

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
11 August 2005 (11.08.2005)

PCT

(10) International Publication Number
WO 2005/073723 A1

(51) International Patent Classification⁷: **G01N 33/53**,
33/566

(21) International Application Number:
PCT/US2005/002638

(22) International Filing Date: 27 January 2005 (27.01.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/539,837 28 January 2004 (28.01.2004) US
60/552,634 12 March 2004 (12.03.2004) US
60/581,696 21 June 2004 (21.06.2004) US

(71) Applicant (for all designated States except US): **EX-ELIXIS, INC** [US/US]; 170 Harbor Way, P.O. Box 511, South San Francisco, CA 94083-0511 (US).

(71) Applicant and

(72) Inventor: **NICOLL, Monique** [US/US]; 224 Naomi Avenue, Pacifica, CA 94044 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **FRIEDMAN, Lori** [US/US]; 113 Arundel Road, San Carlos, CA 94070 (US). **FRANCIS-LANG, Helen** [GB/US]; 1782 Pacific Avenue, Apt. 2, San Francisco, CA 94109 (US). **PARKS, Annette** [US/US]; 83 Clifton Drive, Daly City, Ca 94015 (US). **SHAW, Kenneth, James** [US/US]; 484 Sierra Point Road, Brisbane, CA 94005 (US). **ZHANG, HaiGuang** [US/US]; 4833 El Grande Place, El Sobrante, CA 94803 (US). **BJERKE, Lynn, Margaret** [US/US]; 728 Alabama Street, #201, San Francisco, CA 94110 (US).

ADAMKEWICZ, Joanne [US/US]; 1249 Rhode Island Street, San Francisco, CA 94107 (US). **HITZ, Benjamin C.** [US/US]; 42 Sumner Street, San Francisco, CA 94103 (US). **LICKTEIG, Kim** [US/US]; 1921 Grove Street, San Francisco, CA 94117 (US). **JIN, Yisheng** [CN/US]; 192 36th Avenue, Apt. B, San Mateo, CA 94403 (US).

(74) Agents: **SHAYESTEH, Laleh** et al.; Exelixis, Inc., P.O. Box 511, 170 Harbor Way, South San Francisco, CA 94083-0511 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MIGFRS AS MODIFIERS OF THE IGFR PATHWAY AND METHODS OF USE

(57) Abstract: Human MIGFR genes are identified as modulators of the IGFR pathway and thus are therapeutic targets for disorders associated with defective IGFR function Methods for identifying modulators of IGFR comprising screening for agents that modulate the activity of MIGFR are provided



WO 2005/073723 A1

MIGFRS AS MODIFIERS OF THE IGF1R PATHWAY AND METHODS OF USE

REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. provisional patent applications 60/539,837 filed 1/28/2004, 60/552,634 filed 3/12/2004, and 60/581,696 filed 6/21/2004. The contents of the prior applications are hereby incorporated in their entirety.

BACKGROUND OF THE INVENTION

[0002] Somatic mutations in the PTEN (Phosphatase and Tensin homolog deleted on chromosome 10) gene are known to cause tumors in a variety of human tissues. In addition, germline mutations in PTEN are the cause of human diseases (Cowden disease and Bannayan-Zonana syndrome) associated with increased risk of breast and thyroid cancer (Nelen MR et al. (1997) *Hum Mol Genet*, 8:1383-1387; Liaw D et al. (1997) *Nat Genet*, 1:64-67; Marsh DJ et al. (1998) *Hum Mol Genet*, 3:507-515). PTEN is thought to act as a tumor suppressor by regulating several signaling pathways through the second messenger phosphatidylinositol 3,4,5 triphosphate (PIP3). PTEN dephosphorylates the D3 position of PIP3 and downregulates signaling events dependent on PIP3 levels (Maehama T and Dixon JE (1998) *J Biol Chem*, 273:13375-8). In particular, pro-survival pathways downstream of the insulin-like growth factor (IGF) pathway are regulated by PTEN activity. Stimulation of the IGF pathway, or loss of PTEN function, elevates PIP3 levels and activates pro-survival pathways associated with tumorigenesis (Stambolic V et al. (1998) *Cell*, 95:29-39). Consistent with this model, elevated levels of insulin-like growth factors I and II correlate with increased risk of cancer (Yu H et al (1999) *J Natl Cancer Inst* 91:151-156) and poor prognosis (Takanami I et al, 1996, *J Surg Oncol* 61(3):205-8). In addition, increased levels or activity of positive effectors of the IGF pathway, such as Akt and PI(3) kinase, have been implicated in several types of human cancer (Nicholson KM and Anderson NG (2002) *Cellular Signalling*, 14:381-395).

[0003] In *Drosophila melanogaster*, as in vertebrates, the Insulin Growth Factor Receptor (IGFR) pathway includes the positive effectors PI(3) kinase, Akt, and PDK and the inhibitor, PTEN. These proteins have been implicated in multiple processes, including the regulation of cell growth and size as well as cell division and survival (Oldham S and Hafen E. (2003) *Trends Cell Biol.* 13:79-85; Garafolo RS. (2002) *Trends Endocr. Metab.* 13:156-162; Backman SA et al. (2002) *Curr. Op. Neurobio.* 12:1-7; Tapon N et al. (2001)

Curr Op. Cell Biol. 13:731-737). Activation of the pathway in *Drosophila* can result in increases in cell size, cell number and organ size (Oldham S et al. (2002) Dev. 129:4103-4109; Prober DA and Edgar BA. (2002) Genes&Dev. 16:2286-2299; Potter CJ et al. (2001) Cell 105:357-368; Verdu J et al. (1999) Cell Biol. 1:500-506).

[0004] The ability to manipulate the genomes of model organisms such as *Drosophila* provides a powerful means to analyze biochemical processes that, due to significant evolutionary conservation, have direct relevance to more complex vertebrate organisms. Due to a high level of gene and pathway conservation, the strong similarity of cellular processes, and the functional conservation of genes between these model organisms and mammals, identification of the involvement of novel genes in particular pathways and their functions in such model organisms can directly contribute to the understanding of the correlative pathways and methods of modulating them in mammals (see, for example, Mechler BM et al., 1985 EMBO J 4:1551-1557; Gateff E. 1982 Adv. Cancer Res. 37: 33-74; Watson KL., et al., 1994 J Cell Sci. 18: 19-33; Miklos GL, and Rubin GM. 1996 Cell 86:521-529; Wassarman DA, et al., 1995 Curr Opin Gen Dev 5: 44-50; and Booth DR. 1999 Cancer Metastasis Rev. 18: 261-284). For example, a genetic screen can be carried out in an invertebrate model organism having underexpression (e.g. knockout) or overexpression of a gene (referred to as a “genetic entry point”) that yields a visible phenotype. Additional genes are mutated in a random or targeted manner. When a gene mutation changes the original phenotype caused by the mutation in the genetic entry point, the gene is identified as a “modifier” involved in the same or overlapping pathway as the genetic entry point. When the genetic entry point is an ortholog of a human gene implicated in a disease pathway, such as IGFR, modifier genes can be identified that may be attractive candidate targets for novel therapeutics.

[0005] All references cited herein, including patents, patent applications, publications, and sequence information in referenced Genbank identifier numbers, are incorporated herein in their entireties.

SUMMARY OF THE INVENTION

[0006] We have discovered genes that modify the IGFR pathway in *Drosophila*, and identified their human orthologs, hereinafter referred to as Modifier of IGFR (MIGFR). The invention provides methods for utilizing these IGFR modifier genes and polypeptides to identify MIGFR-modulating agents that are candidate therapeutic agents that can be used in the treatment of disorders associated with defective or impaired IGFR function

and/or MIGFR function. Preferred MIGFR-modulating agents specifically bind to MIGFR polypeptides and restore IGFR function. Other preferred MIGFR-modulating agents are nucleic acid modulators such as antisense oligomers and RNAi that repress MIGFR gene expression or product activity by, for example, binding to and inhibiting the respective nucleic acid (i.e. DNA or mRNA).

[0007] MIGFR modulating agents may be evaluated by any convenient *in vitro* or *in vivo* assay for molecular interaction with an MIGFR polypeptide or nucleic acid. In one embodiment, candidate MIGFR modulating agents are tested with an assay system comprising an MIGFR polypeptide or nucleic acid. Agents that produce a change in the activity of the assay system relative to controls are identified as candidate IGFR modulating agents. The assay system may be cell-based or cell-free. MIGFR-modulating agents include MIGFR related proteins (e.g. dominant negative mutants, and biotherapeutics); MIGFR -specific antibodies; MIGFR -specific antisense oligomers and other nucleic acid modulators; and chemical agents that specifically bind to or interact with MIGFR or compete with MIGFR binding partner (e.g. by binding to an MIGFR binding partner). In one specific embodiment, a small molecule modulator is identified using a binding assay. In specific embodiments, the screening assay system is selected from an apoptosis assay, a cell proliferation assay, an angiogenesis assay, and a hypoxic induction assay.

[0008] In another embodiment, candidate IGFR pathway modulating agents are further tested using a second assay system that detects changes in the IGFR pathway, such as angiogenic, apoptotic, or cell proliferation changes produced by the originally identified candidate agent or an agent derived from the original agent. The second assay system may use cultured cells or non-human animals. In specific embodiments, the secondary assay system uses non-human animals, including animals predetermined to have a disease or disorder implicating the IGFR pathway, such as an angiogenic, apoptotic, or cell proliferation disorder (e.g. cancer).

[0009] The invention further provides methods for modulating the MIGFR function and/or the IGFR pathway in a mammalian cell by contacting the mammalian cell with an agent that specifically binds an MIGFR polypeptide or nucleic acid. The agent may be a small molecule modulator, a nucleic acid modulator, or an antibody and may be administered to a mammalian animal predetermined to have a pathology associated with the IGFR pathway.

DETAILED DESCRIPTION OF THE INVENTION

[0010] A dominant loss of function screen was carried out in *Drosophila* to identify genes that interact with or modulate the IGFR signaling pathway. Modifiers of the IGFR pathway and their orthologs were identified. Accordingly, vertebrate orthologs of these modifiers, and preferably the human orthologs, MIGFR genes (i.e., nucleic acids and polypeptides) are attractive drug targets for the treatment of pathologies associated with a defective IGFR signaling pathway, such as cancer. Table 1 (Example II) lists the modifiers and their orthologs.

[0011] In vitro and in vivo methods of assessing MIGFR function are provided herein. Modulation of the MIGFR or their respective binding partners is useful for understanding the association of the IGFR pathway and its members in normal and disease conditions and for developing diagnostics and therapeutic modalities for IGFR related pathologies. MIGFR-modulating agents that act by inhibiting or enhancing MIGFR expression, directly or indirectly, for example, by affecting an MIGFR function such as enzymatic (e.g., catalytic) or binding activity, can be identified using methods provided herein. MIGFR modulating agents are useful in diagnosis, therapy and pharmaceutical development.

Nucleic acids and polypeptides of the invention

[0012] Sequences related to MIGFR nucleic acids and polypeptides that can be used in the invention are disclosed in Genbank (referenced by Genbank identifier (GI) or RefSeq number), shown in Table 1 and in the appended sequence listing.

[0013] The term “MIGFR polypeptide” refers to a full-length MIGFR protein or a functionally active fragment or derivative thereof. A “functionally active” MIGFR fragment or derivative exhibits one or more functional activities associated with a full-length, wild-type MIGFR protein, such as antigenic or immunogenic activity, enzymatic activity, ability to bind natural cellular substrates, etc. The functional activity of MIGFR proteins, derivatives and fragments can be assayed by various methods known to one skilled in the art (Current Protocols in Protein Science (1998) Coligan *et al.*, eds., John Wiley & Sons, Inc., Somerset, New Jersey) and as further discussed below. In one embodiment, a functionally active MIGFR polypeptide is an MIGFR derivative capable of rescuing defective endogenous MIGFR activity, such as in cell based or animal assays; the rescuing derivative may be from the same or a different species. For purposes herein, functionally active fragments also include those fragments that comprise one or more structural domains of an MIGFR, such as a kinase domain or a binding domain. Protein

domains can be identified using the PFAM program (Bateman A., et al., *Nucleic Acids Res*, 1999, 27:260-2). Methods for obtaining MIGFR polypeptides are also further described below. In some embodiments, preferred fragments are functionally active, domain-containing fragments comprising at least 25 contiguous amino acids, preferably at least 50, more preferably 75, and most preferably at least 100 contiguous amino acids of an MIGFR. In further preferred embodiments, the fragment comprises the entire functionally active domain.

[0014] The term "MIGFR nucleic acid" refers to a DNA or RNA molecule that encodes an MIGFR polypeptide. Preferably, the MIGFR polypeptide or nucleic acid or fragment thereof is from a human, but can also be an ortholog, or derivative thereof with at least 70% sequence identity, preferably at least 80%, more preferably 85%, still more preferably 90%, and most preferably at least 95% sequence identity with human MIGFR. Methods of identifying orthologs are known in the art. Normally, orthologs in different species retain the same function, due to presence of one or more protein motifs and/or 3-dimensional structures. Orthologs are generally identified by sequence homology analysis, such as BLAST analysis, usually using protein bait sequences. Sequences are assigned as a potential ortholog if the best hit sequence from the forward BLAST result retrieves the original query sequence in the reverse BLAST (Huynen MA and Bork P, *Proc Natl Acad Sci* (1998) 95:5849-5856; Huynen MA *et al.*, *Genome Research* (2000) 10:1204-1210). Programs for multiple sequence alignment, such as CLUSTAL (Thompson JD et al, 1994, *Nucleic Acids Res* 22:4673-4680) may be used to highlight conserved regions and/or residues of orthologous proteins and to generate phylogenetic trees. In a phylogenetic tree representing multiple homologous sequences from diverse species (e.g., retrieved through BLAST analysis), orthologous sequences from two species generally appear closest on the tree with respect to all other sequences from these two species. Structural threading or other analysis of protein folding (e.g., using software by ProCeryon, Biosciences, Salzburg, Austria) may also identify potential orthologs. In evolution, when a gene duplication event follows speciation, a single gene in one species, such as *Drosophila*, may correspond to multiple genes (paralogs) in another, such as human. As used herein, the term "orthologs" encompasses paralogs. As used herein, "percent (%) sequence identity" with respect to a subject sequence, or a specified portion of a subject sequence, is defined as the percentage of nucleotides or amino acids in the candidate derivative sequence identical with the nucleotides or amino acids in the subject sequence (or specified portion thereof), after aligning the sequences and introducing gaps,

if necessary to achieve the maximum percent sequence identity, as generated by the program WU-BLAST-2.0a19 (Altschul *et al.*, J. Mol. Biol. (1997) 215:403-410) with all the search parameters set to default values. The HSP S and HSP S2 parameters are dynamic values and are established by the program itself depending upon the composition of the particular sequence and composition of the particular database against which the sequence of interest is being searched. A % identity value is determined by the number of matching identical nucleotides or amino acids divided by the sequence length for which the percent identity is being reported. "Percent (%) amino acid sequence similarity" is determined by doing the same calculation as for determining % amino acid sequence identity, but including conservative amino acid substitutions in addition to identical amino acids in the computation.

[0015] A conservative amino acid substitution is one in which an amino acid is substituted for another amino acid having similar properties such that the folding or activity of the protein is not significantly affected. Aromatic amino acids that can be substituted for each other are phenylalanine, tryptophan, and tyrosine; interchangeable hydrophobic amino acids are leucine, isoleucine, methionine, and valine; interchangeable polar amino acids are glutamine and asparagine; interchangeable basic amino acids are arginine, lysine and histidine; interchangeable acidic amino acids are aspartic acid and glutamic acid; and interchangeable small amino acids are alanine, serine, threonine, cysteine and glycine.

[0016] Alternatively, an alignment for nucleic acid sequences is provided by the local homology algorithm of Smith and Waterman (Smith and Waterman, 1981, Advances in Applied Mathematics 2:482-489; database: European Bioinformatics Institute; Smith and Waterman, 1981, J. of Molec.Biol., 147:195-197; Nicholas et al., 1998, "A Tutorial on Searching Sequence Databases and Sequence Scoring Methods" (www.psc.edu) and references cited therein.; W.R. Pearson, 1991, Genomics 11:635-650). This algorithm can be applied to amino acid sequences by using the scoring matrix developed by Dayhoff (Dayhoff: Atlas of Protein Sequences and Structure, M. O. Dayhoff ed., 5 suppl. 3:353-358, National Biomedical Research Foundation, Washington, D.C., USA), and normalized by Gribskov (Gribskov 1986 Nucl. Acids Res. 14(6):6745-6763). The Smith-Waterman algorithm may be employed where default parameters are used for scoring (for example, gap open penalty of 12, gap extension penalty of two). From the data generated, the "Match" value reflects "sequence identity."

[0017] Derivative nucleic acid molecules of the subject nucleic acid molecules include sequences that hybridize to the nucleic acid sequence of an MIGFR. The stringency of

hybridization can be controlled by temperature, ionic strength, pH, and the presence of denaturing agents such as formamide during hybridization and washing. Conditions routinely used are set out in readily available procedure texts (*e.g.*, Current Protocol in Molecular Biology, Vol. 1, Chap. 2.10, John Wiley & Sons, Publishers (1994); Sambrook *et al.*, Molecular Cloning, Cold Spring Harbor (1989)). In some embodiments, a nucleic acid molecule of the invention is capable of hybridizing to a nucleic acid molecule containing the nucleotide sequence of an MIGFR under high stringency hybridization conditions that are: prehybridization of filters containing nucleic acid for 8 hours to overnight at 65° C in a solution comprising 6X single strength citrate (SSC) (1X SSC is 0.15 M NaCl, 0.015 M Na citrate; pH 7.0), 5X Denhardt's solution, 0.05% sodium pyrophosphate and 100 µg/ml herring sperm DNA; hybridization for 18-20 hours at 65° C in a solution containing 6X SSC, 1X Denhardt's solution, 100 µg/ml yeast tRNA and 0.05% sodium pyrophosphate; and washing of filters at 65° C for 1h in a solution containing 0.1X SSC and 0.1% SDS (sodium dodecyl sulfate).

[0018] In other embodiments, moderately stringent hybridization conditions are used that are: pretreatment of filters containing nucleic acid for 6 h at 40° C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH7.5), 5mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20h at 40° C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH7.5), 5mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml salmon sperm DNA, and 10% (wt/vol) dextran sulfate; followed by washing twice for 1 hour at 55° C in a solution containing 2X SSC and 0.1% SDS.

[0019] Alternatively, low stringency conditions can be used that are: incubation for 8 hours to overnight at 37° C in a solution comprising 20% formamide, 5 x SSC, 50 mM sodium phosphate (pH 7.6), 5X Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured sheared salmon sperm DNA; hybridization in the same buffer for 18 to 20 hours; and washing of filters in 1 x SSC at about 37° C for 1 hour.

Isolation, Production, Expression, and Mis-expression of MIGFR Nucleic Acids and Polypeptides

[0020] MIGFR nucleic acids and polypeptides are useful for identifying and testing agents that modulate MIGFR function and for other applications related to the involvement of MIGFR in the IGFR pathway. MIGFR nucleic acids and derivatives and orthologs thereof may be obtained using any available method. For instance, techniques for isolating cDNA

or genomic DNA sequences of interest by screening DNA libraries or by using polymerase chain reaction (PCR) are well known in the art. In general, the particular use for the protein will dictate the particulars of expression, production, and purification methods. For instance, production of proteins for use in screening for modulating agents may require methods that preserve specific biological activities of these proteins, whereas production of proteins for antibody generation may require structural integrity of particular epitopes. Expression of proteins to be purified for screening or antibody production may require the addition of specific tags (*e.g.*, generation of fusion proteins). Overexpression of an MIGFR protein for assays used to assess MIGFR function, such as involvement in cell cycle regulation or hypoxic response, may require expression in eukaryotic cell lines capable of these cellular activities. Techniques for the expression, production, and purification of proteins are well known in the art; any suitable means therefore may be used (*e.g.*, Higgins SJ and Hames BD (eds.) *Protein Expression: A Practical Approach*, Oxford University Press Inc., New York 1999; Stanbury PF et al., *Principles of Fermentation Technology*, 2nd edition, Elsevier Science, New York, 1995; Doonan S (ed.) *Protein Purification Protocols*, Humana Press, New Jersey, 1996; Coligan JE et al, *Current Protocols in Protein Science* (eds.), 1999, John Wiley & Sons, New York). In particular embodiments, recombinant MIGFR is expressed in a cell line known to have defective IGFR function. The recombinant cells are used in cell-based screening assay systems of the invention, as described further below.

[0021] The nucleotide sequence encoding an MIGFR polypeptide can be inserted into any appropriate expression vector. The necessary transcriptional and translational signals, including promoter/enhancer element, can derive from the native MIGFR gene and/or its flanking regions or can be heterologous. A variety of host-vector expression systems may be utilized, such as mammalian cell systems infected with virus (*e.g.* vaccinia virus, adenovirus, *etc.*); insect cell systems infected with virus (*e.g.* baculovirus); microorganisms such as yeast containing yeast vectors, or bacteria transformed with bacteriophage, plasmid, or cosmid DNA. An isolated host cell strain that modulates the expression of, modifies, and/or specifically processes the gene product may be used.

