Gly Cln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val 385 390 395 400			1200
ctg gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp 405 410 415			1248
aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg cac Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His 420 425 430			1296
gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro 435 440 445			1344
ggc aag Gly Lys 450			1350

<210> 139

<211> 450

<212> PRT

<213> Homo sapiens

<400> 139

Glu Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15
 Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Arg Tyr
 20 25 30
 Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
 35 40 45
 Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
 50 55 60
 Arg Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
 85 90 95
 Ala Arg Arg Met Gly Ala Ala Ser Ala Tyr Phe Asp Asn Trp Gly Gln
 100 105 110
 Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125
 Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140
 Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160
 Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175
 Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190
 Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205
 Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
 210 215 220
 Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
 225 230 235 240
 Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 245 250 255
 Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
 260 265 270
 Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285
 Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
 290 295 300
 Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320
 Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
 325 330 335
 Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Cln Val Tyr
 340 345 350
 Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser Leu
 355 360 365
 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380
 Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400
 Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
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<210> 140

<211> 1359

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1359)

<223>

<400> 140

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1 5 10 15	
tct ctg aag atc tcc tgt aag ggt tct gga tac agt ttt acc agc tac	96
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr	
20 25 30	
tgg atc ggc tgg gtg cgc cag atg ccc ggg aaa ggc ctg gag tgg atg	144
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met	
35 40 45	
ggg atc atc tat cct ggt gac tct gat acc aga tac agc ccg tcc ttc	192
Gly ile ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe	
50 55 60	
caa ggc cag gtc acc atc tca gcc gac aag tcc ata agc acc gcc tac	240
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr	
65 70 75 80	
ctg cag tgg acc agc ctg aag gcc tgg gac acc gcc gtg tat ttc tgt	288
Leu Gln Trp Thr Ser Leu Lys Ala Ser Asp Thr Ala Val Tyr Phe Cys	
85 90 95	
gcg aga ctc ggc gaa ttc cgt aga act gga aat agc tac ttt gac tac	336
Ala Arg Leu Gly Glu Phe Arg Arg Thr Gly Asn Ser Tyr Phe Asp Tyr	
100 105 110	

tgg ggc cag gga acc ctg gtc acc gtc tcg agt gct agc acc aag ggc Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly 115 120 125	384
ccc agc gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly 130 135 140	432
aca gcc gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val 145 150 155 160	480
acc gtg agc tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe 165 170 175	528
ccc gcc gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val 180 185 190	576
acc gtg ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val 195 200 205	624
aac cac aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys 210 215 220	672
agc tgc gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 225 230 235 240	720
ctg ggc gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr 245 250 255	768
ctc atg atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val 260 265 270	816
agc cac gag gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val 275 280 285	864
gag gtg cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser 290 295 300	912
acc tac cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu 305 310 315 320	960
aac gcc aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala 325 330 335	1008
ccc atc gag aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro 340 345 350	1056
cag gtg tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln 355 360 365	1104
gtg tcc ctc acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala 370 375 380	1152
gtg gag tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr 385 390 395 400	1200
ccc cct gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu 405 410 415	1248
acc gtg gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser 420 425 430	1296
gtg atg cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser 435 440 445	1344
ctg agc ccc gcc aag Leu Ser Pro Gly Lys 450	1359

<210> 141

<211> 453

<212> PRT

<213> Homo sapiens

<400> 141

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

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

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
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<210> 142

<211> 1335

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1335)

<223>

<400> 142

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tcc ctg aga ctc tcc tgt gca gcc tct gga ttc acc ttt agc agc tat	96
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr	
20 25 30	
gcc atg ggc tgg gtc cgc cag gct cca ggg aag ggg ctg gag tgg ctt	144
Ala Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu	
35 40 45	
tcg tac att cgg aat gat ggt agt gtc atc tat tac gca gac tct gtg	192
Ser Tyr Ile Arg Asn Asp Gly Ser Val Ile Tyr Tyr Ala Asp Ser Val	

50	55	60	
aag ggt cga ttc acc atc tcc aga gac aat gcc aag aac tca ctg tat lys gly arg phe thr ile ser arg asp asn ala lys asn ser leu tyr 65 70 75 80			240
ctg caa atg aac agc cta aga gcc gag gac acg gct gtg tat tac tgt leu gln met asn ser leu arg ala glu asp thr ala val tyr tyr cys 85 90 95			288
gcg aga aga ggg tac ctc gat ctc tgg ggc cgt gga acc ctg gtc acc ala arg arg gly tyr leu asp leu trp gly arg gly thr leu val thr 100 105 110			336
gtc tcg agt gct agc acc aag gcc ccc agc gtg ttc ccc ctg gcc ccc val ser ser ala ser thr lys gly pro ser val phe pro leu ala pro 115 120 125			384
agc agc aag agc acc agc gcc gcc aca gcc gcc ctg gcc tgc ctg gtg ser ser lys ser thr ser gly gly thr ala ala leu gly cys leu val 130 135 140			432
aag gac tac ttc ccc gag ccc gtg acc gtg agc tgg aac agc gcc gcc lys asp tyr phe pro glu pro val thr val ser trp asn ser gly ala 145 150 155 160			480
ttg acc agc gcc gtg cac acc ttc ccc gcc gtg ctg cag agc agc gcc leu thr ser gly val his thr phe pro ala val leu gln ser ser gly 165 170 175			528
ctg tac agc ctg agc agc gtg gtg acc gtg ccc agc agc agc ctg gcc leu tyr ser leu ser ser val val thr val pro ser ser ser leu cly 180 185 190			576
acc cag acc tac atc tgc aac gtg aac cac aag ccc agc aac acc aag thr gln thr tyr ile cys asn val asn his lys pro ser asn thr lys 195 200 205			624
gtg gac aaa cgc gtg gag ccc aag agc tgc gac aag acc cac acc tgc val asp lys arg val glu pro lys ser cys asp lys thr his thr cys 210 215 220			672
ccc ccc tgc cct gcc ccc gag ctg ctg gcc gga ccc tcc gtg ttc ctg pro pro cys pro ala pro glu leu leu gly gly pro ser val phe leu 225 230 235 240			720
ttc ccc ccc aag ccc aag gac acc ctc atg atc agc cgg acc ccc gag phe pro pro lys pro lys asp thr leu met ile ser arg thr pro glu 245 250 255			768
gtg acc tgc gtg gtg gtg gac gtg agc cac gag gac ccc gag gtg aag val thr cys val val val asp val ser his glu asp pro glu val lys 260 265 270			816
ttc aac tgg tac gtg gac gcc gtg gag gtg cac aac gcc aag acc aag phe asn trp tyr val asp gly val glu val his asn ala lys thr lys 275 280 285			864
ccc cgg gag gag cag tac aac agc acc tac cgg gtg gtg agc gtg ctc pro arg glu glu gln tyr asn ser thr tyr arg val val ser val leu 290 295 300			912
acc gtg ctg cac cag gac tgg ctg aac gcc aag gag tac aag tgc aag thr val leu his gln asp trp leu asn gly lys glu tyr lys cys lys 305 310 315 320			960
gtg agc aac aag gcc ctg cct gcc ccc atc gag aag acc atc agc aag val ser asn lys ala leu pro ala pro ile glu lys thr ile ser lys 325 330 335			1008
gcc aag gcc cag ccc cgg gag ccc cag gtg tac acc ctg ccc ccc agc ala lys gly gln pro arg glu pro gln val tyr thr leu pro pro ser 340 345 350			1056
cgg gag gag atg acc aag aac cag gtg tcc ctc acc tgt ctg gtg aag arg glu glu met thr lys asn gln val ser leu thr cys leu val lys 355 360 365			1104
ggc ttc tac ccc agc gac atc gcc gtg gag tgg gag agc aac gcc cag gly phe tyr pro ser asp ile ala val glu trp glu ser asn gly gln 370 375 380			1152
ccc gag aac aac tac aag acc acc ccc cct gtg ctg gac agc gac gcc pro glu asn asn tyr lys thr thr pro pro val leu asp ser asp gly 385 390 395 400			1200
agc ttc ttc ctg tac agc aag ctc acc gtg gac aag agc cgg tgg cag ser phe phe leu thr ser lys leu thr val asp lys ser arg trp gln 405 410 415			1248
cag gcc aac gtg ttc agc tgc agc gtg atg cac gag gcc ctg cac aac gln gly asn val phe ser cys ser val met his glu ala leu his asn 420 425 430			1296
cac tac acc cag aag agc ctg agc ctg agc ccc gcc aag his tyr thr gln lys ser leu ser leu ser pro gly lys 435 440 445			1335

<210> 143

<211> 445

<212> PRT

<213> Homo sapiens

<400> 143

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

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Cln Pro Arg Cln Pro Cln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Cln Trp Glu Ser Asn Cln Cln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Cln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 144
<211> 1350
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(1350)
<223>

<400> 144

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Cln	Val	Cln	Leu	Val	Cln	Ser	Gly	Gly	Gly	Leu	Val	Cln	Pro	Gly	Gly	
1			5				10			15						

tcc	ctg	aga	gtc	tcc	tgt	gca	gcc	tct	gga	ttc	acg	ttt	agt	agc	tat	96
Ser	Leu	Arg	Val	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr	
			20				25						30			

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

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aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg      912
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290                               295                               300

gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc aag      960
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                               310                               315                               320

gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag      1008
Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325                               330                               335

aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg tac      1056
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340                               345                               350

acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc      1104
Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355                               360                               365

acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag tgg      1152
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370                               375                               380

gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct gtg      1200
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                               390                               395                               400

ctg gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac      1248
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405                               410                               415

aag agc cgg tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg cac      1296
Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420                               425                               430

gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc      1344
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435                               440                               445

ggc aag
Gly Lys
450

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<210> 145

<211> 450

<212> PRT

<213> Homo sapiens

<400> 145

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Ser Leu Arg Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

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

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Cln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

- <210> 146
- <211> 1353
- <212> DNA
- <213> Homo sapiens
- <220>
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tgg atc ggc tgg gtg cgc cag atg ccc ggg aaa ggc ctg gag tgg atg Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met 35 40 45	144
ggg atc atc tat cct ggt gac tct gat acc aga tac agc ccg tcc ttc Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe 50 55 60	192
caa ggc cag gtc acc atc tca gcc gac aag tcc atc agc acc gcc tac Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr 65 70 75 80	240
ctg cag tgg agc agc ctg aag gcc tgc gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95	288
gcg aga cgc gct agt ata gtg gga gct acc cac ttt gac tac tgg ggc Ala Arg Arg Ala Ser Ile Val Gly Ala Thr His Phe Asp Tyr Trp Gly 100 105 110	336
cag gga acc ctg gtc acc gtc tgc agt gct agc acc aag ggc ccc agc Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 115 120 125	384
gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala 130 135 140	432
gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 145 150 155 160	480
agc tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc Ser Trp Asn Ser Gly Ala Leu Thr Ser Ser Gly Val His Thr Phe Pro Ala 165 170 175	528
gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 185 190	576
ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His 195 200 205	624
aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220	672

gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240	720
gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255	768
atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 270	816
gag gac ccc gag gtg aag ttc aac tgg tac gtg gac gcc gtg gag gtg Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285	864
cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr 290 295 300	912
cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac gcc Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 305 310 315 320	960
aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335	1008
gag aag acc atc agc aag gcc aag gcc cag ccc cgg gag ccc cag gtg Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350	1056
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser 355 360 365	1104
ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380	1152
tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc ccc cct Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400	1200
gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415	1248
gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430	1296
cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445	1344
ccc gcc aag Pro Gly Lys 450	1353

<210> 147

<211> 451

<212> PRT

<213> Homo sapiens

<400> 147

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

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

<210> 148

<211> 1353

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1353)

<223>

<400> 148

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

165	170	175	
gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg Val Leu Gln Ser Ser Cys Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 185 190			576
ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac Pro Ser Ser Ser Leu Cys Thr Cln Thr Tyr Ile Cys Asn Val Asn His 195 200 205			624
aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc Lys Pro Ser Ser Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220			672
gac aag acc cac acc tgc ccc ccc tgc cct ggc ccc gag ctg ctg ggc Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240			720
gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255			768
atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac Ile Ser Arg Thr Pro Cln Val Thr Cys Val Val Val Asp Val Ser His 260 265 270			816
gag gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285			864
cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac His Asn Ala Lys Thr Lys Pro Arg Cln Cln Gln Tyr Asn Ser Thr Tyr 290 295 300			912
cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc Arg Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu Asn Gly 305 310 315 320			960
aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335			1008
gag aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350			1056
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc Tyr Thr Leu Pro Pro Ser Arg Cln Cln Met Thr Lys Asn Gln Val Ser 355 360 365			1104
ctc acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380			1152
tgg gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct Trp Glu Ser Asn Gly Cln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400			1200
gtg ctg gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415			1248
gac aag agc cgg tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430			1296
cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc His Glu Ala Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser 435 440 445			1344
ccc gcc aag Pro Cys Lys 450			1353

<210> 149

<211> 451

<212> PRT

<213> Homo sapiens

<400> 149

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ser Ala Ser Gly Phe Thr Phe Ser Asn Tyr
 20 25 30
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Gly Ile Ser Gly Ser Gly Gly Arg Thr Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Gly Ala Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Lys Gly Val Arg Ala Gly Val Pro Tyr Tyr Phe Asp Ser Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140
 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Cln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Cln Pro Arg Glu Pro Cln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 150

<211> 1368

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1368)