[0022] To detect expression of the MIGFR gene product, the expression vector can comprise a promoter operably linked to an MIGFR gene nucleic acid, one or more origins of replication, and, one or more selectable markers (*e.g.* thymidine kinase activity, resistance to antibiotics, *etc.*). Alternatively, recombinant expression vectors can be identified by assaying for the expression of the MIGFR gene product based on the

physical or functional properties of the MIGFR protein in *in vitro* assay systems (*e.g.* immunoassays).

[0023] The MIGFR protein, fragment, or derivative may be optionally expressed as a fusion, or chimeric protein product (*i.e.* it is joined via a peptide bond to a heterologous protein sequence of a different protein), for example to facilitate purification or detection. A chimeric product can be made by ligating the appropriate nucleic acid sequences encoding the desired amino acid sequences to each other using standard methods and expressing the chimeric product. A chimeric product may also be made by protein synthetic techniques, *e.g.* by use of a peptide synthesizer (Hunkapiller *et al.*, Nature (1984) 310:105-111).

[0024] Once a recombinant cell that expresses the MIGFR gene sequence is identified, the gene product can be isolated and purified using standard methods (*e.g.* ion exchange, affinity, and gel exclusion chromatography; centrifugation; differential solubility; electrophoresis). Alternatively, native MIGFR proteins can be purified from natural sources, by standard methods (*e.g.* immunoaffinity purification). Once a protein is obtained, it may be quantified and its activity measured by appropriate methods, such as immunoassay, bioassay, or other measurements of physical properties, such as crystallography.

[0025] The methods of this invention may also use cells that have been engineered for altered expression (mis-expression) of MIGFR or other genes associated with the IGFR pathway. As used herein, mis-expression encompasses ectopic expression, over-expression, under-expression, and non-expression (*e.g.* by gene knock-out or blocking expression that would otherwise normally occur).

Genetically modified animals

[0026] Animal models that have been genetically modified to alter MIGFR expression may be used in *in vivo* assays to test for activity of a candidate IGFR modulating agent, or to further assess the role of MIGFR in an IGFR pathway process such as apoptosis or cell proliferation. Preferably, the altered MIGFR expression results in a detectable phenotype, such as decreased or increased levels of cell proliferation, angiogenesis, or apoptosis compared to control animals having normal MIGFR expression. The genetically modified animal may additionally have altered IGFR expression (*e.g.* IGFR knockout). Preferred genetically modified animals are mammals such as primates, rodents (preferably mice or rats), among others. Preferred non-mammalian species include zebrafish, *C. elegans*, and

Drosophila. Preferred genetically modified animals are transgenic animals having a heterologous nucleic acid sequence present as an extrachromosomal element in a portion of its cells, i.e. mosaic animals (see, for example, techniques described by Jakobovits, 1994, Curr. Biol. 4:761-763.) or stably integrated into its germ line DNA (i.e., in the genomic sequence of most or all of its cells). Heterologous nucleic acid is introduced into the germ line of such transgenic animals by genetic manipulation of, for example, embryos or embryonic stem cells of the host animal.

[0027] Methods of making transgenic animals are well-known in the art (for transgenic mice see Brinster et al., Proc. Nat. Acad. Sci. USA 82: 4438-4442 (1985), U.S. Pat. Nos. 4,736,866 and 4,870,009, both by Leder et al., U.S. Pat. No. 4,873,191 by Wagner et al., and Hogan, B., Manipulating the Mouse Embryo, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., (1986); for particle bombardment see U.S. Pat. No., 4,945,050, by Sanford *et al.*; for transgenic *Drosophila* see Rubin and Spradling, Science (1982) 218:348-53 and U.S. Pat. No. 4,670,388; for transgenic insects see Berghammer A.J. *et al.*, A Universal Marker for Transgenic Insects (1999) Nature 402:370-371; for transgenic Zebrafish see Lin S., Transgenic Zebrafish, Methods Mol Biol. (2000);136:375-3830); for microinjection procedures for fish, amphibian eggs and birds see Houdebine and Chourrout, Experientia (1991) 47:897-905; for transgenic rats see Hammer *et al.*, Cell (1990) 63:1099-1112; and for culturing of embryonic stem (ES) cells and the subsequent production of transgenic animals by the introduction of DNA into ES cells using methods such as electroporation, calcium phosphate/DNA precipitation and direct injection see, e.g., Teratocarcinomas and Embryonic Stem Cells, A Practical Approach, E. J. Robertson, ed., IRL Press (1987)). Clones of the nonhuman transgenic animals can be produced according to available methods (see Wilmut, I. *et al.* (1997) Nature 385:810-813; and PCT International Publication Nos. WO 97/07668 and WO 97/07669).

[0028] In one embodiment, the transgenic animal is a "knock-out" animal having a heterozygous or homozygous alteration in the sequence of an endogenous MIGFR gene that results in a decrease of MIGFR function, preferably such that MIGFR expression is undetectable or insignificant. Knock-out animals are typically generated by homologous recombination with a vector comprising a transgene having at least a portion of the gene to be knocked out. Typically a deletion, addition or substitution has been introduced into the transgene to functionally disrupt it. The transgene can be a human gene (e.g., from a human genomic clone) but more preferably is an ortholog of the human gene derived from the transgenic host species. For example, a mouse MIGFR gene is used to construct a

homologous recombination vector suitable for altering an endogenous MIGFR gene in the mouse genome. Detailed methodologies for homologous recombination in mice are available (see Capecchi, Science (1989) 244:1288-1292; Joyner *et al.*, Nature (1989) 338:153-156). Procedures for the production of non-rodent transgenic mammals and other animals are also available (Houdebine and Chourrout, *supra*; Pursel *et al.*, Science (1989) 244:1281-1288; Simms *et al.*, Bio/Technology (1988) 6:179-183). In a preferred embodiment, knock-out animals, such as mice harboring a knockout of a specific gene, may be used to produce antibodies against the human counterpart of the gene that has been knocked out (Claesson MH *et al.*, (1994) Scan J Immunol 40:257-264; Declerck PJ *et al.*, (1995) J Biol Chem. 270:8397-400).

[0029] In another embodiment, the transgenic animal is a "knock-in" animal having an alteration in its genome that results in altered expression (e.g., increased (including ectopic) or decreased expression) of the MIGFR gene, e.g., by introduction of additional copies of MIGFR, or by operatively inserting a regulatory sequence that provides for altered expression of an endogenous copy of the MIGFR gene. Such regulatory sequences include inducible, tissue-specific, and constitutive promoters and enhancer elements. The knock-in can be homozygous or heterozygous.

[0030] Transgenic nonhuman animals can also be produced that contain selected systems allowing for regulated expression of the transgene. One example of such a system that may be produced is the cre/loxP recombinase system of bacteriophage P1 (Lakso *et al.*, PNAS (1992) 89:6232-6236; U.S. Pat. No. 4,959,317). If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman *et al.* (1991) Science 251:1351-1355; U.S. Pat. No. 5,654,182). In a preferred embodiment, both Cre-LoxP and Flp-Frt are used in the same system to regulate expression of the transgene, and for sequential deletion of vector sequences in the same cell (Sun X *et al.* (2000) Nat Genet 25:83-6).

[0031] The genetically modified animals can be used in genetic studies to further elucidate the IGFR pathway, as animal models of disease and disorders implicating defective IGFR function, and for *in vivo* testing of candidate therapeutic agents, such as those identified in

screens described below. The candidate therapeutic agents are administered to a genetically modified animal having altered MIGFR function and phenotypic changes are compared with appropriate control animals such as genetically modified animals that receive placebo treatment, and/or animals with unaltered MIGFR expression that receive candidate therapeutic agent.

[0032] In addition to the above-described genetically modified animals having altered MIGFR function, animal models having defective IGFR function (and otherwise normal MIGFR function), can be used in the methods of the present invention. For example, a IGFR knockout mouse can be used to assess, *in vivo*, the activity of a candidate IGFR modulating agent identified in one of the *in vitro* assays described below. Preferably, the candidate IGFR modulating agent when administered to a model system with cells defective in IGFR function, produces a detectable phenotypic change in the model system indicating that the IGFR function is restored, i.e., the cells exhibit normal cell cycle progression.

Modulating Agents

[0033] The invention provides methods to identify agents that interact with and/or modulate the function of MIGFR and/or the IGFR pathway. Modulating agents identified by the methods are also part of the invention. Such agents are useful in a variety of diagnostic and therapeutic applications associated with the IGFR pathway, as well as in further analysis of the MIGFR protein and its contribution to the IGFR pathway. Accordingly, the invention also provides methods for modulating the IGFR pathway comprising the step of specifically modulating MIGFR activity by administering an MIGFR-interacting or -modulating agent.

[0034] As used herein, an “MIGFR-modulating agent” is any agent that modulates MIGFR function, for example, an agent that interacts with MIGFR to inhibit or enhance MIGFR activity or otherwise affect normal MIGFR function. MIGFR function can be affected at any level, including transcription, protein expression, protein localization, and cellular or extra-cellular activity. In a preferred embodiment, the MIGFR - modulating agent specifically modulates the function of the MIGFR. The phrases “specific modulating agent”, “specifically modulates”, etc., are used herein to refer to modulating agents that directly bind to the MIGFR polypeptide or nucleic acid, and preferably inhibit, enhance, or otherwise alter, the function of the MIGFR. These phrases also encompass modulating agents that alter the interaction of the MIGFR with a binding partner,

substrate, or cofactor (e.g. by binding to a binding partner of an MIGFR, or to a protein/binding partner complex, and altering MIGFR function). In a further preferred embodiment, the MIGFR- modulating agent is a modulator of the IGFR pathway (e.g. it restores and/or upregulates IGFR function) and thus is also a IGFR-modulating agent.

[0035] Preferred MIGFR-modulating agents include small molecule compounds; MIGFR-interacting proteins, including antibodies and other biotherapeutics; and nucleic acid modulators such as antisense and RNA inhibitors. The modulating agents may be formulated in pharmaceutical compositions, for example, as compositions that may comprise other active ingredients, as in combination therapy, and/or suitable carriers or excipients. Techniques for formulation and administration of the compounds may be found in "Remington's Pharmaceutical Sciences" Mack Publishing Co., Easton, PA, 19th edition.

Small molecule modulators

[0036] Small molecules are often preferred to modulate function of proteins with enzymatic function, and/or containing protein interaction domains. Chemical agents, referred to in the art as "small molecule" compounds are typically organic, non-peptide molecules, having a molecular weight up to 10,000, preferably up to 5,000, more preferably up to 1,000, and most preferably up to 500 daltons. This class of modulators includes chemically synthesized molecules, for instance, compounds from combinatorial chemical libraries. Synthetic compounds may be rationally designed or identified based on known or inferred properties of the MIGFR protein or may be identified by screening compound libraries. Alternative appropriate modulators of this class are natural products, particularly secondary metabolites from organisms such as plants or fungi, which can also be identified by screening compound libraries for MIGFR-modulating activity. Methods for generating and obtaining compounds are well known in the art (Schreiber SL, Science (2000) 151: 1964-1969; Radmann J and Gunther J, Science (2000) 151:1947-1948).

[0037] Small molecule modulators identified from screening assays, as described below, can be used as lead compounds from which candidate clinical compounds may be designed, optimized, and synthesized. Such clinical compounds may have utility in treating pathologies associated with the IGFR pathway. The activity of candidate small molecule modulating agents may be improved several-fold through iterative secondary functional validation, as further described below, structure determination, and candidate modulator modification and testing. Additionally, candidate clinical compounds are

generated with specific regard to clinical and pharmacological properties. For example, the reagents may be derivatized and re-screened using *in vitro* and *in vivo* assays to optimize activity and minimize toxicity for pharmaceutical development.

Protein Modulators

- [0038] Specific MIGFR-interacting proteins are useful in a variety of diagnostic and therapeutic applications related to the IGFR pathway and related disorders, as well as in validation assays for other MIGFR-modulating agents. In a preferred embodiment, MIGFR-interacting proteins affect normal MIGFR function, including transcription, protein expression, protein localization, and cellular or extra-cellular activity. In another embodiment, MIGFR-interacting proteins are useful in detecting and providing information about the function of MIGFR proteins, as is relevant to IGFR related disorders, such as cancer (e.g., for diagnostic means).
- [0039] An MIGFR-interacting protein may be endogenous, i.e. one that naturally interacts genetically or biochemically with an MIGFR, such as a member of the MIGFR pathway that modulates MIGFR expression, localization, and/or activity. MIGFR-modulators include dominant negative forms of MIGFR-interacting proteins and of MIGFR proteins themselves. Yeast two-hybrid and variant screens offer preferred methods for identifying endogenous MIGFR-interacting proteins (Finley, R. L. et al. (1996) in DNA Cloning-Expression Systems: A Practical Approach, eds. Glover D. & Hames B. D (Oxford University Press, Oxford, England), pp. 169-203; Fashema SF et al., Gene (2000) 250:1-14; Drees BL Curr Opin Chem Biol (1999) 3:64-70; Vidal M and Legrain P Nucleic Acids Res (1999) 27:919-29; and U.S. Pat. No. 5,928,868). Mass spectrometry is an alternative preferred method for the elucidation of protein complexes (reviewed in, e.g., Pandley A and Mann M, Nature (2000) 405:837-846; Yates JR 3rd, Trends Genet (2000) 16:5-8).
- [0040] An MIGFR-interacting protein may be an exogenous protein, such as an MIGFR-specific antibody or a T-cell antigen receptor (see, e.g., Harlow and Lane (1988) Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory; Harlow and Lane (1999) Using antibodies: a laboratory manual. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press). MIGFR antibodies are further discussed below.
- [0041] In preferred embodiments, an MIGFR-interacting protein specifically binds an MIGFR protein. In alternative preferred embodiments, an MIGFR-modulating agent binds an MIGFR substrate, binding partner, or cofactor.

Antibodies

[0042] In another embodiment, the protein modulator is an MIGFR specific antibody agonist or antagonist. The antibodies have therapeutic and diagnostic utilities, and can be used in screening assays to identify MIGFR modulators. The antibodies can also be used in dissecting the portions of the MIGFR pathway responsible for various cellular responses and in the general processing and maturation of the MIGFR.

[0043] Antibodies that specifically bind MIGFR polypeptides can be generated using known methods. Preferably the antibody is specific to a mammalian ortholog of MIGFR polypeptide, and more preferably, to human MIGFR. Antibodies may be polyclonal, monoclonal (mAbs), humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab')₂ fragments, fragments produced by a FAb expression library, anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments of any of the above. Epitopes of MIGFR which are particularly antigenic can be selected, for example, by routine screening of MIGFR polypeptides for antigenicity or by applying a theoretical method for selecting antigenic regions of a protein (Hopp and Wood (1981), Proc. Natl. Acad. Sci. U.S.A. 78:3824-28; Hopp and Wood, (1983) Mol. Immunol. 20:483-89; Sutcliffe et al., (1983) Science 219:660-66) to the amino acid sequence of an MIGFR. Monoclonal antibodies with affinities of 10^8 M^{-1} preferably 10^9 M^{-1} to 10^{10} M^{-1} , or stronger can be made by standard procedures as described (Harlow and Lane, *supra*; Goding (1986) Monoclonal Antibodies: Principles and Practice (2d ed) Academic Press, New York; and U.S. Pat. Nos. 4,381,292; 4,451,570; and 4,618,577). Antibodies may be generated against crude cell extracts of MIGFR or substantially purified fragments thereof. If MIGFR fragments are used, they preferably comprise at least 10, and more preferably, at least 20 contiguous amino acids of an MIGFR protein. In a particular embodiment, MIGFR-specific antigens and/or immunogens are coupled to carrier proteins that stimulate the immune response. For example, the subject polypeptides are covalently coupled to the keyhole limpet hemocyanin (KLH) carrier, and the conjugate is emulsified in Freund's complete adjuvant, which enhances the immune response. An appropriate immune system such as a laboratory rabbit or mouse is immunized according to conventional protocols.

[0044] The presence of MIGFR-specific antibodies is assayed by an appropriate assay such as a solid phase enzyme-linked immunosorbent assay (ELISA) using immobilized corresponding MIGFR polypeptides. Other assays, such as radioimmunoassays or fluorescent assays might also be used.

[0045] Chimeric antibodies specific to MIGFR polypeptides can be made that contain different portions from different animal species. For instance, a human immunoglobulin constant region may be linked to a variable region of a murine mAb, such that the antibody derives its biological activity from the human antibody, and its binding specificity from the murine fragment. Chimeric antibodies are produced by splicing together genes that encode the appropriate regions from each species (Morrison et al., Proc. Natl. Acad. Sci. (1984) 81:6851-6855; Neuberger et al., Nature (1984) 312:604-608; Takeda et al., Nature (1985) 31:452-454). Humanized antibodies, which are a form of chimeric antibodies, can be generated by grafting complementary-determining regions (CDRs) (Carlos, T. M., J. M. Harlan. 1994. Blood 84:2068-2101) of mouse antibodies into a background of human framework regions and constant regions by recombinant DNA technology (Riechmann LM, et al., 1988 Nature 323: 323-327). Humanized antibodies contain ~10% murine sequences and ~90% human sequences, and thus further reduce or eliminate immunogenicity, while retaining the antibody specificities (Co MS, and Queen C. 1991 Nature 351: 501-501; Morrison SL. 1992 Ann. Rev. Immun. 10:239-265). Humanized antibodies and methods of their production are well-known in the art (U.S. Pat. Nos. 5,530,101, 5,585,089, 5,693,762, and 6,180,370).

[0046] MIGFR-specific single chain antibodies which are recombinant, single chain polypeptides formed by linking the heavy and light chain fragments of the Fv regions via an amino acid bridge, can be produced by methods known in the art (U.S. Pat. No. 4,946,778; Bird, Science (1988) 242:423-426; Huston et al., Proc. Natl. Acad. Sci. USA (1988) 85:5879-5883; and Ward et al., Nature (1989) 334:544-546).

[0047] Other suitable techniques for antibody production involve in vitro exposure of lymphocytes to the antigenic polypeptides or alternatively to selection of libraries of antibodies in phage or similar vectors (Huse et al., Science (1989) 246:1275-1281). As used herein, T-cell antigen receptors are included within the scope of antibody modulators (Harlow and Lane, 1988, *supra*).

[0048] The polypeptides and antibodies of the present invention may be used with or without modification. Frequently, antibodies will be labeled by joining, either covalently or non-covalently, a substance that provides for a detectable signal, or that is toxic to cells that express the targeted protein (Menard S, et al., Int J. Biol Markers (1989) 4:131-134). A wide variety of labels and conjugation techniques are known and are reported extensively in both the scientific and patent literature. Suitable labels include radionuclides, enzymes, substrates, cofactors, inhibitors, fluorescent moieties, fluorescent

emitting lanthanide metals, chemiluminescent moieties, bioluminescent moieties, magnetic particles, and the like (U.S. Pat. Nos. 3,817,837; 3,850,752; 3,939,350; 3,996,345; 4,277,437; 4,275,149; and 4,366,241). Also, recombinant immunoglobulins may be produced (U.S. Pat. No. 4,816,567). Antibodies to cytoplasmic polypeptides may be delivered and reach their targets by conjugation with membrane-penetrating toxin proteins (U.S. Pat. No. 6,086,900).

[0049] When used therapeutically in a patient, the antibodies of the subject invention are typically administered parenterally, when possible at the target site, or intravenously. The therapeutically effective dose and dosage regimen is determined by clinical studies. Typically, the amount of antibody administered is in the range of about 0.1 mg/kg –to about 10 mg/kg of patient weight. For parenteral administration, the antibodies are formulated in a unit dosage injectable form (e.g., solution, suspension, emulsion) in association with a pharmaceutically acceptable vehicle. Such vehicles are inherently nontoxic and non-therapeutic. Examples are water, saline, Ringer's solution, dextrose solution, and 5% human serum albumin. Nonaqueous vehicles such as fixed oils, ethyl oleate, or liposome carriers may also be used. The vehicle may contain minor amounts of additives, such as buffers and preservatives, which enhance isotonicity and chemical stability or otherwise enhance therapeutic potential. The antibodies' concentrations in such vehicles are typically in the range of about 1 mg/ml to about 10 mg/ml. Immunotherapeutic methods are further described in the literature (US Pat. No. 5,859,206; WO0073469).

Specific biotherapeutics

[0050] In a preferred embodiment, an MIGFR-interacting protein may have biotherapeutic applications. Biotherapeutic agents formulated in pharmaceutically acceptable carriers and dosages may be used to activate or inhibit signal transduction pathways. This modulation may be accomplished by binding a ligand, thus inhibiting the activity of the pathway; or by binding a receptor, either to inhibit activation of, or to activate, the receptor. Alternatively, the biotherapeutic may itself be a ligand capable of activating or inhibiting a receptor. Biotherapeutic agents and methods of producing them are described in detail in U.S. Pat. No. 6,146,628.

[0051] When the MIGFR is a ligand, it may be used as a biotherapeutic agent to activate or inhibit its natural receptor. Alternatively, antibodies against MIGFR, as described in the previous section, may be used as biotherapeutic agents.

[0052] When the MIGFR is a receptor, its ligand(s), antibodies to the ligand(s) or the MIGFR itself may be used as biotherapeutics to modulate the activity of MIGFR in the IGFR pathway.

Nucleic Acid Modulators

[0053] Other preferred MIGFR-modulating agents comprise nucleic acid molecules, such as antisense oligomers or double stranded RNA (dsRNA), which generally inhibit MIGFR activity. Preferred nucleic acid modulators interfere with the function of the MIGFR nucleic acid such as DNA replication, transcription, translocation of the MIGFR RNA to the site of protein translation, translation of protein from the MIGFR RNA, splicing of the MIGFR RNA to yield one or more mRNA species, or catalytic activity which may be engaged in or facilitated by the MIGFR RNA.

[0054] In one embodiment, the antisense oligomer is an oligonucleotide that is sufficiently complementary to an MIGFR mRNA to bind to and prevent translation, preferably by binding to the 5' untranslated region. MIGFR-specific antisense oligonucleotides, preferably range from at least 6 to about 200 nucleotides. In some embodiments the oligonucleotide is preferably at least 10, 15, or 20 nucleotides in length. In other embodiments, the oligonucleotide is preferably less than 50, 40, or 30 nucleotides in length. The oligonucleotide can be DNA or RNA or a chimeric mixture or derivatives or modified versions thereof, single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone. The oligonucleotide may include other appending groups such as peptides, agents that facilitate transport across the cell membrane, hybridization-triggered cleavage agents, and intercalating agents.

[0055] In another embodiment, the antisense oligomer is a phosphothioate morpholino oligomer (PMO). PMOs are assembled from four different morpholino subunits, each of which contain one of four genetic bases (A, C, G, or T) linked to a six-membered morpholine ring. Polymers of these subunits are joined by non-ionic phosphodiamidate intersubunit linkages. Details of how to make and use PMOs and other antisense oligomers are well known in the art (e.g. see WO99/18193; Probst JC, Antisense Oligodeoxynucleotide and Ribozyme Design, Methods. (2000) 22(3):271-281; Summerton J, and Weller D. 1997 Antisense Nucleic Acid Drug Dev. :7:187-95; US Pat. No. 5,235,033; and US Pat No. 5,378,841).

[0056] Alternative preferred MIGFR nucleic acid modulators are double-stranded RNA species mediating RNA interference (RNAi). RNAi is the process of sequence-specific, post-transcriptional gene silencing in animals and plants, initiated by double-stranded RNA (dsRNA) that is homologous in sequence to the silenced gene. Methods relating to the use of RNAi to silence genes in *C. elegans*, *Drosophila*, plants, and humans are known in the art (Fire A, et al., 1998 Nature 391:806-811; Fire, A. Trends Genet. 15, 358-363 (1999); Sharp, P. A. RNA interference 2001. Genes Dev. 15, 485-490 (2001); Hammond, S. M., et al., Nature Rev. Genet. 2, 110-1119 (2001); Tuschl, T. Chem. Biochem. 2, 239-245 (2001); Hamilton, A. et al., Science 286, 950-952 (1999); Hammond, S. M., et al., Nature 404, 293-296 (2000); Zamore, P. D., et al., Cell 101, 25-33 (2000); Bernstein, E., et al., Nature 409, 363-366 (2001); Elbashir, S. M., et al., Genes Dev. 15, 188-200 (2001); WO0129058; WO9932619; Elbashir SM, et al., 2001 Nature 411:494-498; Novina CD and Sharp P. 2004 Nature 430:161-164; Soutschek J et al 2004 Nature 432:173-178).

[0057] Nucleic acid modulators are commonly used as research reagents, diagnostics, and therapeutics. For example, antisense oligonucleotides, which are able to inhibit gene expression with exquisite specificity, are often used to elucidate the function of particular genes (see, for example, U.S. Pat. No. 6,165,790). Nucleic acid modulators are also used, for example, to distinguish between functions of various members of a biological pathway. For example, antisense oligomers have been employed as therapeutic moieties in the treatment of disease states in animals and man and have been demonstrated in numerous clinical trials to be safe and effective (Milligan JF, *et al*, Current Concepts in Antisense Drug Design, J Med Chem. (1993) 36:1923-1937; Tonkinson JL *et al.*, Antisense Oligodeoxynucleotides as Clinical Therapeutic Agents, Cancer Invest. (1996) 14:54-65). Accordingly, in one aspect of the invention, an MIGFR-specific nucleic acid modulator is used in an assay to further elucidate the role of the MIGFR in the IGFR pathway, and/or its relationship to other members of the pathway. In another aspect of the invention, an MIGFR-specific antisense oligomer is used as a therapeutic agent for treatment of IGFR-related disease states.

Assay Systems

[0058] The invention provides assay systems and screening methods for identifying specific modulators of MIGFR activity. As used herein, an "assay system" encompasses all the components required for performing and analyzing results of an assay that detects

and/or measures a particular event. In general, primary assays are used to identify or confirm a modulator's specific biochemical or molecular effect with respect to the MIGFR nucleic acid or protein. In general, secondary assays further assess the activity of an MIGFR modulating agent identified by a primary assay and may confirm that the modulating agent affects MIGFR in a manner relevant to the IGFR pathway. In some cases, MIGFR modulators will be directly tested in a secondary assay.

[0059] In a preferred embodiment, the screening method comprises contacting a suitable assay system comprising an MIGFR polypeptide or nucleic acid with a candidate agent under conditions whereby, but for the presence of the agent, the system provides a reference activity (e.g. binding activity), which is based on the particular molecular event the screening method detects. A statistically significant difference between the agent-biased activity and the reference activity indicates that the candidate agent modulates MIGFR activity, and hence the IGFR pathway. The MIGFR polypeptide or nucleic acid used in the assay may comprise any of the nucleic acids or polypeptides described above.

Primary Assays

[0060] The type of modulator tested generally determines the type of primary assay.

Primary assays for small molecule modulators

[0061] For small molecule modulators, screening assays are used to identify candidate modulators. Screening assays may be cell-based or may use a cell-free system that recreates or retains the relevant biochemical reaction of the target protein (reviewed in Sittampalam GS *et al.*, Curr Opin Chem Biol (1997) 1:384-91 and accompanying references). As used herein the term "cell-based" refers to assays using live cells, dead cells, or a particular cellular fraction, such as a membrane, endoplasmic reticulum, or mitochondrial fraction. The term "cell free" encompasses assays using substantially purified protein (either endogenous or recombinantly produced), partially purified or crude cellular extracts. Screening assays may detect a variety of molecular events, including protein-DNA interactions, protein-protein interactions (e.g., receptor-ligand binding), transcriptional activity (e.g., using a reporter gene), enzymatic activity (e.g., via a property of the substrate), activity of second messengers, immunogenicity and changes in cellular morphology or other cellular characteristics. Appropriate screening assays may use a wide range of detection methods including fluorescent, radioactive, colorimetric,

spectrophotometric, and amperometric methods, to provide a read-out for the particular molecular event detected.

[0062] Cell-based screening assays usually require systems for recombinant expression of MIGFR and any auxiliary proteins demanded by the particular assay. Appropriate methods for generating recombinant proteins produce sufficient quantities of proteins that retain their relevant biological activities and are of sufficient purity to optimize activity and assure assay reproducibility. Yeast two-hybrid and variant screens, and mass spectrometry provide preferred methods for determining protein-protein interactions and elucidation of protein complexes. In certain applications, when MIGFR-interacting proteins are used in screens to identify small molecule modulators, the binding specificity of the interacting protein to the MIGFR protein may be assayed by various known methods such as substrate processing (e.g. ability of the candidate MIGFR-specific binding agents to function as negative effectors in MIGFR-expressing cells), binding equilibrium constants (usually at least about 10^7 M^{-1} , preferably at least about 10^8 M^{-1} , more preferably at least about 10^9 M^{-1}), and immunogenicity (e.g. ability to elicit MIGFR specific antibody in a heterologous host such as a mouse, rat, goat or rabbit). For enzymes and receptors, binding may be assayed by, respectively, substrate and ligand processing.

[0063] The screening assay may measure a candidate agent's ability to specifically bind to or modulate activity of an MIGFR polypeptide, a fusion protein thereof, or to cells or membranes bearing the polypeptide or fusion protein. The MIGFR polypeptide can be full length or a fragment thereof that retains functional MIGFR activity. The MIGFR polypeptide may be fused to another polypeptide, such as a peptide tag for detection or anchoring, or to another tag. The MIGFR polypeptide is preferably human MIGFR, or is an ortholog or derivative thereof as described above. In a preferred embodiment, the screening assay detects candidate agent-based modulation of MIGFR interaction with a binding target, such as an endogenous or exogenous protein or other substrate that has MIGFR –specific binding activity, and can be used to assess normal MIGFR gene function.

[0064] Suitable assay formats that may be adapted to screen for MIGFR modulators are known in the art. Preferred screening assays are high throughput or ultra high throughput and thus provide automated, cost-effective means of screening compound libraries for lead compounds (Fernandes PB, Curr Opin Chem Biol (1998) 2:597-603; Sundberg SA, Curr Opin Biotechnol 2000; 11:47-53). In one preferred embodiment, screening assays uses fluorescence technologies, including fluorescence polarization, time-resolved

fluorescence, and fluorescence resonance energy transfer. These systems offer means to monitor protein-protein or DNA-protein interactions in which the intensity of the signal emitted from dye-labeled molecules depends upon their interactions with partner molecules (*e.g.*, Selvin PR, Nat Struct Biol (2000) 7:730-4; Fernandes PB, *supra*; Hertzberg RP and Pope AJ, Curr Opin Chem Biol (2000) 4:445-451).

[0065] A variety of suitable assay systems may be used to identify candidate MIGFR and IGFR pathway modulators (*e.g.* U.S. Pat. No. 6,165,992 and U.S. Pat. No. 6,720,162 (kinase assays); U.S. Pat. Nos. 5,550,019 and 6,133,437 (apoptosis assays); U.S. Pat. No. 6,114,132 and U.S. Pat. No. 6,720,162 (phosphatase and protease assays), and U.S. Pat. Nos. 5,976,782, 6,225,118 and 6,444,434 (angiogenesis assays), among others). Specific preferred assays are described in more detail below.

[0066] Protein kinases, key signal transduction proteins that may be either membrane-associated or intracellular, catalyze the transfer of gamma phosphate from adenosine triphosphate (ATP) to a serine, threonine or tyrosine residue in a protein substrate. Radioassays, which monitor the transfer from [γ - ^{32}P or ^{33}P]ATP, are frequently used to assay kinase activity. For instance, a scintillation assay for p56 (lck) kinase activity monitors the transfer of the gamma phosphate from [γ - ^{33}P] ATP to a biotinylated peptide substrate. The substrate is captured on a streptavidin coated bead that transmits the signal (Beveridge M *et al.*, J Biomol Screen (2000) 5:205-212). This assay uses the scintillation proximity assay (SPA), in which only radio-ligand bound to receptors tethered to the surface of an SPA bead are detected by the scintillant immobilized within it, allowing binding to be measured without separation of bound from free ligand. Other assays for protein kinase activity may use antibodies that specifically recognize phosphorylated substrates. For instance, the kinase receptor activation (KIRA) assay measures receptor tyrosine kinase activity by ligand stimulating the intact receptor in cultured cells, then capturing solubilized receptor with specific antibodies and quantifying phosphorylation via phosphotyrosine ELISA (Sadick MD, Dev Biol Stand (1999) 97:121-133). Another example of antibody based assays for protein kinase activity is TRF (time-resolved fluorometry). This method utilizes europium chelate-labeled anti-phosphotyrosine antibodies to detect phosphate transfer to a polymeric substrate coated onto microtiter plate wells. The amount of phosphorylation is then detected using time-resolved, dissociation-enhanced fluorescence (Braunwalder AF, *et al.*, Anal Biochem 1996 Jul 1;238(2):159-64). Yet other assays for kinases involve uncoupled, pH sensitive assays that can be used for high-throughput screening of potential inhibitors or for determining

substrate specificity. Since kinases catalyze the transfer of a gamma-phosphoryl group from ATP to an appropriate hydroxyl acceptor with the release of a proton, a pH sensitive assay is based on the detection of this proton using an appropriately matched buffer/indicator system (Chapman E and Wong CH (2002) *Bioorg Med Chem.* 10:551-5).

[0067] Protein phosphatases catalyze the removal of a gamma phosphate from a serine, threonine or tyrosine residue in a protein substrate. Since phosphatases act in opposition to kinases, appropriate assays measure the same parameters as kinase assays. In one example, the dephosphorylation of a fluorescently labeled peptide substrate allows trypsin cleavage of the substrate, which in turn renders the cleaved substrate significantly more fluorescent (Nishikata M *et al.*, *Biochem J* (1999) 343:35-391). In another example, fluorescence polarization (FP), a solution-based, homogeneous technique requiring no immobilization or separation of reaction components, is used to develop high throughput screening (HTS) assays for protein phosphatases. This assay uses direct binding of the phosphatase with the target, and increasing concentrations of target- phosphatase increase the rate of dephosphorylation, leading to a change in polarization (Parker GJ *et al.*, (2000) *J Biomol Screen* 5:77-88).

[0068] Proteases are enzymes that cleave protein substrates at specific sites. Exemplary assays detect the alterations in the spectral properties of an artificial substrate that occur upon protease-mediated cleavage. In one example, synthetic caspase substrates containing four amino acid proteolysis recognition sequences, separating two different fluorescent tags are employed; fluorescence resonance energy transfer detects the proximity of these fluorophores, which indicates whether the substrate is cleaved (Mahajan NP *et al.*, *Chem Biol* (1999) 6:401-409).

[0069] The proteins used in the methods of this invention include enzymes involved in lipid, nucleic acid, and protein metabolism. Many different metabolic enzymes are amenable to high throughput assay development, due to well-characterized substrates and active sites, generally simple reaction mechanisms, and a general conservation in reaction mechanism. Numerous assays for metabolic enzymes (e.g., fatty acid desaturases, glycosyltransferases, mitochondrial enzymes, histone deacetylases, purine biosynthetic enzymes, etc.) have been developed.

[0070] Ubiquitination is a process of attaching ubiquitin to a protein prior to the selective proteolysis of that protein in the cell. Assays based on fluorescence resonance energy transfer to screen for ubiquitination inhibitors are known in the art (Boisclair MD *et al.*, *J Biomol Screen* 2000 5:319-328).

- [0071] G-protein-coupled receptors (GPCRs) comprise a large family of cell surface receptors that mediate a diverse array of biological functions. They selectively respond to a wide variety of extracellular chemical stimuli to activate specific signaling cascades. Assays may measure reporter gene activity or changes in intracellular calcium ions, or other second messengers (Durocher Y *et al.*, Anal Biochem (2000) 284: 316-326; Miller TR *et al.*, J Biomol Screen (1999) 4:249-258). Such assays may utilize chimeric G α proteins that will couple to many different GPCRs and thus facilitate "universal" screening assays (Coward P *et al.*, Anal Biochem (1999) 270:242-248; Milligan G and Rees S *et al.*, Trends Pharmacol Sci (1999) 20:118-124).
- [0072] GPCRs exert their effects through heterotrimeric G proteins, which cycle between active GTP- and inactive GDP-bound forms. Receptors catalyze the activation of G proteins by promoting exchange of GDP for GTP, while G proteins catalyze their own deactivation through their intrinsic GTPase activity. GEFs accelerate GDP dissociation and GTP binding, while GAPs stimulate GTP hydrolysis to GDP. The same assays used to monitor GPCR activity may thus be applied to monitor the activity of GEFs or GAPs. Alternatively, GEF activity may be assayed by the release of labeled GDP from the appropriate GTPase or by the uptake of labelled GTP. GAP activity may be monitored via a GTP hydrolysis assay using labeled GTP (*e.g.*, Jones S *et al.*, Molec Biol Cell (1998) 9:2819-2837).
- [0073] Transporter proteins carry a range of substrates, including nutrients, ions, amino acids, and drugs, across cell membranes. Assays for modulators of transporters may use labeled substrates. For instance, exemplary high throughput screens to identify compounds that interact with different peptide and anion transporters both use fluorescently labeled substrates; the assay for peptide transport additionally uses multiscreen filtration plates (Blevitt JM *et al.*, J Biomol Screen 1999, 4:87-91; Cihlar T and Ho ES, Anal Biochem 2000, 283:49-55).
- [0074] Ion channels mediate essential physiological functions, including fluid secretion, electrolyte balance, bioenergetics, and membrane excitability. Assays for channel activity can incorporate ion-sensitive dyes or proteins or voltage-sensitive dyes or proteins, as reviewed in Gonzalez JE *et al.* (Drug Discovery Today (1999) 4:431-439). Alternative methods measure the displacement of known ligands, which may be radio-labeled or fluorescently labeled (*e.g.*, Schmid EL *et al.*, Anal Chem (1998) 70:1331-1338).
- [0075] Nuclear receptors (NRs) are a superfamily of ligand-dependent transcription factors that mediate the effects of hormones and other endogenous ligands to regulate the

expression of specific genes. High throughput assays for nuclear receptors include fluorescent polarization binding assays (Lin S, et al. (2002) *Anal Biochem* 300(1):15-21), and homogeneous time-resolved fluorescence energy transfer (Zhou G, et al. (2001) *Methods* 25:54-61), among others.

[0076] Hydrolase assays. Hydrolases catalyze the hydrolysis of a substrate such as esterases, lipases, peptidases, nucleotidases, and phosphatases, among others. Enzyme activity assays may be used to measure hydrolase activity. The activity of the enzyme is determined in presence of excess substrate, by spectrophotometrically measuring the rate of appearance of reaction products. High throughput arrays and assays for hydrolases are known to those skilled in the art (Park CB and Clark DS (2002) *Biotech Bioeng* 78:229-235).

[0077] Assays for ATPase activity, such as described in Blackburn et al (Blackburn CL, et al., (1999) *J Org Chem* 64:5565-5570), are known in the art. The ATPase assay is performed using the EnzCheck ATPase kit (Molecular Probes). The assays are performed using an Ultraspec spectrophotometer (Pharmacia), and the progress of the reaction are monitored by absorbance increase at 360 nm.

[0078] High-throughput assays, such as scintillation proximity assays, for synthase enzymes involved in fatty acid synthesis are known in the art (He X et al (2000) *Anal Biochem* 2000 Jun 15;282(1):107-14).

[0079] High throughput adenylyl cyclase assays are known in the art, and are also commercially available (NEN[®] Adenylyl Cyclase Activation FlashPlate[®] Assay, available from Perkin Elmer Life Sciences, Boston, MA). Examples include homogeneous cellular assays that allow direct measurement of receptor-mediated adenylyl cyclase activation/inhibition.

[0080] High throughput intramolecularly quenched fluorescence assays for zinc metallopeptidase have been described. These assays are based on highly sensitive fluorescent substrates (Luciani N et al (2001) *Biochem. J.* 356: 813–819).

[0081] Chemosensor coupled assays for Phosphodiesterases using phosphate chemosensor ensembles have been described (Hans MS and Kim DH (2003) *Bioorg Med Chem Lett.* 13:1079-82).