<223>

<400> 150
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Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
tct ctg aag atc tcc tgt aag gct tct gga tac agt ttt acc agc tac 96
Ser Leu Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
tgg atc gcc tgg gtg cgc cag atg ccc ggg aaa ggc ctg gag tgg atg 144
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
gga atc atc tat ccc ggt gac tct gat acc aga tac agc cgg tcc ttc 192
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
caa gcc cag gtc atc atc tca gcc gac aag tcc atc agc acc gcc tac 240
Gln Gly Gln Val Ile Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
ctg cag tgg agc agc ctg aag gcc tcg gac acc gcc atg tat tac tgt 288
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
gcg aga ttt aag aag agc tca gct gct agg ggc tac tac tac tac tac 336
Ala Arg Phe Lys Lys Ser Ser Ala Ala Arg Gly Tyr Tyr Tyr Tyr Tyr
100 105 110

atg gac gtc tgg ggc aaa ggg acc acg gtc acc gtc tcg agt gct agc 384
Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Ala Ser
115 120 125

acc aag ggc ccc agc gtg ttc ccc ctg gcc ccc agc agc aag agc acc 432
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
130 135 140

agc ggc ggc aca gcc gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc 480
Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145 150 155 160

gag ccc gtg acc gtg agc tgg aac agc ggc ccc ttg acc agc ggc gtg 528
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
165 170 175

cac acc ttc ccc gcc gtg ctg cag agc agc ggc ctg tac agc ctg agc 576
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
180 185 190

agc gtg gtg acc gtg ccc agc agc agc ctg ggc acc cag acc tac atc 624
Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile
195 200 205

tgc aac gtg aac cac aag ccc agc aac acc aag gtg gac aaa cgc gtg 672
Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val
210 215 220

gag ccc aag agc tgc gac aag acc cac acc tgc ccc ccc tgc cct gcc 720
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
225 230 235 240

ccc gag ctg ctg ggc gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc 768
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
245 250 255

aag gac acc ctc atg atc agc cgg acc ccc gag gtg acc tgc gtg gtg 816
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
260 265 270

gtg gac gtg agc cac gag gac ccc gag gtg aag ttc aac tgg tac gtg 864
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
275 280 285

gac ggc gtg gag gtg cac aac gcc aag acc aag ccc cgg gag gag cag 912
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
290 295 300

tac aac agc acc tac cgg gtg gtg agc gtg ctc acc gtg ctg cac cag 960
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
305 310 315 320

gac tgg ctg aac ggc aag gag tac aag tgc aag gtg agc aac aag gcc 1008
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
325 330 335

ctg cct gcc ccc atc gag aag acc atc agc aag gcc aag ggc cag ccc 1056
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
340 345 350

cgg gag ccc cag gtg tac acc ctg ccc ccc agc cgg gag gag atg acc 1104
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
355 360 365

aag aac cag gtg tcc ctc acc tgt ctg gtg aag ggc ttc tac ccc agc 1152
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
370 375 380

gac atc gcc gtg gag tgg gag agc aac ggc cag ccc gag aac aac tac 1200
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
385 390 395 400

aag acc acc ccc cct gtg ctg gac agc gac ggc agc ttc ttc ctg tac 1248
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
405 410 415

agc aag ctc acc gtg gac aag agc cgg tgg cag cag gcc aac gtg ttc 1296
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
420 425 430

agc tgc agc gtg atg cac gag gcc ctg cac aac cac tac acc cag aag 1344
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
435 440 445

agc ctg agc ctg agc ccc ggc aag 1368
Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 151

<211> 456

<212> PRT

<213> Homo sapiens

<400> 151

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

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
 355 360 365

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 370 375 380

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 385 390 395 400

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 405 410 415

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
 420 425 430

Ser Cys Ser Val Met His Cln Ala Leu His Asn His Tyr Thr Cln Lys
 435 440 445

Ser Leu Ser Leu Ser Pro Gly Lys
 450 455

<210> 152

<211> 1347

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1347)

<223>

<400> 152

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Cln Val Cln Leu Val Cln Ser Gly Ala Cln Val Lys Lys Pro Gly Glu	
1 5 10 15	
tct ctg aag atc tcc tgt aag ggt tcc gga tac acc ttt agc agc tac	96
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Ser Ser Tyr	
20 25 30	
tgg atc ggc tgg gtg cgc cag atg ccc ggg aaa ggc ccg gag tgg atg	144
Trp Ile Gly Trp Val Arg Cln Met Pro Gly Lys Gly Pro Glu Trp Met	
35 40 45	
ggg atc atc tat cca ggt gac tct gat acc aga tac agc ccg tcc ttc	192
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe	

50	55	60	
caa ggc cag gtc acc atc tca gcc gac agg tcc atc agc acc gcc tat Gln Gly Gln Val Thr Ile Ser Ala Asp Arg Ser Ile Ser Thr Ala Tyr 65 70 75 80			240
ttg cag tgg agc agc ctg aag gcc tgc gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95			288
gcg aga ctt aat aca gtt atg gtt ggt ttg gac tac tgg gcc cag gga Ala Arg Leu Asn Thr Val Met Val Gly Leu Asp Tyr Trp Gly Gln Gly 100 105 110			336
acc ctg gtc acc gtc tgc agt gct agc acc aag gcc ccc agc gtg ttc Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe 115 120 125			384
ccc ctg gcc ccc agc agc aag agc acc agc gcc gcc aca gcc gcc ctg Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Ser Gly Thr Ala Ala Leu 130 135 140			432
ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc tgg Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp 145 150 155 160			480
aac agc gcc gcc ttg acc agc gcc gtg cac acc ttc ccc gcc gtg ctg Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu 165 170 175			528
cag agc agc gcc ctg tac agc ctg agc agc gtg gtg acc gtg ccc agc Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser 180 185 190			576
agc agc ctg gcc acc cag acc tac atc tgc aac gtg aac cac aag ccc Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro 195 200 205			624
agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac aag Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys 210 215 220			672
acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg gcc gga ccc Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro 225 230 235 240			720
tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc agc Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser 245 250 255			768
cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag gac Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp 260 265 270			816
ccc gag gtg aag ttc aac tgg tac gtg gac gcc gtg gag gtg cac aac Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn 275 280 285			864
gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg gtg Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val 290 295 300			912
gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac gcc aag gag 305 310 315 320			960
tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag aag Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys 325 330 335			1008
acc atc agc aag gcc aag gcc cag ccc cgg gag ccc cag gtg tac acc Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr 340 345 350			1056
ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc acc Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr 355 360 365			1104
tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag tgg gag Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu 370 375 380			1152
agc aac gcc cag ccc gag aac aac tac aag acc acc ccc cct gtg ctg Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu 385 390 395 400			1200
gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg gac aag Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys 405 410 415			1248
agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg cac cag Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu 420 425 430			1296
gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc gcc Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly 435 440 445			1344
aag Lys			1347

<210> 153

<211> 449

<212> PRT

<213> Homo sapiens

<400> 153

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

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Cln Pro Cln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Glu Cln Met Thr Lys Asn Cln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 154
 <211> 1341
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)..(1341)
 <223>

<400> 154

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tcc ctg aga ctc tcc tgt gca gcc tct gga ttc acc ttc agt agc tat Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 20 25 30	96
ggc atg cac tgg gtc cgc cag gct cca ggc aag ggg ctg gag tgg gtg Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45	144
gca gtt ata tca tat gat gga agt aat aaa tac tat gca gac tcc gtg Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val 50 55 60	192
aag ggc cga ttc acc atc tcc aga gac aat tcc aag aac acg ctg tat Lys Gly Val Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 65 70 75 80	240
ctg caa atg aac agc ctg aga gct gag gac acg gct gtg tat tac tgt Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95	288
ggc aaa aat gga ggc aac gct ttt gat atc tgg ggc caa ggg aca atg Ala Lys Asn Gly Ala Asn Ala Phe Asp Ile Trp Gly Gln Gly Thr Met 100 105 110	336
gtc acc gtc tgg agt gct agc acc aag ggc ccc agc gtg ttc ccc ctg Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu 115 120 125	384
gcc ccc agc agc aag agc acc agc ggc ggc aca gcc gcc ctg ggc tgc Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys 130 135 140	432
ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc tgg aac agc Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser 145 150 155 160	480
ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc gtg ctg cag agc Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser 165 170 175	528
agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg ccc agc agc agc Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser 180 185 190	576
ctg ggc acc cag acc tac atc tgc aac gtg aac cac aag ccc agc aac Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn 195 200 205	624
acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac aag acc cac Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His 210 215 220	672
acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc gga ccc tcc gtg Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val 225 230 235 240	720
ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc agc cgg acc Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr 245 250 255	768

ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag gac ccc gag Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu 260 265 270	816
gtg aag ttc aac tgg tac gtg gac ggc gtg gag gtg cac aac gcc aag Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys 275 280 285	864
acc aag ccc cgg gag gag cag tac aac agc acc tac cgg qtg qtg agc Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser 290 295 300	912
gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc aag gag tac aag Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys 305 310 315 320	960
tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag aag acc atc Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile 325 330 335	1008
agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg tac acc ctg ccc Ser Lys Ala Lys Gly Cln Pro Arg Cln Pro Cln Val Tyr Thr Leu Pro 340 345 350	1056
ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc acc tgt ctg Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu 355 360 365	1104
gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag tgg gag agc aac Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn 370 375 380	1152
ggc cag ccc gag aac aac tac aag acc acc ccc cct gtg ctg gac agc Gly Cln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser 385 390 395 400	1200
gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac aag agc cgg Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg 405 410 415	1248
tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg cac gag gcc ctg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu 420 425 430	1296
cac aac cac tac acc cag aag agc ctg agc ctg agc ccc ggc aag His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser Pro Gly Lys 435 440 445	1341

<210> 155

<211> 447

<212> PRT

<213> Homo sapiens

<400> 155

Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Val Val Cln Pro Gly Arg

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1           5           10           15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20           25           30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35           40           45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50           55           60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65           70           75           80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85           90           95

Ala Lys Asn Gly Ala Asn Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
100          105          110

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

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130          135          140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145          150          155          160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165          170          175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180          185          190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195          200          205

Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210          215          220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225          230          235          240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245          250          255

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Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Clu Asp Pro Glu
260 265 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Clu Val His Asn Ala Lys
275 280 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
290 295 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Ala Lys Gly Cln Pro Arg Glu Pro Cln Val Tyr Thr Leu Pro
340 345 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380

Gly Gln Pro Clu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Cln Cln Gly Asn Val Phe Ser Cys Ser Val Met His Clu Ala Leu
420 425 430

His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 156

<211> 1353

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1353)

<223>

<400> 156

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tct ctg aag atc tcc tgt aag ggt tct gga tac agc ttc acc agc tac Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr 20 25 30	96
tgg atc ggc tgg gtg cgc cag ttg ccc ggg aaa ggc ctg gag tgg atg Trp Ile Gly Trp Val Arg Gln Leu Pro Gly Lys Gly Leu Glu Trp Met 35 40 45	144
ggg atc atc tat cct ggt gac tct gat acc aga tac agc cgg tcc ttc Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe 50 55 60	192
caa ggc cag gtc acc atc tca gcc gac aag tcc acc agc acc gcc tac Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Thr Ser Thr Ala Tyr 65 70 75 80	240
ctg cag tgg agc agc ctg aag gcc tgc gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95	288
ggc aga cgc cgt ggt tct acc agc tcc acg gac ttt gac tac tgg ggc Ala Arg Arg Arg Gly Ser Thr Ser Thr Asp Phe Asp Tyr Trp Gly 100 105 110	336
cag gga acc ctg gtc acc gtc tgc agt gct agc acc aag ggc ccc agc Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 115 120 125	384
gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala 130 135 140	432
gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 145 150 155 160	480
agc tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc Ser Trp Asn Ser Gly Ala Leu Thr Ser Ser Gly Val His Thr Phe Pro Ala 165 170 175	528
gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 185 190	576
ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His 195 200 205	624
aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220	672

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gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg gcc 720
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225          230          235          240

gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg 768
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
          245          250          255

atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac 816
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260          265          270

gag gac ccc gag gtg aag ttc aac tgg tac gtg gac gcc gtg gag gtg 864
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275          280          285

cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac 912
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290          295          300

cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac gcc 960
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305          310          315          320

aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc 1008
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
          325          330          335

gag aag acc atc agc aag gcc aag gcc cag ccc cgg gag ccc cag gtg 1056
Glu Lys Thr Ile Ser Lys Ala Lys Glu Glu Met Thr Lys Asn Gln Val Ser
340          345          350

tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc 1104
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355          360          365

ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag 1152
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370          375          380

tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc ccc cct 1200
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385          390          395          400

gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg 1248
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405          410          415

gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg 1296
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420          425          430

cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc 1344
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435          440          445

ccc gcc aag
Pro Gly Lys 1353
450

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<210> 157

<211> 451

<212> PRT

<213> Homo sapiens

<400> 157

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

210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Clu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Clu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Clu Val Lys Phe Asn Trp Tyr Val Asp Cys Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 158
<211> 1353
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(1353)
<223>

<400> 158

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

165	170	175	
gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg Val Leu Gln Ser Ser Cys Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 185 190			576
ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac Pro Ser Ser Ser Leu Cys Thr Cln Thr Tyr Ile Cys Asn Val Asn His 195 200 205			624
aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc Lys Pro Ser Ser Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220			672
gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240			720
gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255			768
atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 270			816
gag gac ccc gag gtg aag ttc aac tgg tac gtg gac gcc gtg gag gtg Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285			864
cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac His Asn Ala Lys Thr Lys Pro Arg Cln Cln Lys Tyr Asn Ser Thr Tyr 290 295 300			912
cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac gcc Arg Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu Asn Gly 305 310 315 320			960
aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335			1008
gag aag acc atc agc aag gcc aag gcc cag ccc cgg gag ccc cag gtg Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350			1056
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc Tyr Thr Leu Pro Pro Ser Arg Cln Cln Met Thr Lys Asn Gln Val Ser 355 360 365			1104
ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380			1152
tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc ccc cct Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400			1200
gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415			1248
gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg 420 425 430			1296
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430			
cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc His Glu Ala Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser 435 440 445			1344
ccc gcc aag Pro Cys Lys 450			1353

<210> 159

<211> 451

<212> PRT

<213> Homo sapiens

<400> 159

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Ser Gly Glu
 1 5 10 15
 Ser Leu Lys Ile Ser Cys Lys Gly Phe Gly Tyr Ser Phe Thr Ser Gln
 20 25 30
 Trp Ile Val Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
 35 40 45
 Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
 50 55 60
 Gln Gly Gln Val Thr Ile Ser Ala Asp Arg Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Asn Ala Met Tyr Tyr Cys
 85 90 95
 Ala Arg Ala Leu Arg Gly Tyr Ser Ser Ser Ser Phe Gly Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140
 Ala Leu Cys Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Cln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Cln Pro Arg Glu Pro Cln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 160

<211> 1344

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1344)

<223>

<400> 160

gag gtc cag ctg gtg cag tct ggg gct gag gtg aag aag cct ggg gcc	48
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala	
1 5 10 15	
tca gtg aag gtt tcc tgc aag gca tct gga tac acc ttc agc aac tac	96
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asn Tyr	
20 25 30	
tat atg cac tgg gtg cga cag gcc cct gga caa ggg ctt gag tgg atg	144
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met	
35 40 45	
gga ata atc aac cct agt ggt ggt agc aca agt tac gca cag aag ttt	192
Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe	
50 55 60	
cag ggc aga ttc acc gtg acc agg gac acg tcc acg agc aca gtc tac	240
Gln Gly Arg Phe Thr Val Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr	
65 70 75 80	
atg gag ctg agc agc ctg aga tct gag gac acg gcc gtg tat tac tgt	288
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys	
85 90 95	
gcg act cga cgc ggg cag cgg tac ttc cag cac tgg gcc cag gcc acc	336
Ala Thr Arg Arg Gly Gln Arg Tyr Phe Gln His Trp Gly Gln Gly Thr	
100 105 110	