[0082] Apoptosis assays. Apoptosis or programmed cell death is a suicide program is activated within the cell, leading to fragmentation of DNA, shrinkage of the cytoplasm, membrane changes and cell death. Apoptosis is mediated by proteolytic enzymes of the

caspase family. Many of the altering parameters of a cell are measurable during apoptosis. Assays for apoptosis may be performed by terminal deoxynucleotidyl transferase-mediated digoxigenin-11-dUTP nick end labeling (TUNEL) assay. The TUNEL assay is used to measure nuclear DNA fragmentation characteristic of apoptosis (Lazebnik *et al.*, 1994, *Nature* 371, 346), by following the incorporation of fluorescein-dUTP (Yonehara *et al.*, 1989, *J. Exp. Med.* 169, 1747). Apoptosis may further be assayed by acridine orange staining of tissue culture cells (Lucas, R., et al., 1998, *Blood* 15:4730-41). Other cell-based apoptosis assays include the caspase-3/7 assay and the cell death nucleosome ELISA assay. The caspase 3/7 assay is based on the activation of the caspase cleavage activity as part of a cascade of events that occur during programmed cell death in many apoptotic pathways. In the caspase 3/7 assay (commercially available Apo-ONE™ Homogeneous Caspase-3/7 assay from Promega, cat# 67790), lysis buffer and caspase substrate are mixed and added to cells. The caspase substrate becomes fluorescent when cleaved by active caspase 3/7. The nucleosome ELISA assay is a general cell death assay known to those skilled in the art, and available commercially (Roche, Cat# 1774425). This assay is a quantitative sandwich-enzyme-immunoassay which uses monoclonal antibodies directed against DNA and histones respectively, thus specifically determining amount of mono- and oligonucleosomes in the cytoplasmic fraction of cell lysates. Mono and oligonucleosomes are enriched in the cytoplasm during apoptosis due to the fact that DNA fragmentation occurs several hours before the plasma membrane breaks down, allowing for accumulation in the cytoplasm. Nucleosomes are not present in the cytoplasmic fraction of cells that are not undergoing apoptosis. The Phospho-histone H2B assay is another apoptosis assay, based on phosphorylation of histone H2B as a result of apoptosis. Fluorescent dyes that are associated with phosphohistone H2B may be used to measure the increase of phosphohistone H2B as a result of apoptosis. Apoptosis assays that simultaneously measure multiple parameters associated with apoptosis have also been developed. In such assays, various cellular parameters that can be associated with antibodies or fluorescent dyes, and that mark various stages of apoptosis are labeled, and the results are measured using instruments such as Cellomics™ ArrayScan® HCS System. The measurable parameters and their markers include anti-active caspase-3 antibody which marks intermediate stage apoptosis, anti-PARP-p85 antibody (cleaved PARP) which marks late stage apoptosis, Hoechst labels which label the nucleus and are used to measure nuclear swelling as a measure of early apoptosis and nuclear condensation as a

measure of late apoptosis, and TOTO-3 fluorescent dye which labels DNA of dead cells with high cell membrane permeability.

[0083] An apoptosis assay system may comprise a cell that expresses an MIGFR, and that optionally has defective IGFR function (e.g. IGFR is over-expressed or under-expressed relative to wild-type cells). A test agent can be added to the apoptosis assay system and changes in induction of apoptosis relative to controls where no test agent is added, identify candidate IGFR modulating agents. In some embodiments of the invention, an apoptosis assay may be used as a secondary assay to test a candidate IGFR modulating agents that is initially identified using a cell-free assay system. An apoptosis assay may also be used to test whether MIGFR function plays a direct role in apoptosis. For example, an apoptosis assay may be performed on cells that over- or under-express MIGFR relative to wild type cells. Differences in apoptotic response compared to wild type cells suggests that the MIGFR plays a direct role in the apoptotic response. Apoptosis assays are described further in US Pat. No. 6,133,437.

[0084] Cell proliferation and cell cycle assays. Cell proliferation may be assayed via bromodeoxyuridine (BRDU) incorporation. This assay identifies a cell population undergoing DNA synthesis by incorporation of BRDU into newly-synthesized DNA. Newly-synthesized DNA may then be detected using an anti-BRDU antibody (Hoshino *et al.*, 1986, Int. J. Cancer 38, 369; Campana *et al.*, 1988, J. Immunol. Meth. 107, 79), or by other means.

[0085] Cell proliferation is also assayed via phospho-histone H3 staining, which identifies a cell population undergoing mitosis by phosphorylation of histone H3. Phosphorylation of histone H3 at serine 10 is detected using an antibody specific to the phosphorylated form of the serine 10 residue of histone H3. (Chadlee, D.N. 1995, J. Biol. Chem 270:20098-105). Cell Proliferation may also be examined using [³H]-thymidine incorporation (Chen, J., 1996, Oncogene 13:1395-403; Jeoung, J., 1995, J. Biol. Chem. 270:18367-73). This assay allows for quantitative characterization of S-phase DNA syntheses. In this assay, cells synthesizing DNA will incorporate [³H]-thymidine into newly synthesized DNA. Incorporation can then be measured by standard techniques such as by counting of radioisotope in a scintillation counter (e.g., Beckman LS 3800 Liquid Scintillation Counter). Another proliferation assay uses the dye Alamar Blue (available from Biosource International), which fluoresces when reduced in living cells and provides an indirect measurement of cell number (Voytik-Harbin SL *et al.*, 1998, In Vitro Cell Dev

Biol Anim 34:239-46). Yet another proliferation assay, the MTS assay, is based on in vitro cytotoxicity assessment of industrial chemicals, and uses the soluble tetrazolium salt, MTS. MTS assays are commercially available, for example, the Promega CellTiter 96[®] Aqueous Non-Radioactive Cell Proliferation Assay (Cat.# G5421).

[0086] Cell proliferation may also be assayed by colony formation in soft agar, or clonogenic survival assay (Sambrook et al., Molecular Cloning, Cold Spring Harbor (1989)). For example, cells transformed with MIGFR are seeded in soft agar plates, and colonies are measured and counted after two weeks incubation.

[0087] Cell proliferation may also be assayed by measuring ATP levels as indicator of metabolically active cells. Such assays are commercially available, for example Cell Titer-Glo[™], which is a luminescent homogeneous assay available from Promega.

[0088] Involvement of a gene in the cell cycle may be assayed by flow cytometry (Gray JW et al. (1986) Int J Radiat Biol Relat Stud Phys Chem Med 49:237-55). Cells transfected with an MIGFR may be stained with propidium iodide and evaluated in a flow cytometer (available from Becton Dickinson), which indicates accumulation of cells in different stages of the cell cycle.

[0089] Involvement of a gene in cell cycle may also be assayed by FOXO nuclear translocation assays. The FOXO family of transcription factors are mediators of various cellular functions including cell cycle progression and cell death, and are negatively regulated by activation of the PI3 kinase pathway. Akt phosphorylation of FOXO family members leads to FOXO sequestration in the cytoplasm and transcriptional inactivation (Medema, R. H et al (2000) Nature 404: 782-787). PTEN is a negative regulator of PI3 kinase pathway. Activation of PTEN, or loss of PI3 kinase or AKT, prevents phosphorylation of FOXO, leading to accumulation of FOXO in the nucleus, transcriptional activation of FOXO regulated genes, and apoptosis. Alternatively, loss of PTEN leads to pathway activation and cell survival (Nakamura, N. et al (2000) Mol Cell Biol 20: 8969-8982). FOXO translocation into the cytoplasm is used in assays and screens to identify members and/or modulators of the PTEN pathway. FOXO translocation assays using GFP or luciferase as detection reagents are known in the art (e.g., Zhang X et al (2002) J Biol Chem 277:45276-45284; and Li et al (2003) Mol Cell Biol 23:104-118).

[0090] Accordingly, a cell proliferation or cell cycle assay system may comprise a cell that expresses an MIGFR, and that optionally has defective IGFR function (e.g. IGFR is over-expressed or under-expressed relative to wild-type cells). A test agent can be added to the assay system and changes in cell proliferation or cell cycle relative to controls where

no test agent is added, identify candidate IGFR modulating agents. In some embodiments of the invention, the cell proliferation or cell cycle assay may be used as a secondary assay to test a candidate IGFR modulating agents that is initially identified using another assay system such as a cell-free assay system. A cell proliferation assay may also be used to test whether MIGFR function plays a direct role in cell proliferation or cell cycle. For example, a cell proliferation or cell cycle assay may be performed on cells that over- or under-express MIGFR relative to wild type cells. Differences in proliferation or cell cycle compared to wild type cells suggests that the MIGFR plays a direct role in cell proliferation or cell cycle.

[0091] Angiogenesis. Angiogenesis may be assayed using various human endothelial cell systems, such as umbilical vein, coronary artery, or dermal cells. Suitable assays include Alamar Blue based assays (available from Biosource International) to measure proliferation; migration assays using fluorescent molecules, such as the use of Becton Dickinson Falcon HTS FluoroBlock cell culture inserts to measure migration of cells through membranes in presence or absence of angiogenesis enhancer or suppressors; and tubule formation assays based on the formation of tubular structures by endothelial cells on Matrigel® (Becton Dickinson). Accordingly, an angiogenesis assay system may comprise a cell that expresses an MIGFR, and that optionally has defective IGFR function (e.g. IGFR is over-expressed or under-expressed relative to wild-type cells). A test agent can be added to the angiogenesis assay system and changes in angiogenesis relative to controls where no test agent is added, identify candidate IGFR modulating agents. In some embodiments of the invention, the angiogenesis assay may be used as a secondary assay to test a candidate IGFR modulating agents that is initially identified using another assay system. An angiogenesis assay may also be used to test whether MIGFR function plays a direct role in cell proliferation. For example, an angiogenesis assay may be performed on cells that over- or under-express MIGFR relative to wild type cells. Differences in angiogenesis compared to wild type cells suggests that the MIGFR plays a direct role in angiogenesis. U.S. Pat. Nos. 5,976,782, 6,225,118 and 6,444,434, among others, describe various angiogenesis assays.

[0092] Hypoxic induction. The alpha subunit of the transcription factor, hypoxia inducible factor-1 (HIF-1), is upregulated in tumor cells following exposure to hypoxia in vitro. Under hypoxic conditions, HIF-1 stimulates the expression of genes known to be

important in tumour cell survival, such as those encoding glycolytic enzymes and VEGF. Induction of such genes by hypoxic conditions may be assayed by growing cells transfected with MIGFR in hypoxic conditions (such as with 0.1% O₂, 5% CO₂, and balance N₂, generated in a Napco 7001 incubator (Precision Scientific)) and normoxic conditions, followed by assessment of gene activity or expression by Taqman®. For example, a hypoxic induction assay system may comprise a cell that expresses an MIGFR, and that optionally has defective IGFR function (e.g. IGFR is over-expressed or under-expressed relative to wild-type cells). A test agent can be added to the hypoxic induction assay system and changes in hypoxic response relative to controls where no test agent is added, identify candidate IGFR modulating agents. In some embodiments of the invention, the hypoxic induction assay may be used as a secondary assay to test a candidate IGFR modulating agents that is initially identified using another assay system. A hypoxic induction assay may also be used to test whether MIGFR function plays a direct role in the hypoxic response. For example, a hypoxic induction assay may be performed on cells that over- or under-express MIGFR relative to wild type cells. Differences in hypoxic response compared to wild type cells suggests that the MIGFR plays a direct role in hypoxic induction.

[0093] Cell adhesion. Cell adhesion assays measure adhesion of cells to purified adhesion proteins, or adhesion of cells to each other, in presence or absence of candidate modulating agents. Cell-protein adhesion assays measure the ability of agents to modulate the adhesion of cells to purified proteins. For example, recombinant proteins are produced, diluted to 2.5g/mL in PBS, and used to coat the wells of a microtiter plate. The wells used for negative control are not coated. Coated wells are then washed, blocked with 1% BSA, and washed again. Compounds are diluted to 2× final test concentration and added to the blocked, coated wells. Cells are then added to the wells, and the unbound cells are washed off. Retained cells are labeled directly on the plate by adding a membrane-permeable fluorescent dye, such as calcein-AM, and the signal is quantified in a fluorescent microplate reader.

[0094] Cell-cell adhesion assays measure the ability of agents to modulate binding of cell adhesion proteins with their native ligands. These assays use cells that naturally or recombinantly express the adhesion protein of choice. In an exemplary assay, cells expressing the cell adhesion protein are plated in wells of a multiwell plate. Cells expressing the ligand are labeled with a membrane-permeable fluorescent dye, such as

BCECF, and allowed to adhere to the monolayers in the presence of candidate agents. Unbound cells are washed off, and bound cells are detected using a fluorescence plate reader.

[0095] High-throughput cell adhesion assays have also been described. In one such assay, small molecule ligands and peptides are bound to the surface of microscope slides using a microarray spotter, intact cells are then contacted with the slides, and unbound cells are washed off. In this assay, not only the binding specificity of the peptides and modulators against cell lines are determined, but also the functional cell signaling of attached cells using immunofluorescence techniques in situ on the microchip is measured (Falsey JR et al., *Bioconjug Chem.* 2001 May-Jun;12(3):346-53).

[0096] Tubulogenesis. Tubulogenesis assays monitor the ability of cultured cells, generally endothelial cells, to form tubular structures on a matrix substrate, which generally simulates the environment of the extracellular matrix. Exemplary substrates include MatrigelTM (Becton Dickinson), an extract of basement membrane proteins containing laminin, collagen IV, and heparin sulfate proteoglycan, which is liquid at 4°C and forms a solid gel at 37°C. Other suitable matrices comprise extracellular components such as collagen, fibronectin, and/or fibrin. Cells are stimulated with a pro-angiogenic stimulant, and their ability to form tubules is detected by imaging. Tubules can generally be detected after an overnight incubation with stimuli, but longer or shorter time frames may also be used. Tube formation assays are well known in the art (e.g., Jones MK et al., 1999, *Nature Medicine* 5:1418-1423). These assays have traditionally involved stimulation with serum or with the growth factors FGF or VEGF. Serum represents an undefined source of growth factors. In a preferred embodiment, the assay is performed with cells cultured in serum free medium, in order to control which process or pathway a candidate agent modulates. Moreover, we have found that different target genes respond differently to stimulation with different pro-angiogenic agents, including inflammatory angiogenic factors such as TNF- α . Thus, in a further preferred embodiment, a tubulogenesis assay system comprises testing an MIGFR's response to a variety of factors, such as FGF, VEGF, phorbol myristate acetate (PMA), TNF- α , ephrin, etc.

[0097] Cell Migration. An invasion/migration assay (also called a migration assay) tests the ability of cells to overcome a physical barrier and to migrate towards pro-angiogenic signals. Migration assays are known in the art (e.g., Paik JH et al., 2001, *J Biol Chem*

276:11830-11837). In a typical experimental set-up, cultured endothelial cells are seeded onto a matrix-coated porous lamina, with pore sizes generally smaller than typical cell size. The matrix generally simulates the environment of the extracellular matrix, as described above. The lamina is typically a membrane, such as the transwell polycarbonate membrane (Corning Costar Corporation, Cambridge, MA), and is generally part of an upper chamber that is in fluid contact with a lower chamber containing pro-angiogenic stimuli. Migration is generally assayed after an overnight incubation with stimuli, but longer or shorter time frames may also be used. Migration is assessed as the number of cells that crossed the lamina, and may be detected by staining cells with hemotoxylin solution (VWR Scientific, South San Francisco, CA), or by any other method for determining cell number. In another exemplary set up, cells are fluorescently labeled and migration is detected using fluorescent readings, for instance using the Falcon HTS FluoroBlok (Becton Dickinson). While some migration is observed in the absence of stimulus, migration is greatly increased in response to pro-angiogenic factors. As described above, a preferred assay system for migration/invasion assays comprises testing an MIGFR's response to a variety of pro-angiogenic factors, including tumor angiogenic and inflammatory angiogenic agents, and culturing the cells in serum free medium.

[0098] Sprouting assay. A sprouting assay is a three-dimensional *in vitro* angiogenesis assay that uses a cell-number defined spheroid aggregation of endothelial cells ("spheroid"), embedded in a collagen gel-based matrix. The spheroid can serve as a starting point for the sprouting of capillary-like structures by invasion into the extracellular matrix (termed "cell sprouting") and the subsequent formation of complex anastomosing networks (Korff and Augustin, 1999, J Cell Sci 112:3249-58). In an exemplary experimental set-up, spheroids are prepared by pipetting 400 human umbilical vein endothelial cells into individual wells of a nonadhesive 96-well plates to allow overnight spheroidal aggregation (Korff and Augustin: J Cell Biol 143: 1341-52, 1998). Spheroids are harvested and seeded in 900 μ l of methocel-collagen solution and pipetted into individual wells of a 24 well plate to allow collagen gel polymerization. Test agents are added after 30 min by pipetting 100 μ l of 10-fold concentrated working dilution of the test substances on top of the gel. Plates are incubated at 37°C for 24h. Dishes are fixed at the end of the experimental incubation period by addition of paraformaldehyde. Sprouting intensity of endothelial cells can be quantitated by an automated image analysis system to determine the cumulative sprout length per spheroid.

Primary assays for antibody modulators

- [0099] For antibody modulators, appropriate primary assays test is a binding assay that tests the antibody's affinity to and specificity for the MIGFR protein. Methods for testing antibody affinity and specificity are well known in the art (Harlow and Lane, 1988, 1999, *supra*). The enzyme-linked immunosorbant assay (ELISA) is a preferred method for detecting MIGFR-specific antibodies; others include FACS assays, radioimmunoassays, and fluorescent assays.
- [0100] In some cases, screening assays described for small molecule modulators may also be used to test antibody modulators.

Primary assays for nucleic acid modulators

- [0101] For nucleic acid modulators, primary assays may test the ability of the nucleic acid modulator to inhibit or enhance MIGFR gene expression, preferably mRNA expression. In general, expression analysis comprises comparing MIGFR expression in like populations of cells (*e.g.*, two pools of cells that endogenously or recombinantly express MIGFR) in the presence and absence of the nucleic acid modulator. Methods for analyzing mRNA and protein expression are well known in the art. For instance, Northern blotting, slot blotting, ribonuclease protection, quantitative RT-PCR (*e.g.*, using the TaqMan®, PE Applied Biosystems), or microarray analysis may be used to confirm that MIGFR mRNA expression is reduced in cells treated with the nucleic acid modulator (*e.g.*, Current Protocols in Molecular Biology (1994) Ausubel FM *et al.*, eds., John Wiley & Sons, Inc., chapter 4; Freeman WM *et al.*, Biotechniques (1999) 26:112-125; Kallioniemi OP, Ann Med 2001, 33:142-147; Blohm DH and Guiseppi-Elie, A Curr Opin Biotechnol 2001, 12:41-47). Protein expression may also be monitored. Proteins are most commonly detected with specific antibodies or antisera directed against either the MIGFR protein or specific peptides. A variety of means including Western blotting, ELISA, or in situ detection, are available (Harlow E and Lane D, 1988 and 1999, *supra*).
- [0102] In some cases, screening assays described for small molecule modulators, particularly in assay systems that involve MIGFR mRNA expression, may also be used to test nucleic acid modulators.

3333

Secondary Assays

[0103] Secondary assays may be used to further assess the activity of MIGFR-modulating agent identified by any of the above methods to confirm that the modulating agent affects MIGFR in a manner relevant to the IGFR pathway. As used herein, MIGFR-modulating agents encompass candidate clinical compounds or other agents derived from previously identified modulating agent. Secondary assays can also be used to test the activity of a modulating agent on a particular genetic or biochemical pathway or to test the specificity of the modulating agent's interaction with MIGFR.

[0104] Secondary assays generally compare like populations of cells or animals (*e.g.*, two pools of cells or animals that endogenously or recombinantly express MIGFR) in the presence and absence of the candidate modulator. In general, such assays test whether treatment of cells or animals with a candidate MIGFR-modulating agent results in changes in the IGFR pathway in comparison to untreated (or mock- or placebo-treated) cells or animals. Certain assays use "sensitized genetic backgrounds", which, as used herein, describe cells or animals engineered for altered expression of genes in the IGFR or interacting pathways.

Cell-based assays

[0105] Cell based assays may detect endogenous IGFR pathway activity or may rely on recombinant expression of IGFR pathway components. Any of the aforementioned assays may be used in this cell-based format. Candidate modulators are typically added to the cell media but may also be injected into cells or delivered by any other efficacious means.

Animal Assays

[0106] A variety of non-human animal models of normal or defective IGFR pathway may be used to test candidate MIGFR modulators. Models for defective IGFR pathway typically use genetically modified animals that have been engineered to mis-express (*e.g.*, over-express or lack expression in) genes involved in the IGFR pathway. Assays generally require systemic delivery of the candidate modulators, such as by oral administration, injection, etc.

[0107] In a preferred embodiment, IGFR pathway activity is assessed by monitoring neovascularization and angiogenesis. Animal models with defective and normal IGFR are used to test the candidate modulator's affect on MIGFR in Matrigel® assays. Matrigel®

is an extract of basement membrane proteins, and is composed primarily of laminin, collagen IV, and heparin sulfate proteoglycan. It is provided as a sterile liquid at 4°C, but rapidly forms a solid gel at 37°C. Liquid Matrigel® is mixed with various angiogenic agents, such as bFGF and VEGF, or with human tumor cells which over-express the MIGFR. The mixture is then injected subcutaneously(SC) into female athymic nude mice (Taconic, Germantown, NY) to support an intense vascular response. Mice with Matrigel® pellets may be dosed via oral (PO), intraperitoneal (IP), or intravenous (IV) routes with the candidate modulator. Mice are euthanized 5 - 12 days post-injection, and the Matrigel® pellet is harvested for hemoglobin analysis (Sigma plasma hemoglobin kit). Hemoglobin content of the gel is found to correlate the degree of neovascularization in the gel.