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ctg gtc act gtc tcg agt gct agc acc aag ggc ccc agc gtg ttc ccc 384
Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc gcc ctg ggc 432
Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140

tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc tgg aac 480
Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145 150 155 160

agc gcc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc gtg ctg cag 528
Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165 170 175

agc agc gcc ctg tac agc ctg agc agc gtg gtg acc gtg ccc agc agc 576
Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180 185 190

agc ctg gcc acc cag acc tac atc tgc aac gtg aac cac aag ccc agc 624
Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195 200 205

aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac aag acc 672
Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
210 215 220

cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc gga ccc tcc 720
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Gly Gly Pro Ser
225 230 235 240

gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc agc cgg 768
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
245 250 255

acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag gac ccc 816
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
260 265 270

gag gtg aag ttc aac tgg tac gtg gac gcc gtg gag gtg cac aac gcc 864
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
275 280 285

aag acc aag ccc cgg gag gag cag tac aac agc acc tac cgg gtg gtg 912
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
290 295 300

agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac gcc aag gag tac 960
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305 310 315 320

aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc gag aag acc 1008
Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
325 330 335

atc agc aag gcc aag gcc cag ccc cgg gag ccc cag gtg tac acc ctg 1056
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340 345 350

ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc ctc acc tgt 1104
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
355 360 365

ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag tgg gag agc 1152
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370 375 380

aac gcc cag ccc gag aac aac tac aag acc acc ccc cct gtg ctg gac 1200
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385 390 395 400

agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg gac aag agc 1248
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
405 410 415

cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg cac gag gcc 1296
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430

ctg cac aac cac tac acc cag aag agc ctg agc ctg agc ccc gcc aag 1344
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

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<210> 161

<211> 448

<212> PRT

<213> Homo sapiens

<400> 161

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asn Tyr
 20 25 30
 Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe
 50 55 60
 Gln Gly Arg Phe Thr Val Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Thr Arg Arg Gly Gln Arg Tyr Phe Gln His Trp Gly Gln Gly Thr
 100 105 110
 Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
 115 120 125
 Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
 130 135 140
 Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
 145 150 155 160
 Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
 165 170 175
 Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
 180 185 190
 Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
 195 200 205
 Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
 210 215 220
 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 225 230 235 240
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 245 250 255
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 260 265 270
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285
 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 290 295 300
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 325 330 335
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350
 Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365

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Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 370                      375                      380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                      390                      395                      400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 405                      410                      415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420                      425                      430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 435                      440                      445

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<210> 162

<211> 1353

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1353)

<223>

<400> 162

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cag gta cag ctg cag cag tca ggt cca gga ctg gtg aag ccc tcg cag      48
Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1                      5                      10                      15

acc ctc tca ctc acc tgt gcc atc tcc gga gac agt gtc tct agc aac      96
Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
20                      25                      30

aga gct gct tgg aac tgg atc aag cag tcc cca tcg aga ggc ctt gag     144
Arg Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35                      40                      45

tgg ctg gga agg sca tac tac agg tcc aag tgg tat aat gat tat gca     192
Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
50                      55                      60

gta tct gtg aaa agt cga ata agc atc aac cca gac gca ttg aag aac     240
Val Ser Val Lys Ser Arg Ile Ser Ile Asn Pro Asp Ala Leu Lys Asn
65                      70                      75                      80

cag ttc tcc ctg cag ctg aac tct gtg act ccc gag gac acg gct gtg     288
Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val

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85	90	95	
tat tac tgt gca aga gat act ggc tgg tac cga ttt gac tcc tgg ggc			336
Tyr Tyr Cys Ala Arg Asp Thr Gly Trp Tyr Arg Phe Asp Ser Trp Gly			
100	105	110	
cag gga acc ctg gtc acc gtc tgg agt gct agc acc aag ggc ccc agc			384
Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser			
115	120	125	
gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca gcc			432
Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala			
130	135	140	
gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc gtg			480
Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val			
145	150	155	160
agc tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc gcc			528
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala			
165	170	175	
gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg			576
Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val			
180	185	190	
ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac			624
Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His			
195	200	205	
aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc			672
Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys			
210	215	220	
gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc			720
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly			
225	230	235	240
gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg			768
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met			
245	250	255	
atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac			816
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His			
260	265	270	
gag gac ccc gag gtg aag ttc aac tgg tac gtg gac gcc gtg gag gtg			864
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val			
275	280	285	
cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac			912
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr			
290	295	300	
cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc			960
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly			
305	310	315	320
aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc			1008
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile			
325	330	335	
gag aag acc atc agc aag gcc aag gcc cag ccc cgg gag ccc cag gtg			1056
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val			
340	345	350	
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc			1104
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser			
355	360	365	
ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag			1152
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu			
370	375	380	
tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc ccc cct			1200
Trp Glu Ser Asn Gly Cln Pro Cln Asn Asn Tyr Lys Thr Thr Pro Pro			
385	390	395	400
gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg			1248
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val			
405	410	415	
gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg			1296
Asp Lys Ser Arg Trp Cln Cln Gly Asn Val Phe Ser Cys Ser Val Met			
420	425	430	
cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc			1344
His Glu Ala Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser			
435	440	445	
ccc gcc aag			1353
Pro Cln Lys			
450			

<210> 163

<211> 451

<212> PRT

<213> Homo sapiens

<400> 163

Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15
 Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
 20 25 30
 Arg Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
 35 40 45
 Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
 50 55 60
 Val Ser Val Lys Ser Arg Ile Ser Ile Asn Pro Asp Ala Leu Lys Asn
 65 70 75 80
 Gln Phe Ser Leu Cln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
 85 90 95
 Tyr Tyr Cys Ala Arg Asp Thr Gly Trp Tyr Arg Phe Asp Ser Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140
 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Cln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Cln Tyr Asn Ser Thr Tyr
 290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Cln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 164
<211> 1353
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(1353)
<223>

<400> 164

gag gtc cag ctg gtg cag tct gga gca gag gtg aaa aag ccc ggg gag	48
Clu Val Cln Leu Val Cln Ser Gly Ala Cln Val Lys Lys Pro Gly Glu	
1 5 10 15	
tct ctg aag atc tcc tgt aag ggt tct gga tac agc ttt acc acc tac	96
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Thr Tyr	
20 25 30	

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

cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr 290 295 300	912
cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac ggc Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 305 310 315 320	960
aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335	1008
gag aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag gtg Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350	1056
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser 355 360 365	1104
ctc acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc gtg gag Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380	1152
tgg gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc cct Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400	1200
gtg ctg gac agc gac ggc agc ttc ttc ctg tac agc aag ctc acc gtg Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415	1248
gac aag agc cgg tgg cag cag ggc aac gtg ttc agc tgc agc gtg atg Asp Lys Ser Arg Trp Cln Cln Cln Asn Val Phe Ser Cys Ser Val Met 420 425 430	1296
cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445	1344
ccc ggc aag Pro Gly Lys 450	1353

<210> 165
<211> 451
<212> PRT
<213> Homo sapiens

<400> 165
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Thr Tyr

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

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

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

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Cys Cln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Cys Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 166
<211> 1359
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(1359)
<223>

<400> 166

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tct ctg aag atc tcc tgt aag ggt tct gga tac acc ttt acc aac tac Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Asn Tyr 20 25 30	96
tgg atc gcc tgg gtg cgc cag aag ccc ggg aaa ggc ctg gag tgg atg Trp Ile Ala Trp Val Arg Gln Lys Pro Gly Lys Gly Leu Glu Trp Met 35 40 45	144
ggg atc atc tat cct ggt gac tct gat acc aga tac agc cgg tcc ttc Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe 50 55 60	192
caa ggc cag gtc acc atc tca gcc gac aag tcc atc agc acc gcc tac Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr 65 70 75 80	240
ctg cag tgg agc agc ctg aag gcc tgc gac acc gcc atg tat tac tgt Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys 85 90 95	288
gcg aga cga tat tgt act act acc agc tgc agt gct ggg ttc gac ccc Ala Arg Arg Tyr Cys Thr Thr Thr Ser Cys Ser Ala Gly Phe Asp Pro 100 105 110	336
tgg ggc cag gga acc ctg gtc acc gtc tgc agt gct agc acc aag ggc Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly 115 120 125	384
ccc agc gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly 130 135 140	432
aca gcc gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val 145 150 155 160	480
acc gtg agc tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe 165 170 175	528
ccc gcc gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val 180 185 190	576
acc gtg ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val 195 200 205	624
aac cac aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Asg Val Glu Pro Lys 210 215 220	672

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agc tgc gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg 720
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

ctg gcc gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc 768
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

ctc atg atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg 816
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

agc cac gag gac ccc gag gtg aag ttc aac tgg tac gtg gac gcc gtg 864
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

gag gtg cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc 912
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

acc tac cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg 960
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

aac gcc aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc 1008
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

ccc atc gag aag acc atc agc aag gcc aag gcc cag ccc cgg gag ccc 1056
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

cag gtg tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag 1104
Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

gtg tcc ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc 1152
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

gtg gag tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc 1200
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

ccc cct gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc 1248
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

acc gtg gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc 1296
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

gtg atg cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc 1344
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

ctg agc ccc gcc aag 1359
Leu Ser Pro Gly Lys
450

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<210> 167

<211> 453

<212> PRT

<213> Homo sapiens

<400> 167

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

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

<210> 168

<211> 1353

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1353)

<223>

<400> 168

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

165	170	175	
gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc gtg Val Leu Cln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 185 190			576
ccc agc agc agc ctg ggc acc cag acc tac atc tgc aac gtg aac cac Pro Ser Ser Ser Leu Cln Thr Cln Thr Tyr Ile Cys Asn Val Asn His 195 200 205			624
aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc tgc Lys Pro Ser Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220			672
gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240			720
gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc atg Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255			768
atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc cac Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 270			816
gag gac ccc gag gtg aag ttc aac tgg tac gtg gac gcc gtg gag gtg Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285			864
cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc tac His Asn Ala Lys Thr Lys Pro Arg Glu Cln Cln Tyr Asn Ser Thr Tyr 290 295 300			912
cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg aac gcc Arg Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu Asn Gly 305 310 315 320			960
aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc atc Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335			1008
gag aag acc atc agc aag gcc aag gcc cag ccc cgg gag ccc cag gtg Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350			1056
tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg tcc Tyr Thr Leu Pro Pro Ser Arg Cln Cln Met Thr Lys Asn Gln Val Ser 355 360 365			1104
ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc gtg gag Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380			1152
tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc ccc cct Trp Glu Ser Asn Gly Cln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400			1200
gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc gtg Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415			1248
gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc gtg atg			1296
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430			
cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg agc His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445			1344
ccc gcc aag Pro Gly Lys 450			1353

<210> 169

<211> 451

<212> PRT

<213> Homo sapiens

<400> 169

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
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 Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Asn Tyr
 20 25 30
 Trp Ile Ala Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
 35 40 45
 Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
 50 55 60
 Gln Gly Gln Val Thr Ile Ser Ala Asp Arg Ser Ile Asn Thr Ala Tyr
 65 70 75 80
 Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Phe Tyr Cys
 85 90 95
 Ala Arg Arg Leu Tyr Gly Ser Gly Arg Pro Tyr Phe Asp Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140
 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Cln Tyr Asn Ser Thr Tyr
 290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Cln Pro Arg Glu Pro Cln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Cln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435 440 445

Pro Gly Lys
 450

<210> 170

<211> 1356

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1356)

<223>

<400> 170

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Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu	
1 5 10 15	
tct ctg aag atc tcc tgt aag ggt tct gga tac agc ttt acc aac tac	96
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Asn Tyr	
20 25 30	
tgg atc ggc tgg gtg cgc cag atg ccc ggg aaa ggc ctg gag tgg atg	144
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met	
35 40 45	
ggg atc atc tat cct ggt gac tct gat acc aga tac agc ccg tcc ttc	192
Gly ile ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe	
50 55 60	
caa ggc cag gtc acc atc tca gcc gac aag tcc atc agc acc gcc tac	240
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr	
65 70 75 80	
ctg cag tgg agc agc ctg aag gcc tgg gac acc gcc atg tat tac tgt	288
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys	
85 90 95	
gcg aga cat acg cag aac aaa aat ggg atg aat act ttt gat atc tgg	336
Ala Arg His Thr Gln Asn Lys Asn Gly Met Asn Thr Phe Asp Ile Trp	
100 105 110	

ggc caa ggg aca atg gtc acc gtc tgg agt gct agc acc aag ggc ccc 384
 Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
 115 120 125
 agc gtg ttc ccc ctg gcc ccc agc agc aag agc acc agc ggc ggc aca 432
 Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
 130 135 140
 gcc gcc ctg ggc tgc ctg gtg aag gac tac ttc ccc gag ccc gtg acc 480
 Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
 145 150 155 160
 gtg agc tgg aac agc ggc gcc ttg acc agc ggc gtg cac acc ttc ccc 528
 Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
 165 170 175
 gcc gtg ctg cag agc agc ggc ctg tac agc ctg agc agc gtg gtg acc 576
 Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
 180 185 190
 gtg ccc agc agc agc ctg gcc acc cag acc tac atc tgc aac gtg aac 624
 Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
 195 200 205
 cac aag ccc agc aac acc aag gtg gac aaa cgc gtg gag ccc aag agc 672
 His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser
 210 215 220
 tgc gac aag acc cac acc tgc ccc ccc tgc cct gcc ccc gag ctg ctg 720
 Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 225 230 235 240
 ggc gga ccc tcc gtg ttc ctg ttc ccc ccc aag ccc aag gac acc ctc 768
 Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 245 250 255
 atg atc agc cgg acc ccc gag gtg acc tgc gtg gtg gtg gac gtg agc 816
 Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 260 265 270
 cac gag gac ccc gag gtg aag ttc aac tgg tac gtg gac ggc gtg gag 864
 His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 275 280 285
 gtg cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc acc 912
 Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 290 295 300
 tac cgg gtg gtg agc gtg ctc acc qtg ctg cac cag gac tgg ctg aac 960
 Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 305 310 315 320
 ggc aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc ccc 1008
 Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 325 330 335
 atc gag aag acc atc agc aag gcc aag ggc cag ccc cgg gag ccc cag 1056
 Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 340 345 350
 gtg tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag gtg 1104
 Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
 355 360 365
 tcc ctc acc tgt ctg gtg aag ggc ttc tac ccc agc gac atc gcc qtg 1152
 Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
 370 375 380
 gag tgg gag agc aac ggc cag ccc gag aac aac tac aag acc acc ccc 1200
 Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 385 390 395 400
 cct gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc acc 1248
 Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
 405 410 415
 gtg gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc qtg 1296
 Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 420 425 430
 atg cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc ctg 1344
 Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 435 440 445
 agc ccc gcc aag 1356
 Ser Pro Gly Lys
 450

<210> 171

<211> 452

<212> PRT

<213> Homo sapiens

<400> 171

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15
 Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Asn Tyr
 20 25 30
 Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
 35 40 45
 Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
 50 55 60
 Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
 85 90 95
 Ala Arg His Thr Cln Asn Lys Asn Gly Met Asn Thr Phe Asp Ile Trp
 100 105 110
 Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
 115 120 125
 Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
 130 135 140
 Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
 145 150 155 160
 Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
 165 170 175
 Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
 180 185 190
 Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
 195 200 205
 His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser
 210 215 220
 Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
 225 230 235 240
 Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 245 250 255
 Met Ile Ser Arg Thr Pro Gln Val Thr Cys Val Val Val Asp Val Ser
 260 265 270
 His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 275 280 285
 Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
 290 295 300
 Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
 305 310 315 320
 Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 325 330 335
 Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Cln
 340 345 350

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

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
370 375 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385 390 395 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
405 410 415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
420 425 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
435 440 445

Ser Pro Gly Lys
450

<210> 172
<211> 1338
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(1338)
<223>

<400> 172
cag gtg cag cta cag cag tgg ggc gca gga ctg ttg aag cct tgg gag 48
Cln Val Cln Leu Cln Cln Trp Cln Ala Cln Leu Leu Lys Pro Ser Glu
1 5 10 15
acc ctg tcc ctc acc tgc gct gtc tat ggt gcg tcc ttc cgt ggt tac 96
Thr Leu Ser Leu Thr Cys Ala Val Tyr Cln Ala Ser Phe Arg Cln Tyr
20 25 30
tac tgg agc tgg atc cgc cag ccc cca ggg aag ggg ctg gag tgg att 144
Tyr Trp Ser Trp Ile Arg Cln Pro Pro Cln Lys Cln Leu Glu Trp Ile
35 40 45
ggg gaa atc aat cat agt gga agc acc aac tac aac ccg tcc ctc aag 192
Cln Cln Ile Asn His Ser Cln Ser Thr Asn Tyr Asn Pro Ser Leu Lys

50	55	60	
agt cga gtc acc ata tca gta gac acg tcc aaa aac cag ttc tcc ctg Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu 65 70 75 80			240
aag ctg agt tct gtg acc gcc gca gac acg gct gtg tat tac tgt gcg Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95			288
aga ggc cgc cct gat tct ttt gat atc tgg ggc caa ggg aca atg gtc Arg Gly Arg Pro Asp Ser Phe Asp Ile Trp Gly Gln Gly Thr Met Val 100 105 110			336
acc gtc tcg agt gct agc acc aag ggc ccc agc gtg ttc ccc ctg gcc Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala 115 120 125			384
ccc agc agc aag agc acc agc ggc ggc aca gcc gcc ctg ggc tgc ctg Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu 130 135 140			432
gtg aag gac tac ttc ccc gag ccc gtg acc gtg agc tgg aac agc ggc Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly 145 150 155 160			480
gcc ttg acc agc ggc gtg cac acc ttc ccc gcc gtg ctg cag agc agc Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser 165 170 175			528
ggc ctg tac agc ctg agc agc gtg gtg acc gtg ccc agc agc agc ctg Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu 180 185 190			576
ggc acc cag acc tac atc tgc aac gtg aac cac aag ccc agc aac acc Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr 195 200 205			624
aag gtg gac aaa cgc gtg gag ccc aag agc tgc gac aag acc cac acc Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr 210 215 220			672
tgc ccc ccc tgc cct gcc ccc gag ctg ctg ggc gga ccc tcc gtg ttc Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe 225 230 235 240			720
ctg ttc ccc ccc aag ccc aag gac acc ctc atg atc agc cgg acc ccc Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro 245 250 255			768
gag gtg acc tgc gtg gtg gtg gac gtg agc cac gag gac ccc gag gtg Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val 260 265 270			816
aag ttc aac tgg tac gtg gac ggc gtg gag gtg cac aac gcc aag acc Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr 275 280 285			864
aag ccc cgg gag gag cag tac aac agc acc tac cgg gtg gtg agc gtg Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val 290 295 300			912
ctc acc gtg ctg cac cag gac tgg ctg aac ggc aag gag tac aag tgc 305 310 315 320			960
aag gtg agc aac aag gcc ctg cct gcc ccc atc gag aag acc atc agc Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser 325 330 335			1008
aag gcc aag ggc cag ccc cgg gag ccc cag gtg tac acc ctg ccc ccc Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro 340 345 350			1056
agc cgg gag gag atg acc aag aac cag gtg tcc ctc acc tgt ctg gtg Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val 355 360 365			1104
aag ggc ttc tac ccc agc gac atc gcc gtg gag tgg gag agc aac gcc Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly 370 375 380			1152
cag ccc gag aac aac tac aag acc acc ccc cct gtg ctg gac agc gac Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp 385 390 395 400			1200
ggc agc ttc ttc ctg tac agc aag ctc acc gtg gac aag agc cgg tgg Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp 405 410 415			1248
cag cag gcc aac gtg ttc agc tgc agc gtg atg cac gag gcc ctg cac Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His 420 425 430			1296
aac cac tac acc cag aag agc ctg agc ctg agc ccc gcc aag Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 435 440 445			1338

<210> 173

<211> 446

<212> PRT

<213> Homo sapiens

<400> 173

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

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
325 330 335

Lys Ala Lys Gly Cln Pro Arg Cln Pro Cln Val Tyr Thr Leu Pro Pro
340 345 350

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
355 360 365

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Cln Trp Cln Ser Asn Gly
370 375 380

Gln Pro Cln Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385 390 395 400

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
405 410 415

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
420 425 430

Asn His Tyr Thr Cln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 174
<211> 1359
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(1359)
<223>

<400> 174

cag	gtg	cag	ctg	gtg	caa	tct	gga	gca	gag	gtg	aaa	aag	cgg	ggg	gag	48
Cln	Val	Cln	Leu	Val	Cln	Ser	Gly	Ala	Cln	Val	Lys	Lys	Pro	Gly	Cln	
1			5				10						15			

tct	ctg	aag	atc	tcc	tgt	aag	ggg	tct	ggg	tac	agc	ttt	acc	aac	tac	96
Ser	Leu	Lys	Ile	Ser	Cys	Lys	Gly	Ser	Gly	Tyr	Ser	Phe	Thr	Asn	Tyr	
		20					25						30			

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

gag gtg cac aac gcc aag acc aag ccc cgg gag gag cag tac aac agc Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser 290 295 300	912
acc tac cgg gtg gtg agc gtg ctc acc gtg ctg cac cag gac tgg ctg Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu 305 310 315 320	960
aac gcc aag gag tac aag tgc aag gtg agc aac aag gcc ctg cct gcc Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala 325 330 335	1008
ccc atc gag aag acc atc agc aag gcc aag gcc cag ccc cgg gag ccc Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro 340 345 350	1056
cag gtg tac acc ctg ccc ccc agc cgg gag gag atg acc aag aac cag Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln 355 360 365	1104
gtg tcc ctc acc tgt ctg gtg aag gcc ttc tac ccc agc gac atc gcc Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala 370 375 380	1152
gtg gag tgg gag agc aac gcc cag ccc gag aac aac tac aag acc acc Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr 385 390 395 400	1200
ccc cct gtg ctg gac agc gac gcc agc ttc ttc ctg tac agc aag ctc Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu 405 410 415	1248
acc gtg gac aag agc cgg tgg cag cag gcc aac gtg ttc agc tgc agc Thr Val Asp Lys Ser Arg Thr Gln Gln Gly Asn Val Phe Ser Cys Ser 420 425 430	1296
gtg atg cac gag gcc ctg cac aac cac tac acc cag aag agc ctg agc Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser 435 440 445	1344
ctg agc ccc gcc aag Leu Ser Pro Gly Lys 450	1359

<210> 175
<211> 453
<212> PRT
<213> Homo sapiens

<400> 175
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Asn Tyr

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Cln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Cln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Cln Pro Arg Glu Pro
340 345 350

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

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Cln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Cln Cln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Cln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 176

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 176

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caa tct gcc ctg act cag cct ccc tcc gcg tcc ggg tct cct gga cag      48
Gln Ser Ala Leu Thr Cln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1      5      10      15

tca gtc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat      96
Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20      25      30

aac tat gtc tcc tgg tac caa cag cac cca ggc aaa gcc ccc aaa ctc      144
Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35      40      45

atg att tat gag gtc agt aag cgg ccc tca ggg gtc cct gat cgc ttc      192
Met Ile Tyr Gln Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50      55      60

tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc gtc tct ggg ctc      240
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65      70      75      80

cag gct gag gat gag gct gat tat tac tgc agc tca tat gca ggc agc      288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
85      90      95

aac aat ttg gta ttc gcc gga ggg acc aag ctg acc gtc cta ggt gcg      336
Asn Asn Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100      105      110

gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc      384
Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115      120      125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc      432
Ser Ser Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130      135      140

agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145      150      155      160

agc ccc gtg aag gcc gcc gtg gag acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165      170      175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180      185      190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc      624
Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195      200      205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210      215      220

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<210> 177

<211> 220

<212> PRT

<213> Homo sapiens

<400> 177

Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Cyl Thr Ser Ser Asp Val Cyl Cyl Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Cln Cln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Clu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Cyl Ser
85 90 95

Asn Asn Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

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

Ser Ser Glu Clu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130 135 140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145 150 155 160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Cln Ser
165 170 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180 185 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195 200 205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215 220

- <210> 178
- <211> 648
- <212> DNA
- <213> Homo sapiens
- <220>
- <221> CDS
- <222> (1)..(648)
- <223>
- <400> 178

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cag tct gtg ttg acg cag ccg ccc tca ctg tcc gtg tcc cca gga cag      48
Gln Ser Val Leu Thr Gln Pro Pro Ser Leu Ser Val Ser Pro Gly Gln
1      5      10      15

aca gcc agc atc tcc tgc tct gga gat aaa tta ggg gat aaa tat gtt      96
Thr Ala Ser Ile Ser Cys Ser Gly Asp Lys Leu Gly Asp Lys Tyr Val
20      25      30

tcc tgg tat cag cag agg cct ggc cag tcc ccc gtc tta gtc atc tat      144
Ser Trp Tyr Gln Gln Arg Pro Gly Gln Ser Pro Val Leu Val Ile Tyr
35      40      45

cac gat act aag cgg ccc tca ggg atc cct gag cga ttc tct ggt acc      192
His Asp Thr Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Thr
50      55      60

aac tct ggg aac aca gcc act ctg acc atc agc ggg acc cag att ctg      240
Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ile Leu
65      70      75      80

gat gag gcc gac tat tac tgt cag gtg tgg gac agg agc act gtg gtt      288
Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Arg Ser Thr Val Val
85      90      95

ttc ggc gga ggg acc cag ctc acc gtt tta agt gcg gcc gca ggc cag      336
Phe Gly Gly Gly Thr Gln Leu Thr Val Leu Ser Ala Ala Ala Gly Gln
100     105     110

ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc tcc tcc gag gag      384
Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
115     120     125

ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc agc gac ttc tac      432
Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
130     135     140

cct ggc gcc gtg acc gtg gcc tgg aag gcc gac agc agc ccc gtg aag      480
Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145     150     155     160

gcc ggc gtg gag acc acc acc ccc agc aag cag agc aac aac aag tac      528
Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
165     170     175

gcc gcc agc agc tac ctg agc ctc acc ccc gag cag tgg aag agc cac      576
Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
180     185     190

cgg agc tac agc tgc cag gtg acc cac gag ggc agc acc gtg gag aag      624
Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
195     200     205

acc gtg gcc ccc acc gag tgc agc                                648
Thr Val Ala Pro Thr Glu Cys Ser
210     215

```

<210> 179

<211> 216

<212> PRT

<213> Homo sapiens

<400> 179

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Gln Ser Val Leu Thr Gln Pro Pro Ser Leu Ser Val Ser Pro Gly Gln
1      5      10      15

Thr Ala Ser Ile Ser Cys Ser Gly Asp Lys Leu Gly Asp Lys Tyr Val
20      25      30

Ser Trp Tyr Gln Gln Arg Pro Gly Gln Ser Pro Val Leu Val Ile Tyr
35      40      45

His Asp Thr Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Thr
50      55      60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ile Leu
65      70      75      80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Arg Ser Thr Val Val
85      90      95

Phe Gly Gly Gly Thr Gln Leu Thr Val Leu Ser Ala Ala Ala Gly Gln
100     105     110

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

```

```

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

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145                      150                      155                      160

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

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
180                      185                      190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
195                      200                      205

Thr Val Ala Pro Thr Clu Cys Ser
210                      215

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<210> 180

<211> 642

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(642)

<223>

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<400> 180
gaa att gtg ttg acg cag tct cca ggc acc ctg tct ttg tct cca ggg      48
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1      5      10      15

gaa aqa gcc acc ctc tcc tgc agg gcc agt cag aqt gtt agc agc agc      96
Clu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20     25     30

tac tta gcc tgg tac cag cag aaa cct ggc cag gct ccc agg ctc ctc      144
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35     40     45

atc tat ggt gca tcc agc agg gcc act ggc atc cca gac agg ttc agt      192
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50     55     60

ggc agt ggg tct ggg aca gac ttc act ctc acc atc agc agc cta gag      240
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu
65     70     75     80

cct gaa gat ttt gca gtg tat tac tgt cag cag tat ggt agc tca tcg      288
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Ser
85     90     95

atc acc ttc ggc caa ggg aca cga ctg gag att aaa cgt gcc gcc gca      336
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Ala Ala Ala
100    105    110

ccc agc gtg ttc atc ttc ccc ccc tcc gac gag cag ctg aag agc ggc      384
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115    120    125

acc gcc agc gtg gtg tgc ctg ctg aac aac ttc tac ccc cgg gag gcc      432
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130    135    140

aag gtg cag tgg aag gtg gac aac gcc ctg cag agc gcc aac agc cag      480
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145    150    155    160

gag agc gtg acc gag cag gac agc aag gac tcc acc tac agc ctg agc      528
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165    170    175

agc acc ctc acc ctg agc aag gcc gac tac gag aag cac aag gtg tac      576
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180    185    190

gcc tgc gag gtg acc cac cag gcc ctg agc agc ccc gtg acc aag agc      624
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195    200    205

ttc aac cgg gcc gag tgt
Phe Asn Arg Gly Glu Cys
210

```

<210> 181

<211> 214

<212> PRT

<213> Homo sapiens

<400> 181

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

<210> 182

<211> 657

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(657)