[0108] In another preferred embodiment, the effect of the candidate modulator on MIGFR is assessed via tumorigenicity assays. Tumor xenograft assays are known in the art (see, e.g., Ogawa K et al., 2000, *Oncogene* 19:6043-6052). Xenografts are typically implanted SC into female athymic mice, 6-7 week old, as single cell suspensions either from a pre-existing tumor or from *in vitro* culture. The tumors which express the MIGFR endogenously are injected in the flank, 1×10^5 to 1×10^7 cells per mouse in a volume of 100 µL using a 27gauge needle. Mice are then ear tagged and tumors are measured twice weekly. Candidate modulator treatment is initiated on the day the mean tumor weight reaches 100 mg. Candidate modulator is delivered IV, SC, IP, or PO by bolus administration. Depending upon the pharmacokinetics of each unique candidate modulator, dosing can be performed multiple times per day. The tumor weight is assessed by measuring perpendicular diameters with a caliper and calculated by multiplying the measurements of diameters in two dimensions. At the end of the experiment, the excised tumors may be utilized for biomarker identification or further analyses. For immunohistochemistry staining, xenograft tumors are fixed in 4% paraformaldehyde, 0.1M phosphate, pH 7.2, for 6 hours at 4°C, immersed in 30% sucrose in PBS, and rapidly frozen in isopentane cooled with liquid nitrogen.

[0109] In another preferred embodiment, tumorigenicity is monitored using a hollow fiber assay, which is described in U.S. Pat No. US 5,698,413. Briefly, the method comprises implanting into a laboratory animal a biocompatible, semi-permeable encapsulation device containing target cells, treating the laboratory animal with a candidate modulating agent, and evaluating the target cells for reaction to the candidate modulator. Implanted cells are generally human cells from a pre-existing tumor or a tumor cell line. After an appropriate

period of time, generally around six days, the implanted samples are harvested for evaluation of the candidate modulator. Tumorigenicity and modulator efficacy may be evaluated by assaying the quantity of viable cells present in the macrocapsule, which can be determined by tests known in the art, for example, MTT dye conversion assay, neutral red dye uptake, trypan blue staining, viable cell counts, the number of colonies formed in soft agar, the capacity of the cells to recover and replicate in vitro, etc.

[0110] In another preferred embodiment, a tumorigenicity assay use a transgenic animal, usually a mouse, carrying a dominant oncogene or tumor suppressor gene knockout under the control of tissue specific regulatory sequences; these assays are generally referred to as transgenic tumor assays. In a preferred application, tumor development in the transgenic model is well characterized or is controlled. In an exemplary model, the "RIP1-Tag2" transgene, comprising the SV40 large T-antigen oncogene under control of the insulin gene regulatory regions is expressed in pancreatic beta cells and results in islet cell carcinomas (Hanahan D, 1985, Nature 315:115-122; Parangi S et al, 1996, Proc Natl Acad Sci USA 93: 2002-2007; Bergers G et al, 1999, Science 284:808-812). An "angiogenic switch," occurs at approximately five weeks, as normally quiescent capillaries in a subset of hyperproliferative islets become angiogenic. The RIP1-TAG2 mice die by age 14 weeks. Candidate modulators may be administered at a variety of stages, including just prior to the angiogenic switch (e.g., for a model of tumor prevention), during the growth of small tumors (e.g., for a model of intervention), or during the growth of large and/or invasive tumors (e.g., for a model of regression). Tumorigenicity and modulator efficacy can be evaluating life-span extension and/or tumor characteristics, including number of tumors, tumor size, tumor morphology, vessel density, apoptotic index, etc.

Diagnostic and therapeutic uses

[0111] Specific MIGFR-modulating agents are useful in a variety of diagnostic and therapeutic applications where disease or disease prognosis is related to defects in the IGFR pathway, such as angiogenic, apoptotic, or cell proliferation disorders. Accordingly, the invention also provides methods for modulating the IGFR pathway in a cell, preferably a cell pre-determined to have defective or impaired IGFR function (e.g. due to overexpression, underexpression, or misexpression of IGFR, or due to gene mutations), comprising the step of administering an agent to the cell that specifically modulates MIGFR activity. Preferably, the modulating agent produces a detectable phenotypic change in the cell indicating that the IGFR function is restored. The phrase "function is

restored”, and equivalents, as used herein, means that the desired phenotype is achieved, or is brought closer to normal compared to untreated cells. For example, with restored IGFR function, cell proliferation and/or progression through cell cycle may normalize, or be brought closer to normal relative to untreated cells. The invention also provides methods for treating disorders or disease associated with impaired IGFR function by administering a therapeutically effective amount of an MIGFR -modulating agent that modulates the IGFR pathway. The invention further provides methods for modulating MIGFR function in a cell, preferably a cell pre-determined to have defective or impaired MIGFR function, by administering an MIGFR -modulating agent. Additionally, the invention provides a method for treating disorders or disease associated with impaired MIGFR function by administering a therapeutically effective amount of an MIGFR -modulating agent. The discovery that MIGFR is implicated in IGFR pathway provides for a variety of methods that can be employed for the diagnostic and prognostic evaluation of diseases and disorders involving defects in the IGFR pathway and for the identification of subjects having a predisposition to such diseases and disorders.

[0112] Various expression analysis methods can be used to diagnose whether MIGFR expression occurs in a particular sample, including Northern blotting, slot blotting, ribonuclease protection, quantitative RT-PCR, and microarray analysis. (*e.g.*, Current Protocols in Molecular Biology (1994) Ausubel FM *et al.*, eds., John Wiley & Sons, Inc., chapter 4; Freeman WM *et al.*, Biotechniques (1999) 26:112-125; Kallioniemi OP, Ann Med 2001, 33:142-147; Blohm and Guiseppi-Elie, Curr Opin Biotechnol 2001, 12:41-47). Tissues having a disease or disorder implicating defective IGFR signaling that express an MIGFR, are identified as amenable to treatment with an MIGFR modulating agent. In a preferred application, the IGFR defective tissue overexpresses an MIGFR relative to normal tissue. For example, a Northern blot analysis of mRNA from tumor and normal cell lines, or from tumor and matching normal tissue samples from the same patient, using full or partial MIGFR cDNA sequences as probes, can determine whether particular tumors express or overexpress MIGFR. Alternatively, the TaqMan® is used for quantitative RT-PCR analysis of MIGFR expression in cell lines, normal tissues and tumor samples (PE Applied Biosystems).

[0113] Various other diagnostic methods may be performed, for example, utilizing reagents such as the MIGFR oligonucleotides, and antibodies directed against an MIGFR, as described above for: (1) the detection of the presence of MIGFR gene mutations, or the detection of either over- or under-expression of MIGFR mRNA relative to the non-

disorder state; (2) the detection of either an over- or an under-abundance of MIGFR gene product relative to the non-disorder state; and (3) the detection of perturbations or abnormalities in the signal transduction pathway mediated by MIGFR.

[0114] Kits for detecting expression of MIGFR in various samples, comprising at least one antibody specific to MIGFR, all reagents and/or devices suitable for the detection of antibodies, the immobilization of antibodies, and the like, and instructions for using such kits in diagnosis or therapy are also provided.

[0115] Thus, in a specific embodiment, the invention is drawn to a method for diagnosing a disease or disorder in a patient that is associated with alterations in MIGFR expression, the method comprising: a) obtaining a biological sample from the patient; b) contacting the sample with a probe for MIGFR expression; c) comparing results from step (b) with a control; and d) determining whether step (c) indicates a likelihood of the disease or disorder. Preferably, the disease is cancer. The probe may be either DNA or protein, including an antibody.

EXAMPLES

[0116] The following experimental section and examples are offered by way of illustration and not by way of limitation.

I. Drosophila IGFR overexpression screen

[0117] A dominant loss of function screen was carried out in *Drosophila* to identify genes that interact with or modulate the IGFR signaling pathway. Activation of the pathway by overexpression of IGFR at early stages in the developing *Drosophila* eye leads to an increase in cell number which results in a larger and rougher adult eye (Potter CJ et al. (2001) Cell 105:357-368; Huang et al., 1999. Dev. 126:5365-5372). We generated a fly stock with an enlarged eye due to overexpression of IGFR and identified modifiers of this phenotype. We then identified human orthologues of these modifiers.

[0118] The screening stock carried two transgenes. The genotype is as follows:

[0119] +; +; P{DmIGFR-pExp-UAS} P{Gal4-pExp-1Xey}/TM6B

Screening stock females of the above genotype were crossed to males from a collection of 3 classes of piggyBac-based transposons. The resulting progeny, which contain both the transgenes and the transposon, were scored for the effect of the transposon on the eye overgrowth phenotype (either enhancement, suppression

or no effect). All data was recorded and all modifiers were retested with a repeat of the original cross.

II. Analysis of Table 1

[0120] BLAST analysis (Altschul et al., *supra*) was employed to identify orthologs of *Drosophila* modifiers. The columns “MIGFR symbol”, and “MIGFR name aliases” provide a symbol and the known name abbreviations for the Targets, where available, from Genbank. “MIGFR RefSeq_NA or GI_NA”, “MIGFR GI_AA”, “MIGFR NAME”, and “MIGFR Description” provide the reference DNA sequences for the MIGFRs as available from National Center for Biology Information (NCBI), MIGFR protein Genbank identifier number (GI#), MIGFR name, and MIGFR description, all available from Genbank, respectively. The length of each amino acid is in the “MIGFR Protein Length” column.

[0121] Names and Protein sequences of *Drosophila* modifiers of IGFR from screen (Example I), are represented in the “Modifier Name” and “Modifier GI_AA” column by GI#, respectively.

Table1

MIGFR symbol	MIGFR name aliases	MIGFR RefSeq_NA or GI_NA	NA SE Q ID NO	MIGFR GI_AA	AA SE Q ID NO	MIGFR name	MIGFR description	MIGFR protein length	Modifier name	Modifier gi_aa
NOS3	nitric oxide synthase 3 (endothelial cell) ECNOS eNOS NOS3	NM_000603	1	40254422	60	nitric oxide synthase 3 (endothelial cell)	nitric oxide synthase; electron transporter; apoptosis inhibitor	1203	Nos	24583543
PRKAG1	AMPK gamma 1 PRKAG1 Protein kinase, AMP-activated, noncatalytic, gamma-1 protein kinase, AMP-activated, gamma 1 non-catalytic subunit	NM_002733	2	4506061	62	protein kinase, AMP-activated, gamma 1 non-catalytic subunit	protein kinase; protein serine/threonine kinase; protein binding	331	SNF4 Agamma	24648661

PRKAG2	AAKG AAKG2 H91620P H91620p protein PRKAG2 WPWS protein kinase, AMP-activated, gamma 2 non-catalytic subunit	NM_016203	3	33186925	63	protein kinase, AMP-activated, gamma 2 non-catalytic subunit	SNF1A/AM P-activated protein kinase; AMP binding	569	SNF4 Agamma	24648661
PRKAG3	AMPK gamma 3 protein kinase, AMP-activated, gamma 3 non-catalytic subunit PRKAG3	NM_017431	4	8394044	64	protein kinase, AMP-activated, gamma 3 non-catalytic subunit	nucleotide binding; protein binding; SNF1A/AM P-activated protein kinase	492	SNF4 Agamma	24648661
NOS2A	HEP-NOS INOS NOS, type II NOS2 NOS2A nitric oxide synthase 2A (inducible, hepatocytes) nitric oxide synthase, macrophage	NM_000625 NM_153292	5	24041029	65	nitric oxide synthase 2A (inducible, hepatocytes)	calcium channel inhibitor; nitric oxide synthase; calmodulin binding; electron transporter; antiviral response protein	1153	Nos	24583543
NOS1	nitric oxide synthase 1 (neuronal) NOS NOS1	NM_000620	6	10835173	66	nitric oxide synthase 1 (neuronal)	nitric oxide synthase; electron transporter	1434	Nos	24583543
KIAA1815	FLJ23309 KIAA1815	XM_291315	7	37540252	67	KIAA1815	na	904	CG11961	24655610
POMT1	POMT1 RT protein-O-mannosyltransferase 1	NM_007171	8	21361382	68	protein-O-mannosyltransferase 1	mannosyltransferase	747	rt	10727985
PTPRN	IA-2 IA-2/PTP IA2 ICA512 PTPRN R-PTP-N islet cell antigen 2 islet cell antigen 512 islet cell autoantigen 3 protein tyrosine phosphatase, receptor type, N protein	NM_002846	9	4506321	69	protein tyrosine phosphatase, receptor type, N	transmembrane receptor protein tyrosine phosphatase; transmembrane receptor protein tyrosine phosphatase	979	ia2	24580758

	tyrosine phosphatase-like N precursor									
PTPRN2	IA-2beta IAR IAR PTPRP IAR/receptor-like protein-tyrosine phosphatase IC AAR KIAA0387 PHOGRIN PTPRN2 PTPRP phogrin protein tyrosine phosphatase receptor pi protein tyrosine phosphatase, receptor type, N polypeptide 2 tyrosine phosphatase IA-2 beta	NM_002847 NM_130843	10	11386149	70	protein tyrosine phosphatase, receptor type, N polypeptide 2	transmembrane receptor protein tyrosine phosphatase	1015	ia2	24580758
SYNJ1	INPP5G SYNJ1 inositol 5'-phosphatase (synaptojanin 1) synaptojanin 1 synaptojanin-1, polyphosphoinositide phosphatase	NM_003895	11	4507335	71	synaptojanin 1	polyphosphoinositide phosphatase; inositol-1,4,5-trisphosphate 5-phosphatase	1575	synaptojanin	18497296
SYNJ2	INPP5H SYNJ2 inositol phosphate 5'-phosphatase 2 (synaptojanin 2) synaptojanin 2	NM_003898	12	26190608	72	synaptojanin 2	protein binding; inositol/phosphatidylinositol phosphatase; inositol-1,4,5-trisphosphate 5-phosphatase	1496	synaptojanin	18497296

LOC284767	na similar to dJ680N4.2 (ubiquitin-conjugating enzyme E2D 3 (homologous to yeast UBC4/5)) LOC284767	XM_209367	13	27485630	73	similar to dJ680N4.2 (ubiquitin-conjugating enzyme E2D 3 (homologous to yeast UBC4/5))	na	147	eff	24646906
LOC51619	ubiquitin-conjugating enzyme HBUCE1 LOC51619	NM_015983	14	8393719	74	ubiquitin-conjugating enzyme HBUCE1	ubiquitin conjugating enzyme;	147	eff	24646906
UBE2D2	ubiquitin-conjugating enzyme E2D 2 (UBC4/5 homolog, yeast) ubiquitin-conjugating enzyme E2-17 kDa 2 ubiquitin carrier protein E2(17) KB2 UBCH5B UBC4/5 PUB C1 UBC4 UBE2D2	NM_003339 NM_181838	15	33188456	75	ubiquitin-conjugating enzyme E2D 2 (UBC4/5 homolog, yeast)	ubiquitin conjugating enzyme;	118	eff	24646906
UBE2D3	ubiquitin-conjugating enzyme E2D 3 (UBC4/5 homolog, yeast) ubiquitin-conjugating enzyme E2-17 kDa 3 ubiquitin carrier protein E2(17) KB3 MGC43926 MGC5416 UBCH5C UBC4/5 UBE2D3	NM_003340 NM_181886 NM_181887 NM_181888 NM_181889 NM_181890 NM_181891 NM_181892 NM_181893	16	33149322	76	ubiquitin-conjugating enzyme E2D 3 (UBC4/5 homolog, yeast)	ubiquitin conjugating enzyme	148	eff	24646906
LOC378372	LOC378372 na similar to dopamine beta-hydroxylase-like	XM_353788	17	37539365	77	similar to dopamine beta-hydroxylase-like	na	451	olf413	28574720

MOXD 1	DKFZP564G2 02 MOX MOX D1 dJ248E1.1 monooxygenas e, DBH-like 1	NM_0155 29	18	37183305	78	monoox ygenase , DBH- like 1	dopamine- beta- monooxygen ase; copper binding; monooxygen ase	613	olf41 3	28574720
ATP2A 1	ATP2A1 ATP 2A SERCA1 c alcium pump 1 SR Ca(2+)- ATPase 1 endoplasmic reticulum class 1/2 Ca(2+) ATPase sarcop lasmic/endopla smic reticulum calcium ATPase 1 calcium- transporting ATPase sarcoplasmic reticulum type, fast twitch skeletal muscle isoform ATPas e, Ca++ transporting, cardiac muscle, fast twitch 1	NM_0043 20 NM_17 3201	19	31873280	79	ATPase, Ca++ transport ing, cardiac muscle, fast twitch 1	ATPase; calcium- transporting ATPase	1054	Ca- P60A	17136664
ATP2A 2	ATP2A2 DD DAR ATP2B S ERCA2 MGC4 5367 calcium pump 2 SR Ca(2+)- ATPase 2 endoplasmic reticulum class 1/2 Ca(2+) ATPase sarcop lasmic/endopla smic reticulum calcium ATPase 2 ATPase, Ca++ dependent, slow-twitch, cardiac muscle- 2 calcium- transporting ATPase sarcoplasmic reticulum type, slow twitch skeletal muscle	NM_0016 81 NM_17 0665	20	24638454	80	ATPase, Ca++ transport ing, cardiac muscle, slow twitch 2	calcium- transporting ATPase; calcium- transporting ATPase	1042	Ca- P60A	17136664

	isoform ATPase, Ca ⁺⁺ transporting, cardiac muscle, slow twitch 2									
ATP2A3	ATP2A3 SERCA3 calcium pump 3 SR Ca(2+)-ATPase 3 adenosine triphosphatase, calcium calcium-translocating P-type ATPase ATPase, Ca(2+)-transporting, ubiquitous sarcoplasmic/endoplasmic reticulum Ca ²⁺ -ATPase sarcoplasmic/endoplasmic reticulum calcium ATPase 3 ATPase, Ca ⁺⁺ transporting, ubiquitous	NM_005173 NM_174953 NM_174954 NM_174955 NM_174956 NM_174957 NM_174958	21	28373105	81	ATPase, Ca ⁺⁺ transporting, ubiquitous	ATPase; calcium-transporting ATPase; calcium-transporting ATPase	1052	Ca-P60A	17136664
BG1	BG1 BGM FLJ30320 MGC14352 bubblegum very long-chain acyl-CoA synthetase lipidosis	NM_015162	22	27477105	82	lipidosis	acyl-CoA ligase	724	bgm	17933690

BGR	BGR PRTD-NY3 DKFZp434K1635 bubbl legum related protein	NM_030924	23	21359960	83	bubbl egum related protein	transferase, transferring acyl groups; long-chain-fatty-acid-CoA-ligase; AMP binding	666	bgm	17933690
CCS	CCS copper chaperone for superoxide dismutase	NM_005125	24	21429608	84	copper chaperone for superoxide dismutase	intracellular copper transporter; intracellular copper transporter; intracellular copper transporter; superoxide dismutase copper chaperone; superoxide dismutase copper chaperone; copper binding; copper binding	274	CCS	24652342
RYK	hydroxyaryl-protein kinase RYK1 RYK receptor-like tyrosine kinase RYK D3S3195	NM_002958	25	11863159	85	RYK receptor-like tyrosine kinase	protein kinase; transmembrane receptor protein tyrosine kinase; transmembrane receptor protein tyrosine kinase; protein kinase binding	604	dnt	24585175
KPNA1	KPNA1 RCH2 SRP1 IPOA5 NPI-1 importin alpha 5 importin-alpha-S1 karyopherin alpha 1 (importin alpha 5)	NM_002264	26	4504895	86	karyopherin alpha 1 (importin alpha 5)	protein binding; nuclear localization sequence binding; nuclear localization sequence binding; nuclear localization sequence binding	538	Kap-alpha 1	17737655

KPNA5	KPNA5 SRP6 IPOA6 importin alpha 6 karyopherin alpha 5 (importin alpha 6)	NM_002269	27	39812229	87	karyopherin alpha 5 (importin alpha 6)	na	539	Kap-alpha 1	17737655
KPNA6	KPNA6 IPOA7 KPNA7 FLJ11249 MGC17918 importin-alpha-S2 importin alpha 7 subunit karyopherin alpha 6 (importin alpha 7)	NM_012316	28	6912478	88	karyopherin alpha 6 (importin alpha 7)	na	536	Kap-alpha 1	17737655
ECE1	endothelin converting enzyme 1 ECE ECE1 3.4.24.71	NM_001397	29	4503443	89	endothelin converting enzyme 1	metallopeptidase; metalloendopeptidase; endothelin-converting enzyme 1	770	Nep2	17737761
ECE2	ECE2 KIAA0604 endothelin converting enzyme 2	NM_014693	30	7662200	90	endothelin converting enzyme 2	endothelin-converting enzyme; metallopeptidase; metalloendopeptidase	765	Nep2	17737761
ECEL1	ECEL1 XCE CEX X converting enzyme endothelin converting enzyme-like 1	NM_004826	31	4758232	91	endothelin converting enzyme-like 1	metallopeptidase; zinc binding	775	Nep2	17737761
KEL	KEL Kell blood group	NM_000420	32	4557691	92	Kell blood group	endothelin-converting enzyme; metalloendopeptidase; neprilysin; endopeptidase	732	Nep2	17737761
MME	membrane metallo-endopeptidase (neutral endopeptidase, enkephalinase, CALLA, CD10) neprilysin CALLA CD10 NEP MME 3.4.24.11	NM_000902 NM_007287 NM_007288 NM_007289	33	6042202	93	membrane metallo-endopeptidase (neutral endopeptidase, enkephalinase, CALLA, CD10)	metallopeptidase; metallopeptidase; endopeptidase	750	Nep2	17737761