<223>

<400> 182

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gac atc cag ttg acc cag tct cca gac tcc ctg gct gtg tct ctg ggc      48
Asp Ile Gln Leu Thr Cln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1      5      10      15

gag agg gcc acc atc aac tgc aag tcc agc cag agt ctt tta tac acc      96
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Tyr Thr
20     25     30

tcc aat aat aag aac ttc tta gct tgg tac caa caa aaa cca gga cag      144
Ser Asn Asn Lys Asn Phe Leu Ala Trp Tyr Cln Cln Lys Pro Gly Cln
35     40     45

cct cct aaa ctg ctc att tac tgg gta tct acc cgg gat tcc ggg gtc      192
Pro Pro Lys Leu Leu Ile Tyr Trp Val Ser Thr Arg Asp Ser Gly Val
50     55     60

cct gac cga ttc agt ggc agc ggg tct ggg aca gat ttc act ctc acc      240
Pro Asp Arg Phe Ser Cln Ser Cln Ser Cln Thr Asp Phe Thr Leu Thr
65     70     75     80

atc agc agc ctg cag gct gag gat gtg gca gtt tat tac tgt cag caa      288
Ile Ser Ser Leu Cln Ala Cln Asp Val Ala Val Tyr Tyr Cys Cln Cln
85     90     95

tat tat act act cgg tac act ttt ggc cag ggg acc aag gtg gag atc      336
Tyr Tyr Thr Thr Pro Tyr Thr Phe Gly Cln Cln Thr Lys Val Glu Ile
100    105    110

aaa cgt ggg gcc gca ccc agc gtg ttc atc ttc ccc ccc tcc gac gag      384
Lys Arg Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115    120    125

cag ctg aag agc ggc acc gcc agc gtg gtg tgc ctg ctg aac aac ttc      432
Gln Leu Lys Ser Cln Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130    135    140

tac ccc cgg gag gcc aag gtg cag tgg aag gtg gac aac gcc ctg cag      480
Tyr Pro Arg Cln Ala Lys Val Cln Trp Lys Val Asp Asn Ala Leu Cln
145    150    155    160

agc ggc aac agc cag gag agc gtg acc gag cag gac agc aag gac tcc      528
Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165    170    175

acc tac agc ctg agc agc acc ctc acc ctg agc aag gcc gac tac gag      576
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180    185    190

aag cac aag gtg tac gcc tgc gag gtg acc cac cag ggc ctg agc agc      624
Lys His Lys Val Tyr Ala Cys Cln Val Thr His Cln Gly Leu Ser Ser
195    200    205

ccc gtg acc aag agc ttc aac cgg ggc gag tgt      657
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210    215

```

<210> 183

<211> 219

<212> PRT

<213> Homo sapiens

<400> 183

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

210 215

<210> 184
 <211> 663
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)..(663)
 <223>

<400> 184

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cag tct gtg ttg acg cag ccg ccc tca gtg tct ggg gcc ccg ggg cag    48
Gln Ser Val Leu Thr Cln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1      5      10      15

agg gtc acc atc tcc tgc act ggg agc agc tcc aac atc ggg gca ggt    96
Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
      20      25      30

tat gat gta cac tgg tac cag cag ctt cca gga aca gcc ccc aaa ctc    144
Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
      35      40      45

ctc atc tat ggt aac agc aat cgg ccc tca ggg gtc cct gac cga ttt    192
Leu Ile Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
      50      55      60

tct ggc tcc aag tct ggc acc tca gcc tcc ctg gcc atc agt ggg ctc    240
Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu
      65      70      75      80

cgg tcc ggg gat gag gct gat tat tac tgc cag tcc tat gac agc agc    288
Arg Ser Gly Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
      85      90      95

ctg agt gat gtg gta ttc ggc gga ggg acc aag ctg acc gtc cta ggt    336
Leu Ser Asp Val Val Phe Gly Gly Thr Lys Leu Thr Val Leu Gly
      100      105      110

gcg gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc    384
Ala Ala Ala Gly Cln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro
      115      120      125

ccc tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc    432
Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu
      130      135      140

atc agc gac ttc tac cct ggc gcc gtg acc gtg gcc tgg aag gcc gac    480
Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp
      145      150      155      160

agc agc ccc gtg aag gcc ggc gtg gag acc acc acc ccc agc aag cag    528
Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Cln
      165      170      175

agc aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag    576
Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu
      180      185      190

cag tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc    624
Cln Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly
      195      200      205

agc acc gtg gag aag acc gtg gcc ccc acc gag tgc agc    663
Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
      210      215      220

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<210> 185

<211> 221

<212> PRT

<213> Homo sapiens

<400> 185

```

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1      5      10      15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
      20      25      30

Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
      35      40      45

Leu Ile Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
      50      55      60

Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu
      65      70      75      80

Arg Ser Gly Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
      85      90      95

Leu Ser Asp Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
      100      105      110

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

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

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```

130          135          140
Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp
145          150          155          160

Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln
165          170          175

Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu
180          185          190

Gln Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly
195          200          205

Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210          215          220

```

<210> 186

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 186

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cag tct gcc ctg act cag cct gcc tcc gtg tct ggg tgg cct gga cag      48
Gln Ser Ala Leu Thr Cln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1          5          10          15

acg atc acc atc tcc tgc tct gga acc agc agt gac gtt ggt ggt tat      96
Thr Ile Thr Ile Ser Cys Ser Gly Thr Ser Ser Asp Val Gly Gly Tyr
20          25          30

aac tat gtc tcc tgg tac caa caa cac cca ggc aaa gcc ccc aaa ctc     144
Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35          40          45

atg att tat gat gtc agt aaa cgg ccc tca ggg gtt tct aat cgc ttc     192
Met Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50          55          60

tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc tct ggg ctc     240
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65          70          75          80

cag gct gag gac gag gct gat tat tac tgc agt tca tct aca cgc agc     288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Ser Thr Arg Ser
85          90          95

agc act ctg gta ttc gcc gga ggg acc aag ctg acc gtc cta ggt gcg     336
Ser Thr Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100         105         110

gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc     384
Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115         120         125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc     432
Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130         135         140

agc gac ttc tac cct ggc gcc gtg acc gtg gcc tgg aag gcc gac agc     480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145         150         155         160

agc ccc gtg aag gcc ggc gtg gag acc acc acc ccc agc aag cag agc     528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165         170         175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag     576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180         185         190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc     624
Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195         200         205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc                       660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210         215         220

```

<210> 187

<211> 220

<212> PRT

<213> Homo sapiens

<400> 187

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

<210> 188

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 188

cag tct gcc ctg act cag cct ccc tcc gcg tcc ggg tct cct gga cag Gln Ser Ala Leu Thr Cln Pro Pro Ser Ala Ser Cly Ser Pro Cly Gln 1 5 10 15	48
tca gtc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr 20 25 30	96
gac tat gtc tcc tgg tac caa caa cac cca ggc aaa gcc ccc aaa ctc Asp Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu 35 40 45	144
atg att tat gat gtc agt aag cgg ccc tca ggg gtc cct gat cgc ttc Met Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe 50 55 60	192
tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc tct ggg ctc Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu 65 70 75 80	240
cag gct gag gat gag gct gat tat tac tgc agc tca tat gca agc aat Cln Ala Glu Asp Clu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Ser Asn 85 90 95	288
agg gat gtg ctt ttc gcc gga ggg acc aag ctg acc gtc cta ggt gcg Arg Asp Val Leu Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala 100 105 110	336
gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro 115 120 125	384
tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile 130 135 140	432
agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser 145 150 155 160	480
agc ccc gtg aag gcc gcc gtg gag acc acc ccc agc aag cag agc Ser Pro Val Lys Ala Gly Val Glu Thr Thr Pro Ser Lys Cln Ser 165 170 175	528
aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln 180 185 190	576
tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc Trp Lys Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Glu Gly Ser 195 200 205	624
acc gtg gag aag acc gtg gcc ccc acc gag tgc agc Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser 210 215 220	660

<210> 189

<211> 220

<212> PRT

<213> Homo sapiens

<400> 189

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

<210> 190

<211> 654

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(654)

<223>

<400> 190

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tct tct gag ctg act cag gac cct gct gag tct gtg gcc ttg gga cag      48
Ser Ser Glu Leu Thr Cln Asp Pro Ala Glu Ser Val Ala Leu Gly Gln
1      5      10      15

aca gtc aag atc aca tgc caa gga gac agt ctc aga agg tat tat gca      96
Thr Val Lys Ile Thr Cys Cln Gly Asp Ser Leu Arg Arg Tyr Tyr Ala
20      25      30

agt tgg tac cag cag aag cca gga cag gcc cct gtt ctt gtc atc tat      144
Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35      40      45

ggc aaa aac aac cgg ccc tca ggg atc cca gac cga ttc tct ggc tcc      192
Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50      55      60

agg tca gga aac aca gct tcc ttg acc ata act ggg gct cag gcg gaa      240
Arg Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65      70      75      80

gat gag gct gtc tat tac tgt aac tcc cgg gac agc agt ggt aac tct      288
Asp Glu Ala Val Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn Ser
85      90      95

gtg gtc ttc ggc gga ggg acc aag ctg acc gtc cta ggt gcg gcc gca      336
Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala Ala Ala
100      105      110

ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc tcc tcc      384
Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
115      120      125

gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc agc gac      432
Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
130      135      140

ttc tac cct ggc gcc gtg acc gtg gcc tgg aag gcc gac agc agc ccc      480
Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
145      150      155      160

gtg aag gcc ggc gtg gag acc acc acc ccc agc aag cag agc aac aac      528

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
165      170      175

aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag tgg aag      576
Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
180      185      190

agc cac cgg agc tac agc tgc cag gtg acc cac gag ggc agc acc gtg      624
Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Cln Gly Ser Thr Val
195      200      205

gag aag acc gtg gcc ccc acc gag tgc agc      654
Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210      215

```

<210> 191

<211> 218

<212> PRT

<213> Homo sapiens

<400> 191

```

Ser Ser Glu Leu Thr Gln Asp Pro Ala Glu Ser Val Ala Leu Gly Gln
1      5      10      15

Thr Val Lys Ile Thr Cys Gln Gly Asp Ser Leu Arg Arg Tyr Tyr Ala
20      25      30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35      40      45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50      55      60

Arg Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Cln Ala Glu
65      70      75      80

Asp Glu Ala Val Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn Ser
85      90      95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala Ala Ala
100      105      110

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

Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
130      135      140

```

```

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
145              150              155              160

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
              165              170              175

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
              180              185              190

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
              195              200              205

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210              215

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<210> 192

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 192

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cag tct gcc ctg act cag cct gcc tcc gtg tct ggg tct cct gga cag      48
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1              5              10              15

tcg atc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat      96
Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
              20              25              30

aac tat gtc tcc tgg tac caa cag cac cca ggc aaa gcc ccc aaa ctc      144
Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
              35              40              45

atg att tat gat gtc att aag cgg ccc tca ggg gtc cct gat cgc ttc      192
Met Ile Tyr Asp Val Ile Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
              50              55              60

tct gcc tcc aag tct gcc aac acg gcc tcc ctg acc atc tct ggg ctc      240
Ser Gly Ser Lys Ser Gln Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
              65              70              75              80

cag gct gag gat gag gct gat tat tac tgc agc tca tat gca ggc agc      288

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
              85              90              95

aac aat gtg gta ttc gcc gga ggg acc aag ctg acc gtc cta ggt gcg      336
Asn Asn Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
              100              105              110

gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc      384
Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
              115              120              125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc      432
Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
              130              135              140

agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
              145              150              155              160

agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
              165              170              175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
              180              185              190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc      624
Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
              195              200              205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
              210              215              220

```

<210> 193

<211> 220

<212> PRT

<213> Homo sapiens

<400> 193

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

<210> 194
<211> 660
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(660)
<223>

<400> 194
cag tct gcc ctg act cag cct ccc tcc gcg tcc ggg tct cct gga cag 48

Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln	
1 5 10 15	
tca gtc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat	96
Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr	
20 25 30	
aac tat gtc tcc tgg tac caa caa cac cca ggc aaa gcc ccc aaa ctc	144
Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu	
35 40 45	
atg att tat gat gtc agt aag cgg ccc tca ggg gtc cct gat cgc ttc	192
Met Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe	
50 55 60	
tct gcc tcc aag tct gcc aac acg gcc tcc ctg acc gtc tct ggg ctc	240
Ser Gly Ser Lys Ser Cys Asn Thr Ala Ser Leu Thr Val Ser Gly Leu	
65 70 75 80	
cag tct gag gat gag gct gat tat tac tgc agc tca tat gca ggc agc	288
Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser	
85 90 95	
acc ggt tat gtc ttc gga act ggg acc aag gtc acc gtc cta ggt gcg	336
Thr Gly Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala	
100 105 110	
gcc gca gcc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc	384
Ala Ala Gly Cln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro	
115 120 125	
tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc	432
Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile	
130 135 140	
agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc	480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser	
145 150 155 160	
agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc	528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser	
165 170 175	
aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag	576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln	
180 185 190	
tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc	624
Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser	
195 200 205	
acc gtg gag aag acc gtg gcc ccc acc gag tgc agc	660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser	
210 215 220	

<210> 195

<211> 220

<212> PRT

<213> Homo sapiens

<400> 195

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

- <210> 196
- <211> 660
- <212> DNA
- <213> Homo sapiens
- <220>
- <221> CDS
- <222> (1)..(660)
- <223>
- <400> 196

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cag tct gtg ttg acg cag ccg ccc tcc gcg tcc ggg tct cct gga cag      48
Gln Ser Val Leu Thr Cln Pro Pro Ser Ala Ser Gly Ser Pro Gly Cln
1      5      10      15

tca gtc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat      96
Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
      20      25      30

aac tat gtc tcc tgg tac caa caa cac cca ggc aaa gcc ccc aaa ctc      144
Asn Tyr Val Ser Trp Tyr Cln Cln His Pro Gly Lys Ala Pro Lys Leu
      35      40      45

atg att tat gag gtc act agg cgg ccc tca ggg gtc tct tat cgc ttc      192
Met Ile Tyr Glu Val Thr Arg Arg Pro Ser Gly Val Ser Tyr Arg Phe
      50      55      60

tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc gtc tct ggg ctc      240
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
      65      70      75      80

cag gct gag gat gag gct gat tat tac tgc agc tca tat gca ggc agc      288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
      85      90      95

aac aat ttg gtc ttc gcc gga ggg acc aag ctg acc gtc cta ggt gcg      336
Asn Asn Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
      100      105      110

gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc      384
Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
      115      120      125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc      432
Ser Ser Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
      130      135      140

agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
      145      150      155      160

agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Cln Val Cln Thr Thr Thr Pro Ser Lys Cln Ser
      165      170      175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
      180      185      190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc      624
Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
      195      200      205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
      210      215      220

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<210> 197

<211> 220

<212> PRT

<213> Homo sapiens

<400> 197

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Cln Ser Val Leu Thr Cln Pro Pro Ser Ala Ser Gly Ser Pro Gly Cln
1      5      10      15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
      20      25      30

Asn Tyr Val Ser Trp Tyr Cln Cln His Pro Gly Lys Ala Pro Lys Leu
      35      40      45

Met Ile Tyr Glu Val Thr Arg Arg Pro Ser Gly Val Ser Tyr Arg Phe
      50      55      60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
      65      70      75      80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
      85      90      95

Asn Asn Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
      100      105      110

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

Ser Ser Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
      130      135      140

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Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145                      150                      155                      160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
                      165                      170                      175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180                      185                      190

Trp Lys Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Cln Cln Ser
195                      200                      205

Thr Val Glu Lys Thr Val Ala Pro Thr Cln Cys Ser
210                      215                      220

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<210> 198

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 198

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cag tct gtc gtg acg cag ccg ccc tca gtg tct gcg gcc cca gga cag      48
Gln Ser Val Val Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln
1      5      10      15

aag gtc acc atc tcc tgc tct gga agc agc tcc aac att ggg aat aat      96
Lys Val Thr Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asn
      20      25      30

tat gta tcc tgg tac caa cag ctc cca gga aca gcc ccc aaa ctc ctc      144
Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
      35      40      45

att tat gac aat aat aag cga ccc tca ggg att cct gac cga ttc tct      192
Ile Tyr Asp Asn Asn Lys Arg Pro Ser Cln Ile Pro Asp Arg Phe Ser
      50      55      60

ggc tcc aag tct ggc acg tca gcc acc ctg ggc atc acc gga ctc cag      240
Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
      65      70      75      80

act ggg gac gag gcc gat tat tac tgc gga aca tgg gag agc agc ctg      288
Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Trp Glu Ser Ser Leu
      85      90      95

agt gct gtg gta ttc ggc gga ggg acc aag ctg acc gtc cta ggt gog      336
Ser Ala Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
      100      105      110

gcc gca gcc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc      384
Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
      115      120      125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc      432
Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
      130      135      140

agc gac ttc tac cct ggc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
      145      150      155      160

agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
      165      170      175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag caa      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
      180      185      190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc      624
Trp Lys Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Cln Gly Ser
      195      200      205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      660
Thr Val Glu Lys Thr Val Ala Pro Thr Cln Cys Ser
      210      215      220

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<210> 199

<211> 220

<212> PRT

<213> Homo sapiens

<400> 199

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

<210> 200

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 200

cag tct gcc ctg act cag cct gcc tcc gtg tct ggg tct cct gga cag 48
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln

1	5	10	15	
tcg atc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat				96
Ser Ile Thr 20	Ile Ser Cys Thr 25	Thr Ser Ser Asp 30	Val Gly Gly Tyr	
aac tat gtc tcc tgg tac caa cac cac cca ggc aaa gcc ccc aaa ctc				144
Asn Tyr Val Ser Trp Tyr 35	Gln His His Pro Gly 40	Lys Ala Pro Lys Leu 45		
atg att tat gat gtc agt gat cgg ccc tca ggg gtt tct aat cgc ttc				192
Met Ile Tyr Asp Val Ser Asp Arg Pro Ser Gly Val Ser Asn Arg Phe 50				
tct ggc tcc aag tct ggc aac gcg gcc tcc ctg acc atc tct ggg ctc				240
Ser Gly Ser Lys Ser Gly Asn Ala Ala Ser Leu Thr Ile Ser Gly Leu 65				
cag gct gag gac gag gct gat tat tac tgc agc tca tat gca ggc agc				288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser 85				
aac aat ttg gtc ttc gga act ggg acc aag gtc acc gtc cta ggt gcg				336
Asn Asn Leu Val Phe Cys Thr Cys Thr Lys Val Thr Val Leu Cys Ala 100				
gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc				384
Ala Ala Gly Cln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro 115				
tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc				432
Ser Ser Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile 130				
agc gac ttc tac cct ggc gcc gtg acc gtg gcc tgg aag gcc gac agc				480
Ser Asp Phe Tyr Pro Cys Ala Val Thr Val Ala Trp Lys Ala Asp Ser 145				
agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc				528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Cln Ser 165				
aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag				576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Cln 180				
tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag ggc agc				624
Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser 195				
acc gtg gag aag acc gtg gcc ccc acc gag tgc agc				660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser 210				

<210> 201

<211> 220

<212> PRT

<213> Homo sapiens

<400> 201

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

<210> 202

<211> 639

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(639)

<223>

<400> 202

gac atc cag atg acc cag tct cca tct tcc gtg tct gca tct gta gga 48
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 1 5 10 15
 gac aga gtc acc atc act tgt cgg gcg agt cag gga att agc agc agg 96
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Arg
 20 25 30
 tta gcc tgg tat cag cag aaa cca ggg aaa gcc cct aag ctc ctg atc 144
 Leu Ala Trp Tyr Cln Cln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45
 tat gct gca tcc agt ttg caa agt ggg gtc cca tca agg ttc agc ggc 192
 Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct 240
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80
 gaa gat ttt gga act tcc tat tgt caa cag gct aag aat ttc cct cgg 288
 Glu Asp Phe Gly Thr Tyr Tyr Cys Gln Gln Ala Lys Asn Phe Pro Arg
 85 90 95
 acc ttc gcc caa ggg aca cga ctg gag att aaa cgt gcg gcc gca ccc 336
 Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Ala Ala Ala Pro
 100 105 110
 agc gtg ttc atc ttc ccc ccc tcc gac gag cag ctg aag agc ggc acc 384
 Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
 115 120 125
 gcc agc gtg gtg tgc ctg ctg aac aac ttc tac ccc cgg gag gcc aag 432
 Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
 130 135 140
 gtg cag tgg aag gtg gac aac gcc ctg cag agc ggc aac agc cag gag 480
 Val Cln Trp Lys Val Asp Asn Ala Leu Cln Ser Gly Asn Ser Cln Glu
 145 150 155 160
 agc gtg acc gag cag gac agc aag gac tcc acc tac agc ctg agc agc 528
 Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
 165 170 175
 acc ctc acc ctg agc aag gcc gac tac gag aag cac aag gtg tac gcc 576
 Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
 180 185 190
 tgc gag gtg acc cac cag gcc ctg agc agc ccc gtg acc aag agc ttc 624
 Cys Glu Val Thr His Cln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
 195 200 205
 aac cgg gcc gag tgt 639
 Asn Arg Gly Glu Cys
 210

<210> 203

<211> 213

<212> PRT

<213> Homo sapiens

<400> 203

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

Ser Val Thr Clu Cln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

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

Asn Arg Gly Glu Cys
210

<210> 204

<211> 642

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(642)

<223>

<400> 204

gaa att gtg ttg acg cag tct cca gcc acc ctg tct ttg tct cca ggg Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly 1 5 10 15	48
gaa aga gcc acc ctg tcc tgc agg gcc agt cag agt gtt agc agc aac Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Cln Ser Val Ser Ser Asn 20 25 30	96
tac tta gcc tgg tac cag cag aaa cct gcc cag gct ccc agg ctg ctg Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu 35 40 45	144
gtc tat ggt gca tcc agc agg gcc act gcc atc cca gac agg ttc agt Val Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser 50 55 60	192
ggc agt ggg tct ggg aca gac ttc act ctg acc atc agc aga ctg gag Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu 65 70 75 80	240
cct gaa gat ttt gca gtg tat cac tgt cag cag tat gct gcc tca ccc Pro Glu Asp Phe Ala Val Tyr His Cys Gln Gln Tyr Ala Gly Ser Pro 85 90 95	288
tgg acg ttc gcc caa ggg acc aag gtg gag atc aaa cgt gcg gcc gca Trp Thr Phe Gly Cln Gly Thr Lys Val Glu Ile Lys Arg Ala Ala Ala 100 105 110	336
ccc agc gtg ttc atc ttc ccc ccc tcc gac gag cag ctg aag agc ggc Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 115 120 125	384
acc gcc agc gtg gtg tgc ctg ctg aac aac ttc tac ccc cgg gag gcc Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140	432
aag gtg cag tgg aag gtg gac aac gcc ctg cag agc gcc aac agc cag Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 155 160	480
gag agc gtg acc gag cag gac agc aag gac tcc acc tac agc ctg agc Glu Ser Val Thr Glu Cln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 175	528
agc acc ctg acc ctg agc aag gcc gac tac gag aag cac aag gtg tac Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190	576
gcc tgc gag gtg acc cac cag gcc ctg agc agc ccc gtg acc aag agc Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205	624
ttc aac cgg gcc gag tgt Phe Asn Arg Gly Glu Cys 210	642

<210> 205

<211> 214

<212> PRT

<213> Homo sapiens

<400> 205

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

<210> 206
<211> 660
<212> DNA
<213> Homo sapiens

<220>
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<222> (1)..(660)
<223>

<400> 206
caa tct gcc ctg act cag cct ccc tcc gcg tcc ggg tct cct gga cag 48
Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

tca gtc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr 20 25 30	96
aac tat gtc tcc tgg tac caa cag cac cca ggc aaa gcc ccc aaa ctc Asn Tyr Val Ser Trp Tyr Cln Cln His Pro Gly Lys Ala Pro Lys Leu 35 40 45	144
atg att tat gag gtc agt aag cgg ccc tca ggg gtc cct gat cgc ttc Met Ile Tyr Glu Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe 50 55 60	192
tct gcc tcc aag tct gcc aac acg gcc tcc ctg acc gtc tct ggg ctc Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu 65 70 75 80	240
cag gct gag gat gag gct gat tat tac tgc agc tca tat gca gcc agc Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser 85 90 95	288
aac aat ttg gta ttc gcc gga ggg acc aag ctg acc gtc cta ggt gcg Asn Asn Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala 100 105 110	336
gcc gca gcc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro 115 120 125	384
tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile 130 135 140	432
agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser 145 150 155 160	480
agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser 165 170 175	528
aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln 180 185 190	576
tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser 195 200 205	624
acc gtg gag aag acc gtg gcc ccc acc gag tgc agc Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser 210 215 220	660

<210> 207

<211> 220

<212> PRT

<213> Homo sapiens

<400> 207

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

<210> 208

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 208

cag tct gcc ctg act cag cct cgc tca gtg tcc ggg tct cct gga cag Gln Ser Ala Leu Thr Cln Pro Arg Ser Val Ser Cln Ser Pro Cln Gln 1 5 10 15	48
tca gtc acc atc tcc tgc act gga acc agc agt gat att ggt ggt tat Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Ile Gly Gly Tyr 20 25 30	96
aac ttt gtc tcc tgg tac caa caa cac cca ggc aaa gcc ccc aaa ctc Asn Phe Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu 35 40 45	144
atg att tat gat gtc agt aat cgg ccc tca ggg gtt tct aat cgc ttc Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe 50 55 60	192
tct ggc tcc aag tct ggc aaa atg gcc tcc ctg acc atc tct ggg ctc Ser Gly Ser Lys Ser Gly Lys Met Ala Ser Leu Thr Ile Ser Cln Leu 65 70 75 80	240
cag gct gag gac gag gct gat tac tac tgc gcc tca tat aca agc aga Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Tyr Thr Ser Arg 85 90 95	288
agc act ctc gtc ttc gga act ggg acc aag gtc acc gtc cta ggt gcg Ser Thr Leu Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala 100 105 110	336
gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro 115 120 125	384
tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile 130 135 140	432
agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser 145 150 155 160	480
agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc Ser Pro Val Lys Ala Cln Val Cln Thr Thr Thr Pro Ser Lys Cln Ser 165 170 175	528
aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln 180 185 190	576
tgq aag agc cac cgg agc tac agc tgc caq gtg acc cac gag gcc agc Trp Lys Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Cln Gly Ser 195 200 205	624
acc gtg gag aag acc gtg gcc ccc acc gag tgc agc Thr Val Cln Lys Thr Val Ala Pro Thr Cln Cys Ser 210 215 220	660

<210> 209

<211> 220

<212> PRT

<213> Homo sapiens

<400> 209

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

<210> 210

<211> 639

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(639)

<223>

<400> 210

gac atc cag atg acc cag tct cca tcc tcc ctg tct gca tct gta gga	48
Asp ile Cln Met Thr Cln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly	
1 5 10 15	
gac aga gtc acc atc act tgc cgg gca agt cag agc att agc agc tat	96
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr	
20 25 30	
tta aat tgg tat cag cag aaa cca ggg aaa gcc cct aag ctc ctg atc	144
Leu Asn Trp Tyr Cln Cln Lys Pro Cys Lys Ala Pro Lys Leu Leu Ile	
35 40 45	
tat gct gca tcc agt ttg caa agt ggg gtc cca tca agg ttt agc ggc	192
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	
agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct	240
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro	
65 70 75 80	
gaa gat ttt gca act tac tat tgt caa cag gct aac agt ttc ccg ctc	288
Glu Asp Phe Ala Thr Tyr Tyr Cys Cln Cln Ala Asn Ser Phe Pro Leu	
85 90 95	
act ttc ggc gga ggg acc aag gtg gaa atc aaa cgt gcg gcc gca ccc	336
Thr Phe Gly Gly Cys Thr Lys Val Clu ile Lys Arg Ala Ala Ala Pro	

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100          105          110
agc gtg ttc atc ttc ccc ccc tcc gac gag cag ctg aag agc ggc acc 384
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115          120          125

gcc agc gtg gtg tgc ctg ctg aac aac ttc tac ccc cgg gag gcc aag 432
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130          135          140

gtg cag tgg aag gtg gac aac gcc ctg cag agc ggc aac agc cag gag 480
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145          150          155          160

agc gtg acc gag cag gac agc aag gac tcc acc tac agc ctg agc agc 528
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165          170          175

acc ctc acc ctg agc aag gcc gac tac gag aag cac aag gtg tac gcc 576
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180          185          190

tgc gag gtg acc cac cag gcc ctg agc agc ccc gtg acc aag agc ttc 624
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195          200          205

aac cgg gcc gag tgt 639
Asn Arg Gly Glu Cys
210

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<210> 211

<211> 213

<212> PRT

<213> Homo sapiens

<400> 211

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Asp Ile Cln Met Thr Cln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1      5      10      15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20     25     30

Leu Asn Trp Tyr Cln Cln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35     40     45

Tyr Ala Ala Ser Ser Leu Cln Ser Gly Val Pro Ser Arg Phe Ser Gly
50     55     60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Cln Pro
65     70     75     80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Leu
85     90     95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Ala Ala Ala Pro
100    105    110

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

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130    135    140

Val Gln Trp Lys Val Asp Asn Ala Leu Cln Ser Gly Asn Ser Cln Glu
145    150    155    160

Ser Val Thr Glu Cln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165    170    175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180    185    190

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

Asn Arg Gly Glu Cys
210

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<210> 212

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 212

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cag tct gcc ctg act cag cct ccc tcc gcg tcc ggg tct cct gga cag      48
Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1      5      10      15

tca gtc acc atc tcc tgc act gga acc agc agt gat gtt ggt ggt tat      96
Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr

                20                25                30

aac tat gtc tcc tgg tac caa cac ccc cca ggc aaa gcc ccc aaa ctc      144
Asn Tyr Val Ser Trp Tyr Gln His His Pro Gly Lys Ala Pro Lys Leu
35      40      45

atg att tat gat gtc agt aat cgg ccc tca ggg gtt tct aat cgc ttc      192
Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50      55      60

tct ggc tcc aag tct gcc aac acg gcc tcc ctg acc atc tct ggg ctc      240
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65      70      75      80

cag gct gag gac gag gct gat tat tac tgc agc tca tat aca agc agc      288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85      90      95

agc act ctt gtc ttc gga act ggg acc aag gtc acc gtc cta ggt gcg      336
Ser Thr Leu Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
100     105     110

gcc gca gcc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc      384
Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115     120     125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc      432
Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130     135     140

agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145     150     155     160

agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165     170     175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180     185     190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc      624
Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195     200     205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210     215     220

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<210> 213

<211> 220

<212> PRT

<213> Homo sapiens

<400> 213

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

<210> 214

<211> 663

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(663)

<223>

<400> 214

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cag tct gcc ctg act cag cct ccc tcc gcg tcc ggg tct cct gga cag      48
Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1      5      10      15

tca gtc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tac      96
Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20     25     30

aac tat gtc tcc tgg tac caa cag cgc cca ggc aaa gcc ccc aaa ctc      144
Asn Tyr Val Ser Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Leu
35     40     45

atg att tat gat gtc agt aat cgg ccc tca ggg gtt tct gat cgc ttc      192
Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asp Arg Phe
50     55     60

tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc tct ggg ctc      240
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65     70     75     80

cag gct gaa gac gag gct gat tat tac tgc agc tca tat aca act ggc      288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Gly
85     90     95

agc act ctc gtg gtc ttc ggc qga ggg acc aag ctg acc gtc cta qgt      336
Ser Thr Leu Val Val Phe Gly Gly Thr Lys Leu Thr Val Leu Gly
100    105    110

gcg gcc gaa ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc      384
Ala Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro
115    120    125

ccc tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc      432
Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu
130    135    140

atc agc gac ttc tac cct ggc gcc gtg acc gtg gcc tgg aag gcc gac      480
Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp
145    150    155    160

agc agc ccc gtg aag gcc ggc gtg gag acc acc acc ccc agc aag cag      528
Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln
165    170    175

agc aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag      576
Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu
180    185    190

cag tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag ggc      624
Gln Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly
195    200    205

agc acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      663
Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210    215    220

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<210> 215

<211> 221

<212> PRT

<213> Homo sapiens

<400> 215

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

<210> 216

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 216

cag tct gcc ctg act cag cct ccc tcc gcg tcc ggg tct cct gga cag Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln 1 5 10 15	48
tca gtc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr 20 25 30	96
aac tat gtc tcc tgg tac caa cag cac cca ggc aaa gcc ccc aaa ctc Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu 35 40 45	144
atg att tat gag gtc agt aag cgg ccc tca ggg gtc cct gat cgc ttc Met Ile Tyr Glu Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe 50 55 60	192
tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc gtc tct ggg ctc Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu 65 70 75 80	240
cag gct gag gat gag gct gat tat tac tgc agc tca tat gga ggc agc Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Gly Gly Ser 85 90 95	288
aac aat gtg gta ttc gcc gga ggg acc aag ctg acc gtc cta ggt gcg Asn Asn Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala 100 105 110	336

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gcc gca ggc cag ecc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc      384
Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
      115      120      125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc      432
Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
      130      135      140

agc gac ttc tac cct ggc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
      145      150      155      160

agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
      165      170      175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
      180      185      190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc      624
Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
      195      200      205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
      210      215      220

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<210> 217

<211> 220

<212> PRT

<213> Homo sapiens

<400> 217

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Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1      5      10      15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20      25      30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35      40      45

Met Ile Tyr Glu Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50      55      60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65      70      75      80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Gly Gly Ser
85      90      95

Asn Asn Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100      105      110

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

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

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145      150      155      160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165      170      175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180      185      190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195      200      205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210      215      220

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<210> 218

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 218

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tgg atc acc atc tcc tgc act gga acc agc agt gac gtt ggt gct tat Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ala Tyr 20 25 30	96
aac tat gtc tcc tgg tac caa caa cac cca ggc aaa gcc ccc aaa ctc Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu 35 40 45	144
atg att tat gat gtc agt aat cgg ccc tca ggg gtt tct aat cgc ttc Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe 50 55 60	192
tct gcc tcc aag tct gcc aac acg gcc tcc ctg acc atc tct ggg ctc Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu 65 70 75 80	240
cag gct gag gac gag gct gat tat tac tgc agc tca tat gca ggc agc Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser 85 90 95	288
aac agt gtg gta ttc gcc gga ggg acc aag ctc acc gtc cta ggt gcg Asn Ser Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala 100 105 110	336
gcc gca gcc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro 115 120 125	384
tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile 130 135 140	432
agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser 145 150 155 160	480
agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser 165 170 175	528
aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln 180 185 190	576
tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser 195 200 205	624
acc gtg gag aag acc gtg gcc ccc acc gag tgc agc Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser 210 215 220	660

<210> 219

<211> 220

<212> PRT

<213> Homo sapiens

<400> 219

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln 1 5 10 15
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Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ala Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
85 90 95

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

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

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

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145 150 155 160

Ser Pro Val Lys Ala Gly Val Cln Thr Thr Thr Pro Ser Lys Cln Ser
165 170 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180 185 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195 200 205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215 220

<210> 220

<211> 639

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(639)

<223>

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<400> 220
gac atc caq ttg acc caq tct cca tct tcc gtg tct gca tct gta gga 48
Asp ile Gln leu thr Cln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

ggc aga gtc acc atc act tgt cgg gcg agt caq ggt att agc agc tgg 96
Gly Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
20 25 30

tta gcc tgg tat caq caq aga cca ggg aaa gcc cct aac ctc ctg atc 144
Leu Ala Trp Tyr Cln Cln Arg Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45

tat ggt gca tcc aac ttg caa agt ggg gtc ccc tca agg ttc agc ggc 192
Tyr Gly Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt ggg tct ggg aca gat ttc agt ctc acc atc agc agc ctg caa cct 240
Ser Gly Ser Gly Thr Asp Phe Ser Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

gaa gat ttt gca act tac tac tgt caa cag gct aag agt ttc cgg ctc 288
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Lys Ser Phe Pro Leu
85 90 95

act ttc gcc ggc ggg acc aag gtg gaa atc aaa cgt gcg gcc gca ccc 336
Thr Phe Gly Gly Cln Thr Lys Val Cln ile Lys Arg Ala Ala Ala Pro
100 105 110

agc gtg ttc atc ttc ccc ccc tcc gac gag cag ctg aag agc ggc acc 384
Ser Val Phe ile Phe Pro Pro Ser Asp Glu Gln leu Lys Ser Cln Thr
115 120 125

gcc agc gtg gtg tgc ctg ctg aac aac ttc tac ccc cgg gag gcc aag 432
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

gtg cag tgg aag gtg gac aac gcc ctg cag agc ggc aac agc cag gag 480
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

agc gtg acc gag cag gac agc aag gac tcc acc tac agc ctg agc agc 528
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser leu Ser Ser
165 170 175

acc ctc acc ctg agc aag gcc gac tac gag aag cac aag gtg tac gcc 576
Thr leu Thr leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

tgc gag gtg acc cac cag gcc ctg agc agc ccc gtg acc aag agc ttc 624
Cys Glu Val Thr His Gln Gly leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

aac cgg gcc gag tgt 639
Asn Arg Gly Glu Cys
210

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<210> 221

<211> 213

<212> PRT

<213> Homo sapiens

<400> 221

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

<210> 222

<211> 657

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(657)

<223>

<400> 222

gat gtt gtg atg act cag tct cca gac tcc ctg gct gtg tct ctg ggc	48
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly	
1 5 10 15	
gag agg gcc acc atc aac tgc aag tcc agc cag agt gtt ttt tac agc	96
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Phe Tyr Ser	
20 25 30	
tcc aac aat aag aac tac tta gct tgg tac cag cac aaa cca gga cag	144
Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln His Lys Pro Gly Gln	
35 40 45	
cct cct aag ttg ctc att tac tgg gca tct acc cgg caa tcc ggg gtc	192
Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Gln Ser Gly Val	
50 55 60	
cct gac cga ttc agt gcc agc ggg tct ggg aca gat ttc act ctc acc	240
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr	
65 70 75 80	
atc aac agc ctg cag gct gaa gat gtg gca gtt tat tac tgt cag caa	288
Ile Asn Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln	
85 90 95	
tat tat agt act cct ccc act ttc gcc gga ggg acc aag gtg gaa atc	336
Tyr Tyr Ser Thr Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile	
100 105 110	
aaa cgt gcg gcc gca ccc agc gtg ttc atc ttc ccc ccc tcc gac gag	384
Lys Arg Ala Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu	

115	120	125	
cag ctg aag agc gcc acc gcc agc gtg gtg tgc ctg ctg aac aac ttc			432
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe			
130	135	140	
tac ccc cgg gag gcc aag gtg cag tgg aag gtg gac aac gcc ctg cag			480
Tyr Pro Arg Clu Ala Lys Val Cln Trp Lys Val Asp Asn Ala Leu Cln			
145	150	155	160
agc gcc aac agc cag gag agc gtg acc gag cag gac agc aag gac tcc			528
Ser Cly Asn Ser Cln Clu Ser Val Thr Cln Cln Asp Ser Lys Asp Ser			
165	170	175	
acc tac agc ctg agc agc acc ctc acc ctg agc aag gcc gac tac gag			576
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu			
180	185	190	
aag cac aag gtg tac gcc tgc gag gtg acc cac cag gcc ctg agc agc			624
Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser			
195	200	205	
ccc gtg acc aag agc ttc aac cgg gcc gag tgt			657
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys			
210	215		

<210> 223

<211> 219

<212> PRT

<213> Homo sapiens

<400> 223

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

<210> 224

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 224

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cag tct gcc ctg act cag cct cgc tca gtg tcc ggg tct cct gga cag      48
Gln Ser Ala Leu Thr Cln Pro Arg Ser Val Ser Gly Ser Pro Gly Gln
1          5          10          15

gca gtc acc ctc tcc tgc aat gga acc agc agg gat gtt ggt ggt tat      96
Ala Val Thr Leu Ser Cys Asn Gly Thr Ser Arg Asp Val Gly Gly Tyr
20          25          30

aat tat gtc tcc tgg tac caa caa cac cca ggc aaa gcc ccc aaa ctc      144
Asn Tyr Val Ser Trp Tyr Cln Cln His Pro Gly Lys Ala Pro Lys Leu
35          40          45

atg att tat gat gtc act aag cgg ccc tca ggg gtc cct gat cgc ttc      192
Met Ile Tyr Asp Val Thr Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50          55          60

tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc tct gga ctc      240
Ser Gly Ser Lys Ser Cln Asn Thr Ala Ser Leu Thr Ile Ser Cln Leu
65          70          75          80

cag gct gag gat gag gct gat tat tac tgc aac tca tac gca ggc agc      288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Tyr Ala Gly Ser
85          90          95

aac act tgg gtg ttc ggc gga ggg acc aag ctg acc gtc cta ggt gcg      336
Asn Thr Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100         105         110

gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc      384
Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115         120         125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc      432
Ser Ser Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130         135         140

agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Cln Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145         150         155         160

agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165         170         175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180         185         190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc      624
Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195         200         205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210         215         220

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<210> 225

<211> 220

<212> PRT

<213> Homo sapiens

<400> 225

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Gln Ser Ala Leu Thr Gln Pro Arg Ser Val Ser Gly Ser Pro Gly Gln
1          5          10          15