MMEL2	MMEL2 NL2 zinc metalloproteinase membrane metallo-endopeptidase-like 2	NM_033467	34	15991813	94	membrane metallo-endopeptidase-like 2	metalloendopeptidase	770	Nep2	17737761
PHEX	phosphate regulating endopeptidase homolog, X-linked (hypophosphatemia, vitamin D resistant rickets) phosphate regulating gene with homologies to endopeptidases on the X chromosome (hypophosphatemia, vitamin D resistant rickets) Phosphate regulating gene with homologies to endopeptidases on the X chromosome (hypophosphatemia, vitamin D resistant rickets) HPDR1 HYP1 HPDR XLH PEX HYP PHEX phosphate regulating gene with homologies to endopeptidases on the X chromosome	NM_000444	35	40254424	95	phosphate regulating endopeptidase homolog, X-linked (hypophosphatemia, vitamin D resistant rickets)	metalloendopeptidase; metalloendopeptidase; endopeptidase; zinc binding	749	Nep2	17737761
MTHFR	MTHFR Methylenetetrahydrofolate reductase 5,10-methylenetetrahydrofolate reductase (NADPH)	NM_005957	36	40254829	96	5,10-methylenetetrahydrofolate reductase (NADPH)	electron transporter; methylenetetrahydrofolate reductase (NADPH); methylenetetrahydrofolate reductase (NADPH)	65660	CG7560	24662658
GLA	GLA GALA galactosidase, alpha	NM_000169	37	178246	97	galactosidase, alpha	alpha-galactosidase	403	CG5731	24583253

NAGA	3.2.1.49 NAG A GALB D22S 674 Acetylgalactosaminidase, alpha-N-(alpha-galactosidase B) N-acetylgalactosaminidase, alpha-[alpha-N-acetylgalactosaminidase	NM_000262	38	4557781	98	N-acetylgalactosaminidase, alpha-	alpha-N-acetylgalactosaminidase; alpha-N-acetylgalactosaminidase	411	CG5731	24583253
PDE10A	PDE10A phosphodiesterase 10A	NM_006661	39	5729972	99	phosphodiesterase 10A	cAMP-specific phosphodiesterase; 3',5'-cyclic-nucleotide phosphodiesterase; 3',5'-cyclic-nucleotide phosphodiesterase; cGMP-specific phosphodiesterase	779	Pde11	24584985
PDE2A	PDE2A Human cGMP-stimulated 3',5'-cyclic nucleotide phosphodiesterase PDE2A3 (PDE2A) mRNA, complete cds phosphodiesterase 2A, cGMP-stimulated	NM_002599	40	4505657	100	phosphodiesterase 2A, cGMP-stimulated	cGMP-stimulated cyclic-nucleotide phosphodiesterase	941	Pde11	24584985
PDE5A	PDE5A CN5A PDE5 PDE5A1 CGB-PDE cGMP-binding cGMP-specific 3',5'-cyclic nucleotide phosphodiesterase phosphodiesterase 5A, cGMP-specific	NM_001083 NM_033430 NM_033431 NM_033437	41	15812216	101	phosphodiesterase 5A, cGMP-specific	cyclic nucleotide binding; cGMP-specific phosphodiesterase	823	Pde11	24584985

PDE6A	PDE6A PDEA CGPR-A phosphodiesterase 6A, cGMP-specific, rod, alpha	NM_000440	42	4585864	102	phosphodiesterase 6A, cGMP-specific, rod, alpha	cGMP-specific phosphodiesterase; cGMP-specific phosphodiesterase	860	Pde11	24584985
PDE6B	PDE6B PDEB CSNB3 phosphodiesterase 6B, cGMP-specific, rod, beta (congenital stationary night blindness 3, autosomal dominant)	NM_000283	43	4505669	103	phosphodiesterase 6B, cGMP-specific, rod, beta (congenital stationary night blindness 3, autosomal dominant)	cGMP-specific phosphodiesterase; cGMP-specific phosphodiesterase	854	Pde11	24584985
PDE6C	PDE6C PDEA2 phosphodiesterase 6C, cGMP-specific, cone, alpha prime	NM_006204	44	21361308	104	phosphodiesterase 6C, cGMP-specific, cone, alpha prime	cGMP-specific phosphodiesterase; cGMP-specific phosphodiesterase	858	Pde11	24584985
PHLDB1	PHLDB1 LL5A FLJ00141 KIAA0638 LL5a phal pleckstrin homology-like domain, family B, member 1	NM_015157 XM_290497	45	38424073	105	pleckstrin homology-like domain, family B, member 1	na	1377	CG5004	24642721
SLC26A11	SLC26A11 MGC46523 solute carrier family 26, member 11	NM_173626	46	27734748	106	solute carrier family 26, member 11	na	589	Esp	24649801
SLC8A1	SLC8A1 NCX1 solute carrier family 8 (sodium-calcium exchanger), member 1 Solute carrier family 8, member 1 (sodium-calcium	NM_021097	47	10863913	107	solute carrier family 8 (sodium/calcium exchanger), member 1	calcium ion transporter; sodium transporter	973	Calx	24648584

	exchanger-1) solute carrier family 8 (sodium/calcium exchanger), member 1									
SLC8A2	SLC8A2 NCX2 KIAA1087 DKFZp761D171 sodium-calcium exchanger 2 Na+/Ca2+-exchanging protein Nac2 solute carrier family 8 (sodium-calcium exchanger), member 2	5689510	48	5689511	108	solute carrier family 8 (sodium-calcium exchanger), member 2	cation transporter	952	Calx	24648584
SLC8A3	SLC8A3 NCX3 sodium-calcium exchanger 3 Na+/Ca2+ exchanger isoform 3 Na(+)/Ca(2+)-exchange protein 3 sodium-calcium exchanger form 3 sodium/calcium exchanger SLC8A3 solute carrier family 8 (sodium-calcium exchanger), member 3	NM_033262 NM_058240 NM_182932 NM_182933 NM_182936 NM_183002	49	17865805	109	solute carrier family 8 (sodium-calcium exchanger), member 3	porter; calcium:sodium antiporter; transporter	924	Calx	24648584
TPH1	TPH1 TPH1 TPRH tryptophan 5-monooxygenase tryptophan hydroxylase 1 (tryptophan 5-monooxygenase)	NM_004179	50	4759248	110	tryptophan 5-hydroxylase 1 (tryptophan 5-monooxygenase)	tryptophan 5-monooxygenase; tryptophan 5-monooxygenase	444	CG9122	24654994

TPH2	TPH2 NTPH F LJ37295 neuro nal tryptophan hydroxylase tr yptophan hydroxylase 2	NM_1733 53	51	31795563	111	tryptophan hydroxy lase 2	na	490	CG91 22	24654994
UNC93 A	UNC93A dJ36 6N23.1 dJ366 N23.2 unc-93 homolog A (C. elegans)	NM_0189 74	52	29336077	112	unc-93 homolo g A (C. elegans)	na	457	CG21 21	19921816
UNC93 B1	UNC93B1 UN C93 UNC93B unc-93 related protein unc93 (C.elegans) homolog B unc-93 homolog B1 (C. elegans)	NM_0309 30	53	13569893	113	unc-93 homolo g B1 (C. elegans)	na	597	CG21 21	19921816
IDH1	IDH1 IDH IDP PICD NADP+ -specific ICDH oxalosu ccinate decarboxylase NADP- dependent isocitrate dehydrogenase , cytosolic NAD P-dependent isocitrate dehydrogenase , peroxisomal is ocitrate dehydrogenase 1 (NADP+), soluble	NM_0058 96	54	28178825	114	isocitrat e dehydro genase 1 (NADP +), soluble	electron transporter; isocitrate dehydrogena se (NADP+)	414	Idh	24660860
IDH2	IDH2 IDH IDP IDHM ICD- M mNADP- IDH NADP+- specific ICDH oxalosu ccinate decarboxylase isocitrate dehydrogenase , mitochondrial i socitrate dehydrogenase 2 (NADP+), mitochondrial	NM_0021 68	55	28178832	115	isocitrat e dehydro genase 2 (NADP +), mitocho ndrial	electron transporter; isocitrate dehydrogena se (NADP+)	452	Idh	24660860

ACVR1 B	serine(threonine) protein kinase receptor R2 serine(threonine) protein kinase activin receptor-like kinase 4 activin A receptor, type II-like kinase 4 activin A receptor, type IB SKR2 ALK4 ACVRLK4 ACVR1B ACTRIB	NM_004302 NM_020327 NM_020328	56	4757720	116	activin A receptor, type IB	transmembrane receptor protein serine/threonine kinase; transmembrane receptor protein serine/threonine kinase	505	babo	17136928
ACVR1 C	similar to transforming growth factor, beta receptor I (activin A receptor type II-like kinase, 53kD) activin receptor-like kinase 7 activin A receptor, type IC ALK7 ACVRLK7 ACVR1C	NM_145259	57	21687098	117	activin A receptor, type IC	transmembrane receptor protein serine/threonine kinase; transforming growth factor-beta receptor	493	babo	17136928
TGFBR 1	ALK-5 ACVRLK4 transforming growth factor, beta receptor I (activin A receptor type II-like kinase, 53kD) TGFBR1 transforming growth factor, beta receptor I (activin A receptor type II-like kinase, 53kDa) TGFBR1 activin A receptor type II-like kinase, 53kD	NM_004612	58	4759226	118	transforming growth factor, beta receptor I (activin A receptor type II-like kinase, 53kDa)	type I transforming growth factor-beta receptor; type I transforming growth factor-beta receptor; enzyme binding; enzyme binding; receptor signaling protein serine/threonine kinase; receptor signaling protein serine/threonine kinase; transmembrane receptor	503	babo	17136928

KIAA0935	KIAA0935 epididymis-specific alpha-mannosidase precursor mannosidase alpha class 2B member 2	XM_052620	59	22042434	119	mannosidase alpha class 2B member 2	alpha-mannosidase ; mannosidase ; hydrolase, hydrolyzing O-glycosyl compounds	1009	CG6206	19921088
LMLN	leishmanolysin-like (metallopeptidase M8 family) leishmanolysin-2 Gp63 Msp LMLN	NM_033029	60	14719422	120	leishmanolysin-like (metallopeptidase M8 family)	metalloendopeptidase	655	l(3)IX-14	21357023

IV. High-Throughput In Vitro Fluorescence Polarization Assay

[0122] Fluorescently-labeled MIGFR peptide/substrate are added to each well of a 96-well microtiter plate, along with a test agent in a test buffer (10 mM HEPES, 10 mM NaCl, 6 mM magnesium chloride, pH 7.6). Changes in fluorescence polarization, determined by using a Fluorolite FPM-2 Fluorescence Polarization Microtiter System (Dynatech Laboratories, Inc), relative to control values indicates the test compound is a candidate modifier of MIGFR activity.

V. High-Throughput In Vitro Binding Assay.

[0123] ³³P-labeled MIGFR peptide is added in an assay buffer (100 mM KCl, 20 mM HEPES pH 7.6, 1 mM MgCl₂, 1% glycerol, 0.5% NP-40, 50 mM beta-mercaptoethanol, 1 mg/ml BSA, cocktail of protease inhibitors) along with a test agent to the wells of a Neutralite-avidin coated assay plate and incubated at 25°C for 1 hour. Biotinylated substrate is then added to each well and incubated for 1 hour. Reactions are stopped by washing with PBS, and counted in a scintillation counter. Test agents that cause a difference in activity relative to control without test agent are identified as candidate IGFR modulating agents.

VI. Immunoprecipitations and Immunoblotting

[0124] For coprecipitation of transfected proteins, 3 × 10⁶ appropriate recombinant cells containing the MIGFR proteins are plated on 10-cm dishes and transfected on the following day with expression constructs. The total amount of DNA is kept constant in each transfection by adding empty vector. After 24 h, cells are collected, washed once with phosphate-buffered saline and lysed for 20 min on ice in 1 ml of lysis buffer

containing 50 mM Hepes, pH 7.9, 250 mM NaCl, 20 mM -glycerophosphate, 1 mM sodium orthovanadate, 5 mM p-nitrophenyl phosphate, 2 mM dithiothreitol, protease inhibitors (complete, Roche Molecular Biochemicals), and 1% Nonidet P-40. Cellular debris is removed by centrifugation twice at $15,000 \times g$ for 15 min. The cell lysate is incubated with 25 μ l of M2 beads (Sigma) for 2 h at 4 °C with gentle rocking.

[0125] After extensive washing with lysis buffer, proteins bound to the beads are solubilized by boiling in SDS sample buffer, fractionated by SDS-polyacrylamide gel electrophoresis, transferred to polyvinylidene difluoride membrane and blotted with the indicated antibodies. The reactive bands are visualized with horseradish peroxidase coupled to the appropriate secondary antibodies and the enhanced chemiluminescence (ECL) Western blotting detection system (Amersham Pharmacia Biotech).

VII. Kinase assay

[0126] A purified or partially purified MIGFR is diluted in a suitable reaction buffer, e.g., 50 mM Hepes, pH 7.5, containing magnesium chloride or manganese chloride (1-20 mM) and a peptide or polypeptide substrate, such as myelin basic protein or casein (1-10 μ g/ml). The final concentration of the kinase is 1-20 nM. The enzyme reaction is conducted in microtiter plates to facilitate optimization of reaction conditions by increasing assay throughput. A 96-well microtiter plate is employed using a final volume 30-100 μ l. The reaction is initiated by the addition of ^{33}P -gamma-ATP (0.5 μ Ci/ml) and incubated for 0.5 to 3 hours at room temperature. Negative controls are provided by the addition of EDTA, which chelates the divalent cation (Mg^{2+} or Mn^{2+}) required for enzymatic activity. Following the incubation, the enzyme reaction is quenched using EDTA. Samples of the reaction are transferred to a 96-well glass fiber filter plate (MultiScreen, Millipore). The filters are subsequently washed with phosphate-buffered saline, dilute phosphoric acid (0.5%) or other suitable medium to remove excess radiolabeled ATP. Scintillation cocktail is added to the filter plate and the incorporated radioactivity is quantitated by scintillation counting (Wallac/Perkin Elmer). Activity is defined by the amount of radioactivity detected following subtraction of the negative control reaction value (EDTA quench).

VIII. Expression analysis

[0127] All cell lines used in the following experiments are NCI (National Cancer Institute) lines, and are available from ATCC (American Type Culture Collection, Manassas, VA

20110-2209). Normal and tumor tissues are obtained from Impath, UC Davis, Clontech, Stratagene, Ardaïs, Genome Collaborative, and Ambion.

[0128] TaqMan® analysis is used to assess expression levels of the disclosed genes in various samples.

[0129] RNA is extracted from each tissue sample using Qiagen (Valencia, CA) RNeasy kits, following manufacturer's protocols, to a final concentration of 50ng/μl. Single stranded cDNA is then synthesized by reverse transcribing the RNA samples using random hexamers and 500ng of total RNA per reaction, following protocol 4304965 of Applied Biosystems (Foster City, CA).

[0130] Primers for expression analysis using TaqMan® assay (Applied Biosystems, Foster City, CA) are prepared according to the TaqMan® protocols, and the following criteria: a) primer pairs are designed to span introns to eliminate genomic contamination, and b) each primer pair produced only one product. Expression analysis is performed using a 7900HT instrument.

[0131] TaqMan® reactions are carried out following manufacturer's protocols, in 25 μl total volume for 96-well plates and 10 μl total volume for 384-well plates, using 300nM primer and 250 nM probe, and approximately 25ng of cDNA. The standard curve for result analysis is prepared using a universal pool of human cDNA samples, which is a mixture of cDNAs from a wide variety of tissues so that the chance that a target will be present in appreciable amounts is good. The raw data are normalized using 18S rRNA (universally expressed in all tissues and cells).

[0132] For each expression analysis, tumor tissue samples are compared with matched normal tissues from the same patient. A gene is considered overexpressed in a tumor when the level of expression of the gene is 2 fold or higher in the tumor compared with its matched normal sample. In cases where normal tissue is not available, a universal pool of cDNA samples is used instead. In these cases, a gene is considered overexpressed in a tumor sample when the difference of expression levels between a tumor sample and the average of all normal samples from the same tissue type is greater than 2 times the standard deviation of all normal samples (i.e., $\text{Tumor} - \text{average}(\text{all normal samples}) > 2 \times \text{STDEV}(\text{all normal samples})$).

[0133] A modulator identified by an assay described herein can be further validated for therapeutic effect by administration to a tumor in which the gene is overexpressed. A decrease in tumor growth confirms therapeutic utility of the modulator. Prior to treating a patient with the modulator, the likelihood that the patient will respond to treatment can be

diagnosed by obtaining a tumor sample from the patient, and assaying for expression of the gene targeted by the modulator. The expression data for the gene(s) can also be used as a diagnostic marker for disease progression. The assay can be performed by expression analysis as described above, by antibody directed to the gene target, or by any other available detection method.

WHAT IS CLAIMED IS:

1. A method of identifying a candidate IGFR pathway modulating agent, said method comprising the steps of:
 - (a) providing an assay system comprising an MIGFR polypeptide or nucleic acid;
 - (b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and
 - (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate IGFR pathway modulating agent.
2. The method of Claim 1 wherein the assay system comprises cultured cells that express the MIGFR polypeptide.
3. The method of Claim 2 wherein the cultured cells additionally have defective IGFR function.
4. The method of Claim 1 wherein the assay system includes a screening assay comprising an MIGFR polypeptide, and the candidate test agent is a small molecule modulator.
5. The method of Claim 4 wherein the assay is a binding assay.
6. The method of Claim 1 wherein the assay system is selected from the group consisting of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system.
7. The method of Claim 1 wherein the assay system includes a binding assay comprising an MIGFR polypeptide and the candidate test agent is an antibody.

8. The method of Claim 1 wherein the assay system includes an expression assay comprising an MIGFR nucleic acid and the candidate test agent is a nucleic acid modulator.

9. The method of claim 8 wherein the nucleic acid modulator is an antisense oligomer.

10. The method of Claim 8 wherein the nucleic acid modulator is a PMO.

11. The method of Claim 1 additionally comprising:

(d) administering the candidate IGFR pathway modulating agent identified in (c) to a model system comprising cells defective in IGFR function and, detecting a phenotypic change in the model system that indicates that the IGFR function is restored.

12. The method of Claim 11 wherein the model system is a mouse model with defective IGFR function.

13. A method for modulating a IGFR pathway of a cell comprising contacting a cell defective in IGFR function with a candidate modulator that specifically binds to an MIGFR polypeptide, whereby IGFR function is restored.

14. The method of claim 13 wherein the candidate modulator is administered to a vertebrate animal predetermined to have a disease or disorder resulting from a defect in IGFR function.

15. The method of Claim 13 wherein the candidate modulator is selected from the group consisting of an antibody and a small molecule.

16. The method of Claim 1, comprising the additional steps of:

(d) providing a secondary assay system comprising cultured cells or a non-human animal expressing MIGFR ,

(e) contacting the secondary assay system with the test agent of (b) or an agent derived therefrom under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and

(f) detecting an agent-biased activity of the second assay system,
wherein a difference between the agent-biased activity and the reference activity of the second assay system confirms the test agent or agent derived therefrom as a candidate IGFR pathway modulating agent,
and wherein the second assay detects an agent-biased change in the IGFR pathway.

17. The method of Claim 16 wherein the secondary assay system comprises cultured cells.

18. The method of Claim 16 wherein the secondary assay system comprises a non-human animal.

19. The method of Claim 18 wherein the non-human animal mis-expresses a IGFR pathway gene.

20. A method of modulating IGFR pathway in a mammalian cell comprising contacting the cell with an agent that specifically binds an MIGFR polypeptide or nucleic acid.

21. The method of Claim 20 wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with the IGFR pathway.

22. The method of Claim 20 wherein the agent is a small molecule modulator, a nucleic acid modulator, or an antibody.

23. A method for diagnosing a disease in a patient comprising:
obtaining a biological sample from the patient;
contacting the sample with a probe for MIGFR expression;
comparing results from step (b) with a control;
determining whether step (c) indicates a likelihood of disease.

24. The method of claim 23 wherein said disease is cancer.

EX05-002patentin.txt
SEQUENCE LISTING

<110> EXELIXIS, INC.

<120> MIGFRS AS MODIFIERS OF THE IGFR PATHWAY AND METHODS OF USE

<130> EX05-002C-PC

<150> US 60/539,837
<151> 2004-01-28

<150> US 60/552,634
<151> 2004-03-12

<150> US 60/581,696
<151> 2004-06-21

<160> 120

<170> PatentIn version 3.2

<210> 1
<211> 4338
<212> DNA
<213> Homo sapiens

<400> 1
aaactagggg caaggagacg aagagaacat gaaagttaaa cttaagatg aagaacaaag 60
ctgaacatac tgatgcattg gatctttgga gaggatctca gaactcattg tacttaattt 120
acaggctaaa accttagaag aggaatttat tatatcctac acaagactcc agggaagcac 180
atggccttg gactgaaggct ggcattctgga agctgtcagc caccagcacc ttctgcagca 240
ggaaaaggcc agggctctgc tggagcaggc agcagagtgg acgcacagta acatgggcaa 300
cttgaagagc gtggcccagg agcctgggac accctgcggc ctggggctgg ggctgggcct 360
tgggctgtgc ggcaagcagg gccagccac cccggcccct gagcccagcc gggcccagc 420
atccctactc ccaccagcgc cagaacacag ccccccagc tccccgctaa cccagcccc 480
agagggggcc aagttccctc gtgtgaagaa ctgggaggtg gggagcatca cctatgacac 540
cctcagcgcc caggcgcagc aggatgggac ctgcacccca agacgctgcc tgggctccct 600
ggatattcca cggaactac agggccggcc ctccccggc ccccgggcc ctgagcagct 660
gctgagtcag gcccgggact tcatcaacca gtactacagc tccattaaga ggagcggctc 720
ccaggccac gaacagcggc ttcaagaggt ggaagccgag gtggcagcca caggcaccta 780
ccagcttagg gagagcgagc tgggtgttcg ggctaagcag gcctggcgca acgctccccg 840
ctgcgtgggc cggatccagt gggggaagct gcaggtgttc gatgccggg actgcaggtc 900
tgcacaggaa atgttcacct acatctgcaa ccacatcaag tatgccacca accggggcaa 960
ccttcgctcg gccatcacag tgttcccgca gcgctgccct ggccgaggag acttccgaat 1020
ctggaacagc cagctgggtg gctacgcggg ctaccggcag caggatggct ctgtgcgggg 1080
ggaccagcc aacgtggaga tcaccgagct ctgcattcag cacggctgga cccaggaaa 1140
cggctcgttc gacgtgctgc ccctgctgct gcaggcccca gatgatcccc cagaactctt 1200
ccttctgccc cccgagctgg tccttgaggt gccctggag caccacgc tggagtgggt 1260

EX05-002patentin.txt

tgcagccctg	ggcctgcgct	ggtacgccct	cccggcagtg	tccaacatgc	tgctggaaat	1320
tgggggcctg	gagttccccg	cagccccctt	cagtggctgg	tacatgagca	ctgagatcgg	1380
cacgaggaac	ctgtgtgacc	ctcaccgcta	caacatcctg	gaggatgtgg	ctgtctgcat	1440
ggacctggat	acccggacca	cctcgtccct	gtggaaagac	aaggcagcag	tggaaatcaa	1500
cgtggccgtg	ctgcacagtt	accagctagc	caaagtcacc	atcgtggacc	accacgccgc	1560
cacggcctct	ttcatgaagc	acctggagaa	tgagcagaag	gccagggggg	gctgccctgc	1620
agactggggc	tggatcgtgc	cccccatctc	gggcagcctc	actcctgttt	tccatcagga	1680
gatggtcaac	tatttcctgt	ccccggcctt	ccgctaccag	ccagaccctt	ggaaggggag	1740
tgccgccaag	ggcaccggca	tcaccaggaa	gaagaccttt	aaagaagtgg	ccaacgccgt	1800
gaagatctcc	gcctcgtca	tgggcacggt	gatggcgaag	cgagtgaagg	cgacaatcct	1860
gtatggctcc	gagaccggcc	gggcccagag	ctacgcacag	cagctgggga	gactcttccg	1920
gaaggctttt	gatccccggg	tcctgtgtat	ggatgagtat	gacgtggtgt	ccctcgaaca	1980
cgagacgctg	gtgctggtgg	taaccagcac	atttggaat	ggggatcccc	cggagaatgg	2040
agagagcttt	gcagctgccc	tgatggagat	gtccggcccc	tacaacagct	cccctcggcc	2100
ggaacagcac	aagagttata	agatccgctt	caacagcatc	tcctgctcag	accactggt	2160
gtcctcttgg	cggcggaaga	ggaaggagtc	cagtaacaca	gacagtgcag	gggccctggg	2220
caccctcagg	ttctgtgtgt	tcgggctcgg	ctcccgggca	tacccccact	tctgcgcctt	2280
tgctcgtgcc	gtggacacac	ggctggagga	actgggctgg	gagcggctgc	tgacgtggg	2340
ccagggcgac	gagctgtgct	gccaggagga	ggccttcgga	ggctggggcc	aggctgcctt	2400
ccagggcgcc	tgtgagacct	tctgtgtggg	agaggatgcc	aaggccgccc	cccagacat	2460
cttcagcccc	aaacggagct	ggaagcgcca	gaggtaccgg	ctgagcgccc	aggccgaggg	2520
cctgcagttg	ctgccaggtc	tgatccacgt	gcacaggcgg	aagatgttcc	aggctacaat	2580
ccgctcagtg	gaaaacctgc	aaagcagcaa	gtccacgagg	gccaccatcc	tggtgctgct	2640
ggacaccgga	ggccaggagg	ggctgcagta	ccagccgggg	gaccacatag	gtgtctgccc	2700
gccaaccgga	cccggccttg	tggaggcgct	gctgagccgc	gtggaggacc	cgccggcgcc	2760
cactgagccc	gtggcagtag	agcagctgga	gaagggcagc	cctggtggcc	ctcccccg	2820
ctgggtgcgg	gacccccggc	tgcccccggt	cacgctgcgc	caggctctca	ccttcttctt	2880
ggacatcacc	tccccaccca	gccctcagct	cttgccggctg	ctcagcacct	tggcagaaga	2940
gcccagggaa	cagcaggagc	tggaggccct	cagccaggat	ccccgacgct	acgaggagt	3000
gaagtgggtc	cgctgcccc	cgctgctgga	gggtgctggg	cagttcccgt	cggtggcgct	3060
gcctgcccc	ctgctcctca	cccagctgcc	tctgctccag	ccccggtact	actcagtcag	3120
ctcggcacc	agcaccacc	caggagagat	ccacctcact	gtagctgtgc	tggcatacag	3180
gactcaggat	gggctggggc	ccctgcacta	tggagtctgc	tccacgtggc	taagccagct	3240
caagcccgga	gaccctgtgc	cctgcttcat	ccgggggggt	ccctccttcc	ggctgccacc	3300

EX05-002patentin.txt

```

cgatcccagc ttgccctgca tcctgggtggg tccaggcact ggcattgccc ccttccgggg 3360
attctggcag gagcggctgc atgacattga gagcaaaggg ctgcagccca ctcccatgac 3420
tttgggtgttc ggctgccgat gctcccaact tgaccatctc taccgcgacg aggtgcagaa 3480
cgcccagcag cgcgggggtgt ttggccgagt cctcaccgcc ttctcccggg aacctgacaa 3540
ccccaagacc tacgtgcagg acatcctgag gacggagctg gctgcggagg tgcaccgcgt 3600
gctgtgcctc gagcgggggcc acatgtttgt ctgcggcgat gttaccatgg caaccaacgt 3660
cctgcagacc gtgcagcgca tcctggcgac ggagggcgac atggagctgg acgaggccgg 3720
cgacgtcatc ggcgtgctgc gggatcagca acgctaccac gaagacattt tcgggctcac 3780
gctgcgcacc caggagggtga caagccgat acgcaccag agcttttcct tgcaggagcg 3840
tcagttgcgg ggcgcagtgc cctgggcgtt cgaccctccc ggctcagaca ccaacagccc 3900
ctgagagccg cctggctttc ccttccagtt ccgggagagc ggctgcccga ctcagggtccg 3960
cccgaccagg atcagccccg ctctccctc cttgaggtgg tgccttctca catctgtcca 4020
gaggctgcaa ggattcagca ttattcctcc aggaaggagc aaaacgcctc ttttcctct 4080
ctaggcctgt tgcctcgggc ctgggtccgc cttaatctgg aaggcccctc ccagcagcgg 4140
taccacaggg cctactgcca ccgcttcct gtttcttagt cgaatgttag attcctcttg 4200
cctctctcag gagtatctta cctgtaaagt ctaatctcta aatcaagtat ttattattga 4260
agatttacca taagggactg tgccagatgt taggagaact actaaagtgc ctacccagc 4320
ccaaaaaaaa aaaaaaaaaa 4338

```

```

<210> 2
<211> 1578
<212> DNA
<213> Homo sapiens

```

```

<400> 2
gcgcccttaa agatggtgag ggggctcatg ctctgagtag aagggtggtga cctccaggag 60
cgggtgggatg atgagggccc gggcgctctc tgcaatggag acggtcattt cttcagatag 120
ctccccagct gtggaaaatg agcatcctca agagacccca gaatccaaca atagcgtgta 180
tacttccttc atgaagtctc atcgctgcta tgacctgatt cccacaagct ccaaattggt 240
tgtatttgat acgtccctgc aggtgaagaa agcttttttt gctttggtga ctaacggtgt 300
acgagctgcc ctttatggg atagtaagaa gcaaagtttt gtgggcatgc tgaccatcac 360
tgatttcac aatatcctgc accgctacta taaatcagcc ttggtacaga tctatgagct 420
agaagaacac aagatagaaa cttggagaga ggtgtatctc caggactcct ttaaaccgct 480
tgtctgcatt tctcctaata ccagcttggt tgatgctgtc tcttcattaa ttcggaacaa 540
gatccacagg ctgccagtta ttgaccaga atcaggcaat actttgtaca tcctcaccca 600
caagcgcatt ctgaagtcc tcaaattggt tatcactgag ttccccaagc cagagttcat 660
gtccaagtct ctggaagagc tacagattgg cacctatgcc aatattgcta tggttcgcac 720

```

EX05-002patentin.txt

taccaccccc	gtctatgtgg	ctctggggat	ttttgtacag	catcgagtct	cagccctgcc	780
agtgggtggat	gagaaggggc	gtgtggtgga	catctactcc	aagtttgatg	ttatcaatct	840
ggcagcagaa	aagacctaca	acaacctaga	tgtatctgtg	actaaagcct	tgcaacatcg	900
atcacattac	tttgaggggtg	ttctcaagtg	ctacctgcat	gagactctgg	agaccatcat	960
caacaggcta	gtggaagcag	aggttcaccg	acttgtagtg	gtggatgaaa	atgatgtggt	1020
caaggggaatt	gtatcactgt	ctgacatcct	gcaggccctg	gtgctcacag	gtggagagaa	1080
gaagccctga	gctgggggaa	ggggtcatgc	agcaccaggg	gatatgcca	actcactgcc	1140
tgctggaagc	tctgtgggaa	tcagatgaaa	cttgagggaa	ttgtgactct	gttccctgtt	1200
caggggtcccc	tgcccttcta	tctgggagct	aggggaaggta	tgggggagga	aagagaatgg	1260
atztatagct	acccttacct	tcacacatac	acttgaaaaa	actttcagcc	tagccagttc	1320
tagcccctgt	cctcttagat	atatccccct	ttctgggtga	actataggct	ctgtgcctct	1380
cagacaaatt	ctgatctcta	agagatcccc	agacctcact	tgccctctgcc	tccatcttgg	1440
ccctgattca	accctaagat	aatagcacia	caaaattctt	cataaagata	tttttattca	1500
cctgtttccgt	gctatatgga	ggaggccaag	tccatttagt	gacatttctt	cccataatgt	1560
gagtggggag	gattgtgg					1578

<210> 3
 <211> 2062
 <212> DNA
 <213> Homo sapiens

<400> 3	
gcggctccag	tccgaaggca gcggccgggg gagggaaagga ggggaccgaa cccccgagga 60
gtttcgcaga	atcaacttct ggtagagtt atgggaagcg cggttatgga caccaagaag 120
aaaaaagatg	tttccagccc cggcgggagc ggcggaaga aaaatgccag ccagaagagg 180
cgttcgcgtc	gcgtgcacat tccggacctg agctccttcg ccatgccgct cctggacgga 240
gacctggagg	gttccggaaa gcattcctct cgaaagggtg acagcccctt cggcccgggc 300
agcccctcca	aagggttctt ctccagaggc cccagcccc ggccctccag ccccatgtct 360
gcacctgtga	ggcccaagac cagccccggc tctcccaaaa ccgtgttccc gttctcctac 420
caggagtccc	cgccacgctc ccctcgacgc atgagcttca gtgggatctt ccgctcctcc 480
tccaaagagt	cttcccccaa ctccaaccct gctacctcgc ccgggggcat cagggtttttc 540
tcccgctcca	gaaaaacctc cggcctctcc tcctctccgt caacaccac ccaagtgacc 600
aagcagcaca	cgtttcccct ggaatcctat aagcacgagc ctgaacggtt agagaatcgc 660
atctatgcct	cgcttcccc cccggacaca gggcagaggt tctgcccgtc ttccttccag 720
agcccgacca	ggcctccact ggcatcaccg acacactatg ctccctccaa agccgcggcg 780
ctggcggcgg	ccctgggacc cgcggaagcc ggcagtctgg agaagctgga gttcgaggac 840
gaagcagtag	aagactcaga aagtgggtgt tacatgcgat tcatgaggtc acacaagtgt 900
tatgacatcg	ttccaaccag ttcaaagctt gttgtctttg atactacatt acaagttaaa 960

EX05-002patentin.txt

```

aaggccttct ttgctttggt agccaacggt gtccgagcag cgccactgtg ggagagtaaa 1020
aaacaaagtt ttgtaggaat gctaacaatt acagatttca taaatatact acatagatac 1080
tataaatcac ctatggtaca gattttatgaa ttagaggaac ataaaattga aacatggagg 1140
gagcttttatt tacaagaaac atttaagcct ttagtgaata tatctccaga tgcaagcctc 1200
ttcgatgctg tataactcctt gatcaaaaat aaaatccaca gattgcccgt tattgaccct 1260
atcagtggga atgcacttta tatacttacc cacaaaagaa tcctcaagtt cctccagctt 1320
tttatgtctg atatgccaaa gcctgctttc atgaagcaga acctggatga gcttggaata 1380
ggaacgtacc acaacattgc cttcatacat ccagacactc ccatcatcaa agccttgaac 1440
atatttgtgg aaagacgaat atcagctctg cctgttgtgg atgagtcagg aaaagttgta 1500
gatattttatt ccaaatttga tgtaattaat cttgctgctg agaaaacata caataaccta 1560
gatatcacgg tgacccaggc ccttcagcac cgttcacagt attttgaagg tgttgtgaag 1620
tgcaataagc tggaaatact ggagaccatc gtggacagaa tagtaagagc tgaggtccat 1680
cggttggtgg tggtaaataga agcagatagt attgtgggta ttatttcctt gtcggacatt 1740
ctgcaagccc tgatcctcac accagcaggt gccaaacaaa aggagacaga aacggagtga 1800
ccgccgtgaa tgtagacgcc ctaggaggag aacttgaaca aagtctctgg gtcacgtttt 1860
gcctcatgaa cactggctgc aagtggttaa gaatgtatat cagggtttta cgataggtat 1920
ttcttccagt gatgttgaag ttaagcttaa aaaagaaaga ttttatgtgc ttgaaaattc 1980
aggcttgcac taaaaaactg ttttcagacc ttgtctgaag gattttaaat gctgtatgtc 2040
attaaagtgc actgtgtccc tg 2062

```

```

<210> 4
<211> 2290
<212> DNA
<213> Homo sapiens

```

```

<400> 4
acttggctctg gggctggcca catggagccc gggctggagc acgcactgcg caggaccctt 60
tcctggagca gccttggggg ttctgagcat caagagatga gcttcctaga gcaagaaaac 120
agcagctcat ggccatcacc agctgtgacc agcagctcag aaagaatccg tgggaaacgg 180
agggccaaag ccttgagatg gacaaggcag aagtcggtgg aggaagggga gccaccaggt 240
cagggggaag gtccccggtc caggccagct gctgagtcca ccgggctgga ggccacattc 300
cccaagacca cacccttggc tcaagctgat cctgccgggg tgggcactcc accaacaggg 360
tgggactgcc tcccctctga ctgtacagcc tcagctgcag gctccagcac agatgatgtg 420
gagctggcca cgagattccc agccacagag gcctgggagt gtgagctaga aggcctgctg 480
gaagagaggc ctgccctgtg cctgtccccg caggccccat ttcccaagct gggctgggat 540
gacgaactgc ggaaacccgg cgcccagatc tacatgcgct tcatcgagga gcacacctgc 600
tacgatgcc tggcaactag ctccaagcta gtcattctcg acaccatgct ggagatcaag 660

```

EX05-002patentin.txt

```

aaggccttct ttgctctggt ggccaacggt gtgcgggcag cccctctatg ggacagcaag 720
aagcagagct ttgtggggat gctgaccatc actgacttca tcctgggtgct gcatcgctac 780
tacaggcccc ccctgggtcca gatctatgag attgaacaac ataagattga gacctggagg 840
gagatctacc tgcaaggctg cttcaagcct ctgggtctcca tctctcctaa tgatagcctg 900
tttgaagctg tctacaccct catcaagaac cggatccatc gcctgcctgt tcttgacccg 960
gtgtcaggca acgtactcca catcctcaca cacaaacgcc tgctcaagtt cctgcacatc 1020
tttgggtccc tgctgccccg gccctccttc ctctaccgca ctatccaaga tttgggcatc 1080
ggcacattcc gagacttggc tgtgggtgctg gagacagcac ccatcctgac tgcactggac 1140
atctttgtgg accggcggtg gtctgcactg cctgtggtca acgaatgtgg tcaggctcgtg 1200
ggcctctatt cccgctttga tgtgattcac ctggctgccc agcaaacctt caaccacctg 1260
gacatgagtg tgggagaagc cctgaggaag aggacactat gtctggaggg agtcctttcc 1320
tgccagcccc acgagagctt gggggaagtg atcgacagga ttgctcggga gcaggtagac 1380
aggctggtgc tagtgagcga gaccagcat ctcttgggcg tgggtctcct ctccgacatc 1440
cttcaggcac tggtgctcag ccctgctggc atcgatccct cggggcctga gaagatctga 1500
gtcctcaatc ccaagccacc tgcacacctg gaagccaatg aagggaactg gagaactcag 1560
ccttcattct cccccacccc catttgctgg ttcagctatg attcaggctt cttcaggccc 1620
tcccaaattg cccttgccct accagagctc ccagaagccc tcggcatgcc agtgcacat 1680
gggatgatga aattaaggag aacagctgag tcaagcttgg aggtccctga accagaggca 1740
ctaggattac ccagggcca tctgtgctcc atgcccgcct atccccttgc cgcctgactg 1800
ggtcggatgg ccccgagtgg gtttagtcag ggcttctgga tcctcggttt ctgggctacc 1860
tatgcttcac cttcagctcc tgggagttcc cagcaacgct gccactgccc ctctactct 1920
ccaggggttg gtcatttcaa ggctgctgaa atgctgcatt tcagggggcc accatggagc 1980
agccgttatt tatagaactg ccctgttggg ggtggggagt cctccctcca ttcttgtcca 2040
gaaaactcct tagctctcgc agtgagccca tgttcttagt ctccagggat ggatggcctt 2100
gtatatggac ccctgagaat gagcaattga gaaaacaaaa caaaagggaac aatccatgaa 2160
cttagatttt attggtttca ctcaaatgc tgcagtcatt tgacctgaac ttgtggcaag 2220
agacttgtgc tttctaaatt caaagactag aagggaatg gataaaaatc acaagtgccg 2280
tttctcttgc 2290

```

<210> 5
 <211> 4221
 <212> DNA
 <213> Homo sapiens

```

<400> 5
ataactttgt agcgagtcga aaactgaggc tccggccgca gagaactcag cctcattcct 60
gctttaaaat ctctcgcca cctttgatga ggggactggg cagttctaga cagtcccga 120
gttctcaagg cacaggctctc ttcctggttt gactgtcctt accccgggga ggcagtgcag 180