```

Ala Val Thr Leu Ser Cys Asn Gly Thr Ser Arg Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Thr Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Tyr Ala Gly Ser
85 90 95

Asn Thr Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

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

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

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145 150 155 160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Cln Ser
165 170 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180 185 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Glu Gly Ser
195 200 205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215 220

<210> 226

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 226

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cag tct gcc ctg act cag cct ccc tcc gcg tcc ggg tct cct gga cag      48
Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1      5      10      15

tca gtc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat      96
Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20     25     30

aac tat gtc tcc tgg tac caa caa cac cca ggc aaa gcc ccc aaa ctc      144
Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35     40     45

atg att tat gat gtc agt aag cgg ccc tca ggg gtc cct gat cgc ttc      192
Met Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50     55     60

tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc gtc tct ggg ctc      240
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65     70     75     80

cag tct gag gat gag gct gat tat tac tgc agc tca tat gca ggc agc      288
Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
85     90     95

acc ggt tat gtc ttc gga act ggg acc aag gtc acc gtc cta ggt gcg      336
Thr Gly Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
100    105    110

gcc gca gcc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc      384
Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115    120    125

tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc atc      432
Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130    135    140

agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145    150    155    160

agc ccc gtg aag gcc gcc gtg gag acc acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Cln Ser
165    170    175

aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180    185    190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc agc      624
Trp Lys Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Glu Gly Ser
195    200    205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc      660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210    215    220

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<210> 227

<211> 220

<212> PRT

<213> Homo sapiens

<400> 227

Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65 70 75 80

Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
85 90 95

Thr Gly Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

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

Ser Ser Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130 135 140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145 150 155 160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165 170 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Cln
180 185 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195 200 205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215 220

<210> 228

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(660)

<223>

<400> 228

cag tct gcc ctg act cag cct ccc tcc gag tcc ggg tct cct gga cag Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln 1 5 10 15	48
tca gtc acc atc tcc tgc act gga acc agc agt gac gtt ggt ggt tat Ser Val Thr Ile Ser Cys Thr Cly Thr Ser Ser Asp Val Gly Gly Tyr 20 25 30	96
aac tat gtc tcc tgg tac caa caa tac cca ggc aaa gcc ccc aaa ctc Asn Tyr Val Ser Trp Tyr Gln Gln Tyr Pro Gly Lys Ala Pro Lys Leu 35 40 45	144
atg att tat gat gtc agt aat cgg ccc tca ggg gtt tct aat cgc ttc Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe 50 55 60	192
tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc tct ggg ctc Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu 65 70 75 80	240
cag gct gag gac gag gct gat tat tac tgc agc tca tat aca agc agc Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser 85 90 95	288
agc act ctt gtc ttc gga act ggg acc aag gtc acc gtc cta ggt gog Ser Thr Leu Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala 100 105 110	336
gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro 115 120 125	384

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tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc etc atc      432
Ser Ser Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130                      135                      140

agc gac ttc tac cct ggc gcc gtg acc gtg gcc tgg aag gcc gac agc      480
Ser Asp Phe Tyr Pro Cln Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145                      150                      155                      160

agc ccc gtg aag gcc ggc gtg gag acc acc acc ccc agc aag cag agc      528
Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Cln Ser
165                      170                      175

aac aac aag tac gcc gcc agc agc tac ctg agc etc acc ccc gag cag      576
Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Cln Cln
180                      185                      190

tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag ggc agc      624
Trp Lys Ser Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Glu Cln Ser
195                      200                      205

acc gtg gag aag acc gtg gcc ccc acc gag tgc agc                      660
Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210                      215                      220

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<210> 229

<211> 220

<212> PRT

<213> Homo sapiens

<400> 229

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Cln Ser Ala Leu Thr Cln Pro Pro Ser Ala Ser Gly Ser Pro Gly Cln
1                      5                      10                      15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20                      25                      30

Asn Tyr Val Ser Trp Tyr Cln Cln Tyr Pro Gly Lys Ala Pro Lys Leu
35                      40                      45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50                      55                      60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                      70                      75                      80

Cln Ala Cln Asp Cln Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85                      90                      95

Ser Thr Leu Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
100                     105                     110

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

Ser Ser Glu Glu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130                     135                     140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145                     150                     155                     160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Cln Ser
165                     170                     175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Cln Cln
180                     185                     190

Trp Lys Ser Ser His Arg Ser Tyr Ser Cys Cln Val Thr His Glu Gly Ser
195                     200                     205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210                     215                     220

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<210> 230

<211> 663

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(663)

<223>

<400> 230

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cag tct gcc ctg act cag cct ccc tcc ggc tcc ggg tct cct gga cag    48
Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1      5      10      15

tca gtc acc atc tcc tgc act gga acc agc agt gac att ggt ggt tat    96
Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Ile Gly Gly Tyr
20     25     30

aac tat gtc tcc tgg tac caa cag cac cca ggc aaa gcc ccc aaa ctc    144
Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35     40     45

atg att tat gag gtc agt aat cgg ccc cca ggg gtt tct aat cgc ttc    192
Met Ile Tyr Glu Val Ser Asn Arg Pro Pro Gly Val Ser Asn Arg Phe
50     55     60

tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc tct ggg ctc    240
Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65     70     75     80

cag gct gag gac gag gct gat tat tac tgc agc tca tac tca acc acc    288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ser Thr Thr
85     90     95

acc acc cga gtg ata ttc gcc gga ggg acc aag ctg acc gtc cta ggt    336
Thr Thr Arg Val Ile Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100    105    110

ggc gcc gca ggc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc    384
Ala Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro
115    120    125

ccc tcc tcc gag gag ctg cag gcc aac aag gcc acc ctg gtg tgc ctc    432
Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu
130    135    140

atc agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac    480
Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp
145    150    155    160

agc agc ccc gtg aag gcc ggc gtg gag acc acc acc ccc agc aag cag    528
Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln
165    170    175

agc aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag    576
Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu
180    185    190

cag tgg aag agc cac cgg agc tac agc tgc cag gtg acc cac gag gcc    624
Gln Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly
195    200    205

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85 90 95

Thr Thr Arg Val Ile Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

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

Pro Ser Ser Clu Clu Leu Cln Ala Asn Lys Ala Thr Leu Val Cys Leu
130 135 140

Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp
145 150 155 160

Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln
165 170 175

Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu
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gcc gca gcc cag ccc aag gcc gct ccc agc gtg acc ctg ttc ccc ccc Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro 115 120 125	384
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agc gac ttc tac cct gcc gcc gtg acc gtg gcc tgg aag gcc gac agc Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser 145 150 155 160	480
agc ccc gtg aag gcc gcc gtg gag acc acc ccc agc aag cag agc Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Cln Ser 165 170 175	528
aac aac aag tac gcc gcc agc agc tac ctg agc ctc acc ccc gag cag Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln 180 185 190	576
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acc gtg gag aag acc gtg gcc ccc acc gag tgc agc Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser	660

210 215 220

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Ile Tyr Glu Asn Asn Lys Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Asp Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Ala Trp Asp Gly Ser Leu
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130 135 140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
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Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
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Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
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85     90     95

agc act ctc gta ttc ggc gga ggg acc aag ctg acc gtc cta ggt gcg      336
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100    105    110

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115    120    125

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Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
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Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
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Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
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Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
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Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
 210 215 220

REFERENCES CITED IN THE DESCRIPTION

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Patentkrav

1. Humant monoklonalt antistof, der binder specifikt til og har opsonisk fagocytisk dræberaktivitet mod mindst to forskellige Staphylococcus-arter og mod mindst 3 forskellige stammer af Staphylococcus aureus, der er kendetegnet ved, at antistoffet er et antistof med en tung kæde, der omfatter den variable region ifølge SEQ ID NO: 30, og en let kæde, der omfatter den variable region ifølge SEQ ID NO: 36.

2. Humant monoklonalt antistof ifølge krav 1, der er kendetegnet ved, at det har den opsoniske fagocytiske dræberaktivitet, når Staphylococcus-arten er i logaritmisk vækstfase og i statisk fase.

3. Humant monoklonalt antistof ifølge krav 1 eller 2, der er kendetegnet ved, at Staphylococcus-arten er udvalgt fra gruppen, der består af S. aureus, S. auricularis, S. capitis, S. caprae, S. caseolyticus, S. chromogenes, S. cohnii, S. epidermidis, S. haemolyticus, S. hominis, S. hyicus, S. intermedium, S. lentus, S. lugdunensis, S. saprophyticus, S. schleiferi, S. sciuri, S. simulans, S. warneri og S. xylosus.

4. Immunkonjugat, der omfatter et humant monoklonalt antistof ifølge et hvilket som helst af kravene 1-3, hvilket immunkonjugat yderligere omfatter mindst ét tag.

5. Nukleinsyremolekyle, der koder for et humant monoklonalt antistof ifølge et hvilket som helst af kravene 1-3.

6. Vektor, der omfatter mindst ét nukleinsyremolekyle ifølge krav 5.

7. Værtscelle, der omfatter mindst én vektor ifølge krav 6.

8. Fremgangsmåde til fremstilling af et humant monoklonalt antistof ifølge et hvilket som helst af kravene 1-3, hvor fremgangsmåden omfatter trinene:

a) dyrkning af en værtscelle ifølge krav 7 under betingelser, der bidrager til ekspresion af det humane monoklonale antistof, og eventuelt

b) indvindning af det udtrykte humane monoklonale antistof.

5

9. Farmaceutisk sammensætning, der omfatter et humant monoklonalt antistof ifølge et hvilket som helst af kravene 1-3 eller et immunkonjugat ifølge krav 4, hvilken farmaceutiske sammensætning yderligere omfatter mindst ét farmaceutisk

10 acceptabelt excipiens.

10. Farmaceutisk sammensætning ifølge krav 9, der yderligere omfatter mindst ét andet terapeutisk middel.

15 11. Anvendelse af et humant monoklonalt antistof ifølge et hvilket som helst af kravene 1-3, immunkonjugat ifølge krav 4 eller farmaceutisk sammensætning ifølge krav 9 eller 10 til diagnosticering, profylakse, behandling eller en kombination deraf af en stafylokokinfektion.

DRAWINGS

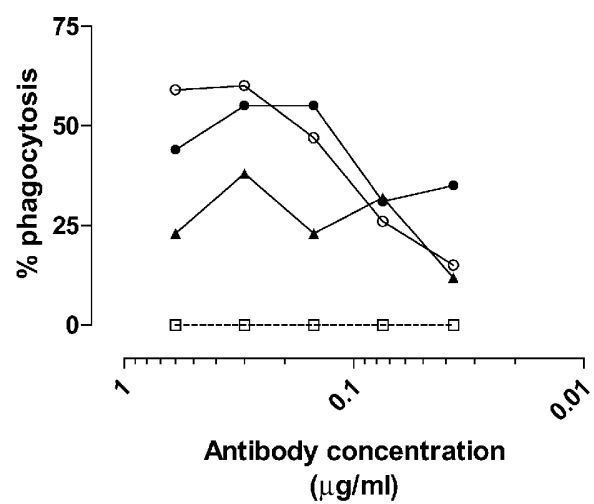


FIG. 1

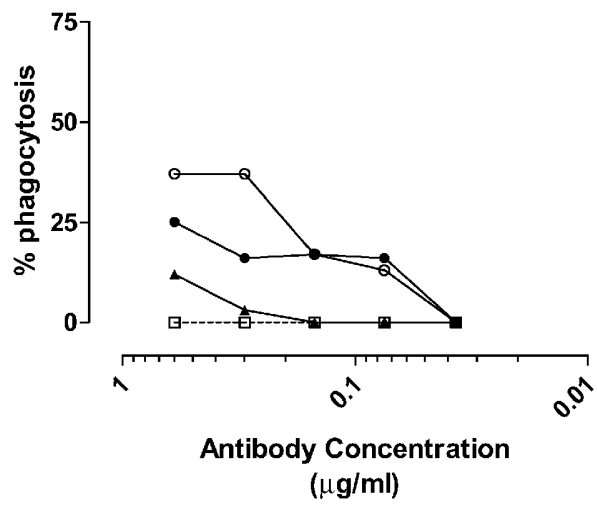


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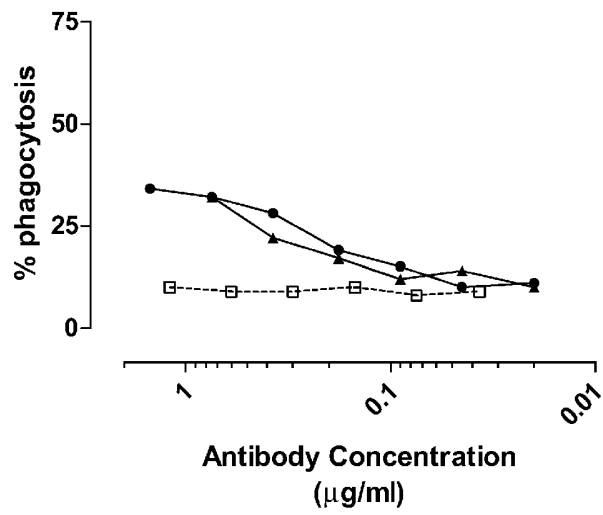


FIG. 3

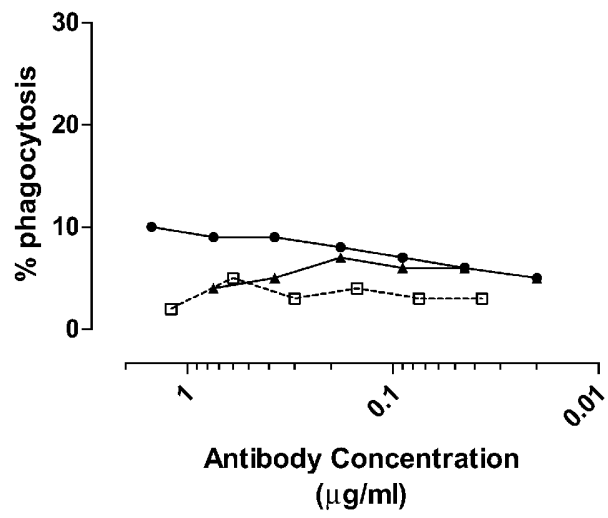


FIG. 4

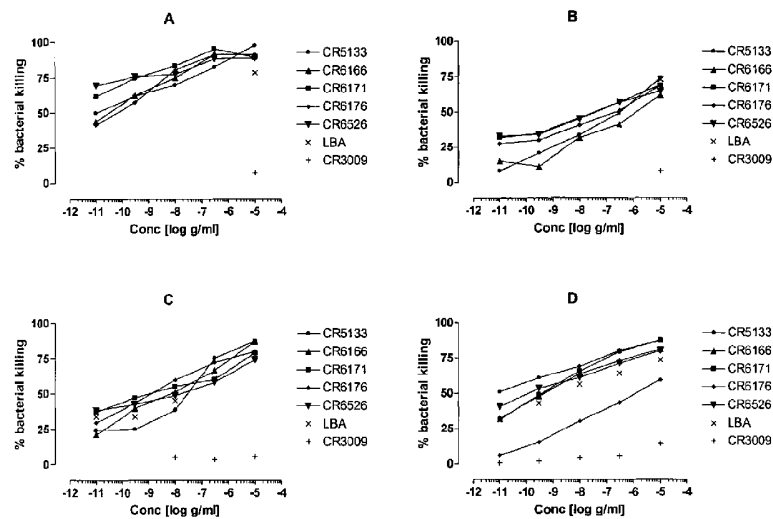


FIG. 5

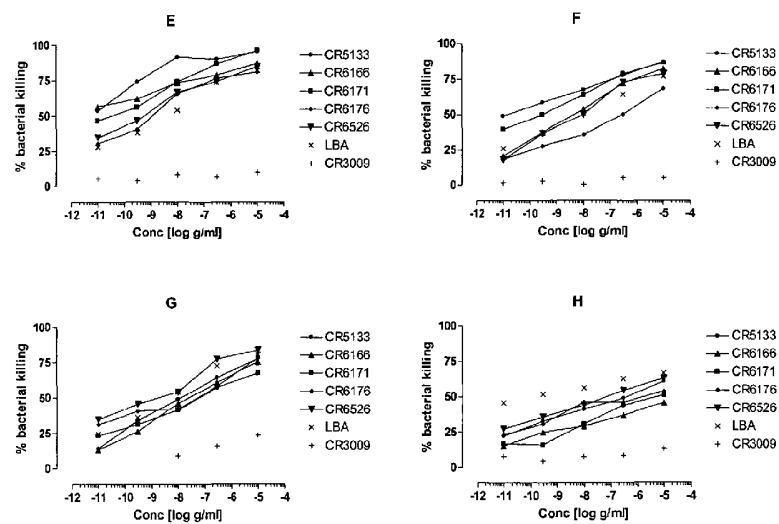


FIG. 5 cont'd