```

EX05-002patentin.txt

ccagctgcaa	gccccacagt	gaagaacatc	tgagctcaaa	tccagataag	tgacataagt	240
gacctgcttt	gtaaagccat	agagatggcc	tgctccttga	aatttctgtt	caagacccaaa	300
ttccaccagt	atgcaatgaa	tggggaaaaa	gacatcaaca	acaatgtgga	gaaagcccc	360
tgtgccacct	ccagtccagt	gacacaggat	gaccttcagt	atcacaacct	cagcaagcag	420
cagaatgagt	ccccgcagcc	cctcgtggag	acgggaaaga	agtctccaga	atctctggtc	480
aagctggatg	caacccatt	gtcctcccca	cggcatgtga	ggatcaaaaa	ctggggcagc	540
gggatgactt	tccaagacac	acttcacat	aaggccaaag	ggattttaac	ttgcagggtcc	600
aaatcttgcc	tggggtccat	tatgactccc	aaaagtgtga	ccagaggacc	cagggacaag	660
cctacccctc	cagatgagct	tctacctcaa	gctatcgaat	ttgtcaacca	atattacggc	720
tccttcaaag	aggcaaaaat	agaggaacat	ctggccaggg	tggaagcggg	aacaaaggag	780
atagaaacaa	caggaaccta	ccaactgacg	ggagatgagc	tcattcttcg	caccaagcag	840
gcctggcgca	atgccccacg	ctgcattggg	aggatccagt	ggtccaacct	gcagggtcttc	900
gatgcccgc	gctgttccac	tgcccgggaa	atgtttgaac	acatctgcag	acacgtgcgt	960
tactccacca	acaatggcaa	catcaggtcg	gccatcaccg	tgttccccca	gcggagtgat	1020
ggcaagcacg	acttccgggt	gtggaatgct	cagctcatcc	gctatgctgg	ctaccagatg	1080
ccagatggca	gcatcagagg	ggaccctgcc	aacgtggaat	tcactcagct	gtgcatcgac	1140
ctgggctgga	agcccaagta	cggccgcttc	gatgtggtcc	ccctggtcct	gcaggccaat	1200
ggccgtgacc	ctgagctctt	cgaaatccca	cctgaccttg	tgcttgaggt	ggccatggaa	1260
catcccaa	acgagtgggt	tcgggaactg	gagctaaagt	ggtacgccct	gcctgcagtg	1320
gccaacatgc	tgcttgaggt	gggcggcctg	gagttcccag	ggtgccccct	caatggctgg	1380
tacatgggca	cagagatcgg	agtccgggac	ttctgtgacg	tccagcgcta	caacatcctg	1440
gaggaagtgg	gcaggagaat	gggcctggaa	acgcacaagc	tggcctcgct	ctggaaagac	1500
caggctgtcg	ttgagatcaa	cattgctgtg	ctccatagtt	tccagaagca	gaatgtgacc	1560
atcatggacc	accactcggc	tgacagaatc	ttcatgaagt	acatgcagaa	tgaataccgg	1620
ttccgtgggg	gctgcccggc	agactggatt	tggctggtcc	ctcccatgtc	tgggagcatc	1680
acccccgtgt	ttcaccagga	gatgctgaac	tacgtcctgt	cccctttcta	ctactatcag	1740
gtagaggcct	ggaaaaccca	tgtctggcag	gacgagaagc	ggagacccaa	gagaagagag	1800
attccattga	aagtcttggt	caaagctgtg	ctctttgcct	gtatgctgat	gcgcaagaca	1860
atggcgtccc	gagtcagagt	caccatcctc	tttgcgacag	agacaggaaa	atcagaggcg	1920
ctggcctggg	acctgggggc	cttattcagc	tgtgccttca	accccaaggt	tgtctgcatg	1980
gataagtaca	ggctgagctg	cctggaggag	gaacggctgc	tggttggtgg	gaccagtacg	2040
tttggaatg	gagactgccc	tggcaatgga	gagaaactga	agaaatcgct	cttcatgctg	2100
aaagagctca	acaacaaatt	caggtacgct	gtgtttggcc	tcggctccag	catgtaccct	2160
cggttctg	cctttgctca	tgacattgat	cagaagctgt	cccacctggg	ggcctctcag	2220

EX05-002patentin.txt

```

ctcaccccgga tgggagaagg ggatgagctc agtgggcagg aggacgcctt ccgcagctgg 2280
gccgtgcaaa ctttcaaggc agcctgtgag acgtttgatg tccgaggcaa acagcacatt 2340
cagatcccca agctctacac ctccaatgtg acctgggacc cgcaccacta caggctcgtg 2400
caggactcac agccttttga cctcagcaaa gccctcagca gcatgcatgc caagaacgtg 2460
ttcaccatga ggctcaaate tcggcagaat ctacaaagtc cgacatccag ccgtgccacc 2520
atcctggtgg aactctcctg tgaggatggc caaggcctga actacctgcc gggggagcac 2580
cttggggttt gcccaggcaa ccagccggcc ctgggtccaag gtatcctgga gcgagtgggtg 2640
gatggcccca caccacacca gacagtgcgc ctggaggccc tggatgagag tggcagctac 2700
tgggtcagtg acaagaggct gccccctgc tctctcagcc aggccctcac ctacttcctg 2760
gacatcacca ccccccaac ccagctgctg ctccaaaagc tggcccaggt ggccacagaa 2820
gagcctgaga gacagaggct ggaggccctg tgccagccct cagagtacag caagtggag 2880
ttcaccaaca gcccacatt cctggagggtg ctagaggagt tcccgctcct gcgggtgtct 2940
gctggcttcc tgctttccca gctccccatt ctgaagcca ggttctactc catcagctcc 3000
tcccgggatc acacgccac agagatccac ctgactgtgg ccgtggtcac ctaccacacc 3060
cgagatggcc aggggtcccct gcaccacggc gtctgcagca catggctcaa cagcctgaag 3120
cccaagacc cagtgccttg ctttgtgcgg aatgccagcg gcttcacct ccccgaggat 3180
ccctcccatc cttgcatcct catcgggcct ggacaggca tcgcgccctt ccgcagtttc 3240
tggcagcaac ggctccatga ctcccagcac aagggtgtgc ggggaggccg catgacctg 3300
gtgtttgggt gccgccgccc agatgaggac cacatctacc aggaggagat gctggagatg 3360
gccagaagg ggggtgtgca tgcggtgcac acagcctatt cccgcctgcc tggcaagccc 3420
aagggtctatg ttcaggacat cctgcggcag cagctggcca gcgagggtgct ccgtgtgctc 3480
cacaaggagc caggccacct ctatgtttgc ggggatgtgc gcatggcccg ggacgtggcc 3540
cacaccctga agcagctggg ggctgccaa gtgaaattga atgaggagca ggtcgaggac 3600
tatttctttc agctcaagag ccagaagcgc tatcacgaag atatctttgg tgctgtattt 3660
ccttacgagg cgaagaagga cagggtggcg gtgcagcca gcagcctgga gatgtcagcg 3720
ctctgagggc ctacaggagg ggttaaagct gccggcacag aacttaagga tggagccagc 3780
tctgcattat ctgaggtcac agggcctggg gagatggagg aaagtgatat cccccagcct 3840
caagtcttat ttcctcaacg ttgctccca tcaagccctt tacttgacct cctaacaagt 3900
agcaccctgg attgatcgga gcctcctctc tcaaactggg gcctccctgg tcccttggag 3960
acaaaatctt aaatgccagg cctggcaagt gggtgaaaga tggaaactgc tgctgagtgc 4020
accacttcaa gtgaccacca ggaggtgcta tcgcaccact gtgtatttaa ctgccttggtg 4080
tacagttatt tatgcctctg tatttaaaaa actaacacc agtctgttcc ccatggccac 4140
ttgggtcttc cctgtatgat tccttgatgg agatatttac atgaattgca ttttacttta 4200
atcacaaaaa aaaaaaaaaa a 4221

```


EX05-002patentin.txt

<210> 6
 <211> 7124
 <212> DNA
 <213> Homo sapiens

<400> 6
 agagcgggctc ttttaatgag ggttgcgacg tctccctccc cacacccata aaccagtcgg 60
 gttggacgctc actgctaatt cgtttcagtg atgataggat aaaggaggga cattaagaaa 120
 taaattcccc ctcacgaccc tcgctgagct cacggctcag tccctacata tttatgccgc 180
 gtttccagcc gctgggtgag gagctactta gcgccgcggc tcctccgagg ggcggccggg 240
 cagcgagcag cggccgagcg gacgggctca tgatgcctca gatctgatcc gcatctaaca 300
 ggctggcaat gaagataccc agagaatagt tcacatctat catgcgtcac ttctagacac 360
 agccatcaga cgcatctcct cccctttctg cctgacctta ggacacgtcc caccgcctct 420
 cttgacgtct gcctgggtcaa ccatcacttc cttagagaat aaggagagag gcggatgcag 480
 gaaatcatgc caccgacggg ccaccagcca tgagtgggtg acgctgagct gacgtcaaag 540
 acagagaggg ctgaagcctt gtcagcacct gtcaccccgg ctctgtctct ccgtgtagcc 600
 tgaagcctgg atcctcctgg tgaaatcatc ttggcctgat agcattgtga ggtcttcaga 660
 caggaccctt cggaagctag ttaccatgga ggatcacatg ttcggtgttc agcaaattcca 720
 gcccaatgtc atttctgttc gtctcttcaa gcgcaaagtt gggggcctgg gatttctggt 780
 gaaggagcgg gtcagtaagc cgcccgtgat catctctgac ctgattcgtg ggggcgccgc 840
 agagcagagt ggcctcatcc aggccggaga catcattctt gcggtcaacg gccggccctt 900
 ggtggacctg agctatgaca gcgccctgga ggtactcaga ggcatcgcct ctgagaccca 960
 cgtggtcctc attctgaggg gccctgaagg tttcaccacg cacctggaga ccacctttac 1020
 aggtgatggg accccaaga ccatccgggt gacacagccc ctgggtcccc ccaccaaagc 1080
 cgtggatctg tcccaccagc caccggccgg caaagaacag cccctggcag tggatggggc 1140
 ctcgggtccc gggaatgggc ctcagcatgc ctacgatgat gggcaggagg ctggctcact 1200
 ccccatgcc aacggcctgg ccccaggcc cccaggccag gaccccgca agaaagcaac 1260
 cagagtcagc ctccaaggca gaggggagaa caatgaactg ctcaaggaga tagagcctgt 1320
 gctgagcctt ctcaccagtg ggagcagagg ggtcaaggga ggggcacctg ccaaggcaga 1380
 gatgaaagat atgggaatcc aggtggacag agatttggac ggcaagtcac acaaacctct 1440
 gccctcggc gtggagaacg accgagtctt caatgacctt tgggggaagg gcaatgtgcc 1500
 tgtcgtcctc aacaacccat attcagagaa ggagcagccc cccacctcag gaaaacagtc 1560
 cccacaaaag aatggcagcc cctccaagtg tccacgcttc ctcaagggtca agaactggga 1620
 gactgaggtg gttctcactg acaccctcca ccttaagagc acattggaaa cgggatgcac 1680
 tgagtacatc tgcatgggct ccatcatgca tccttctcag catgcaagga ggcctgaaga 1740
 cgtccgcaca aaaggacagc tcttccctct cgccaaagag ttatttgatc aatactattc 1800

EX05-002patentin.txt

atcaattaa	agatttggct	ccaaagccca	catggaaagg	ctggaagagg	tgaacaaaga	1860
gatcgacacc	actagcactt	accagctcaa	ggacacagag	ctcatctatg	gggccaagca	1920
cgcctggcgg	aatgcctcgc	gctgtgtggg	caggatccag	tggtccaagc	tgcaggtatt	1980
cgatgcccgt	gactgcacca	cggcccacgg	gatgttcaac	tacatctgta	accatgtcaa	2040
gtatgccacc	aacaaagggg	acctcaggtc	tgccatcacc	atattcccc	agaggacaga	2100
cggcaagcac	gacttccgag	tctggaactc	ccagctcatc	cgctacgctg	gctacaagca	2160
gcctgacggc	tccaccctgg	gggaccagc	caatgtgcag	ttcacagaga	tatgcataca	2220
gcagggctgg	aaaccgccta	gaggccgctt	cgatgtcctg	ccgctcctgc	ttcaggccaa	2280
cggcaatgac	cctgagctct	tccagattcc	tccagagctg	gtgttggaag	ttcccatcag	2340
gcacccaag	tttgagtggg	tcaaggacct	ggggctgaag	tggtacggcc	tccccgccgt	2400
gtccaacatg	ctcctagaga	ttggcggcct	ggagttcagc	gcctgtccct	tcagtggctg	2460
gtacatgggc	acagagattg	gtgtccgcga	ctactgtgac	aactcccgt	acaatatcct	2520
ggaggaagtg	gccaagaaga	tgaacttaga	catgaggaag	acgtcctccc	tgtggaagga	2580
ccaggcgctg	gtggagatca	atatcgcggt	tctctatagc	ttccagagtg	acaaagtgc	2640
cattgttgac	catcactccg	ccaccgagtc	cttcattaag	cacatggaga	atgagtaccg	2700
ctgccggggg	ggctgccctg	ccgactgggt	gtggatcgtg	cccccatgt	ccggaagcat	2760
caccctgtg	ttccaccagg	agatgtctaa	ctaccggctc	acccctcct	tcgaatacca	2820
gcctgatccc	tggaacacgc	atgtctggaa	aggcaccaac	gggaccccca	caaagcggcg	2880
agccatcggc	ttcaagaagc	tagcagaagc	tgtcaagttc	tcggccaagc	tgatggggca	2940
ggctatggcc	aagaggggtg	aagcgaccat	cctctatgcc	acagagacag	gcaaatcgca	3000
agcttatgcc	aagaccttgt	gtgagatctt	caaacacgcc	tttgatgcca	aggtgatgtc	3060
catggaagaa	tatgacattg	tgcacctgga	acatgaaact	ctggtccttg	tggtcaccag	3120
cacctttggc	aatggagatc	cccctgagaa	tggggagaaa	ttcggctgtg	ctttgatgga	3180
aatgaggcac	cccaactctg	tgcaggaaga	aaggaagagc	tacaagggtc	gattcaacag	3240
cgtctcctcc	tactctgact	cccaaaaatc	atcaggcgat	gggcccgaac	tcagagacaa	3300
ctttgagagt	gctggacccc	tggccaatgt	gaggttctca	gtttttggcc	tcggctcacg	3360
agcataccct	cacttttgcg	ccttcggaca	cgctgtggac	accctcctgg	aagaactggg	3420
aggggagagg	atcctgaaga	tgaggggaagg	ggatgagctc	tgtgggcagg	aagaggcttt	3480
caggacctgg	gccaagaagg	tcttcaaggc	agcctgtgat	gtcttctgtg	tgggagatga	3540
tgtcaacatt	gaaaaggcca	acaattccct	catcagcaat	gatcgagct	ggaagagaaa	3600
caagttccgc	ctcacctttg	tggccgaagc	tccagaactc	acacaaggtc	tatccaatgt	3660
ccacaaaaag	cgagtctcag	ctgcccggct	ccttagccgt	caaaacctcc	agagccctaa	3720
atccagtcgg	tcaactatct	tcgtgctgtc	ccacaccaac	gggagccagg	agctgcagta	3780
ccagcctggg	gaccacctgg	gtgtcttccc	tggcaaccac	gaggacctcg	tgaatgcctt	3840

EX05-002patentin.txt

gatcgagcgg	ctggaggacg	cgccgcctgt	caaccagatg	gtgaaagtgg	aactgctgga	3900
ggagcggaac	acggccttag	gtgtcatcag	taactggaca	gacgagctcc	gcctcccgcc	3960
ctgcaccatc	ttccaggcct	tcaagtacta	cctggacatc	accacgccac	caacgcctct	4020
gcagctgcag	cagtttgcct	ccctagctac	cagcgagaag	gagaagcagc	gtctgctggt	4080
cctcagcaag	ggtttgcagg	agtacgagga	atggaaatgg	ggcaagaacc	ccaccatcgt	4140
ggaggtgctg	gaggagtcc	catctatcca	gatgccggcc	accctgctcc	tgaccagct	4200
gtccctgctg	cagccccgct	actattccat	cagctcctcc	ccagacatgt	accctgatga	4260
agtgcacctc	actgtggcca	tcgtttccta	ccgcactcga	gatggagaag	gaccaattca	4320
ccacggcgta	tgctcctcct	ggctcaaccg	gatacaggct	gacgaactgg	ttccctgttt	4380
cgtgagagga	gcaccagct	tccacctgcc	ccggaacccc	caagtcccct	gcctcctcgt	4440
tggaccaggc	accggcattg	cccctttccg	aagcttctgg	caacagcggc	aatttgatat	4500
ccaacacaaa	ggaatgaacc	cctgccccat	ggctctgggtc	ttcggtgccc	ggcaatccaa	4560
gatagatcat	atctacaggg	aagagaccct	gcaggccaag	aacaaggggg	tcttcagaga	4620
gctgtacacg	gcttactccc	gggagccaga	caaaccaaag	aagtacgtgc	aggacatcct	4680
gcaggagcag	ctggcgaggt	ctgtgtaccg	agccctgaag	gagcaagggg	gccacatata	4740
cgtctgtggg	gacgtcacca	tggctgctga	tgtcctcaaa	gccatccagc	gcctcatgac	4800
ccagcagggg	aagctctcgg	cagaggacgc	cggcgtattc	atcagccgga	tgagggatga	4860
caaccgatac	catgaggata	tttttggagt	caccctgcga	acgtacgaag	tgaccaaccg	4920
ccttagatct	gagtccattg	ccttcattga	agagagcaaa	aaagacaccg	atgaggtttt	4980
cagctcctaa	ctggaccctc	ttgcccagcc	ggctgcaagt	tttgtaagcg	cggacagaca	5040
ctgctgaacc	tttcctctgg	gacccctgt	ggccctcgct	ctgcctcctg	tccttgctgc	5100
tgtgccctgg	tttcctcct	cgggcttctc	gcccctcagt	ggtttcctcg	gccctcctgg	5160
gtttactcct	tgagttttcc	tgctgcgatg	caatgctttt	ctaacttgca	gtggctctta	5220
caaaactctg	ttccactcc	ctctcttgcc	gacaagggca	actcacgggt	gcctgaaacc	5280
actggaacat	ggccgtcgct	gtgggggttt	ttttctctgg	ggttcccctg	gaaaggctgc	5340
aggaactagg	cacaagctct	ctgagccagt	ccctcagcca	ctgaagtccc	cctttctcct	5400
tttttatgat	gacattttgg	ttgtgcgtgc	ctgtgtgtgt	gtgtgtgtgt	gtgtgtgtgt	5460
gtgtgatggg	ccaggctctc	gtccgtcctc	ttccctgcac	aagtgtgtcg	atcttagatt	5520
gccactgctt	tcattgaaga	ccctcaatgc	caagaaacgt	gtccctggcc	catattaatc	5580
cctcgtgtgt	ccataattag	ggccacgcc	catgtacctg	aaacatttgg	aagccccata	5640
attgttctag	ttagaaaggg	ttcagggcat	ggggagagga	gtgggaaatt	gattaaaggg	5700
gctgtctccc	aatgaaagag	gcattcccag	aatttgctgc	atttagattt	tgataccagt	5760
gagcagagcc	ctcatgtgac	atgaacccat	ccaatggatt	gtgcaaattc	cctccccaaa	5820
cccaccata	ccagctagaa	tcacttgact	ttgccacatc	cattgactga	ccccctcctc	5880

EX05-002patentin.txt

cagcaatagc atccaagggg cctggaagtt atgttggtca aagaagcctg gtggcaataa 5940
 ggatcttccc actttgccac tggatgactt tggatgggtc acttgtcctc agtttttcct 6000
 agtcataatg tcatacgaac ctaaagaata tgaatggatt aaatgttaaa gctttgggtgc 6060
 ctggaacaa tatcaagtaa caatatgatt attatttttt tattccccca aagcgggctt 6120
 gctgcttcac ccttggggat gaaataatgg aagctggtta aagtggatga ggttggaag 6180
 agttgccata atgaggtccc acgtggcttc ttcgatagga gccacaactt ggggtgggaa 6240
 gaacttgctc ctcaggcttg ttgccctctg cagttgatct ccaaagtttt aaacctgtta 6300
 aattaatttt gacaaataag ttaccctcaa ctcagatcaa aaatgggcag ccaagtcttc 6360
 ggtaggaatt ggagccggtg taattcctcc ctaagaggca acctgttgaa ttactctct 6420
 cagagtaaat ggtgggaagg gatccctttg tatacttttt taaatactac aaattagtgt 6480
 caggcagttc ccagaaagag acaagaaatc ctagtggcct cccagactgc aggggtcccca 6540
 aggatggaaa gggaatgttc tgctggttct accctgtttg ttgtgtcttg ctatacagaa 6600
 aaaccacatt tcttttatat actgtacgtg ggcatatctt gttgttcagt ttgggtgtct 6660
 gctaaagagg aagtgcactg gccctctttg aaagggtttt acagtggggg caccaagacc 6720
 ccaaaggccc aggccaggag actgttaaag tgaaaaggca atctatgact caccttgctc 6780
 tgccatccct ggcagcccc accggtgtcc tgttcctgcc acatggagct tgacttcatg 6840
 ccagctataa tctcccctgc cttcctttaa tcccaatttc ccctgctcac tcttcacag 6900
 atataaagaa caaacactta gcatcccaca ctcaccctt ctaatcctga agggaagccc 6960
 attctaaact cttttcctgc aaaccattt ccagctccta gtagctttcc tcccaaaggc 7020
 tttctttcca atcctttata gctttggaga cgctcccca attcccagg gaaggaaact 7080
 gttgtgtcca atccccatta aagacaaatt gatcagtgtc tccc 7124

<210> 7
 <211> 5340
 <212> DNA
 <213> Homo sapiens

<400> 7
 ggccggggct gtcgcggtt gggcggtt ggctggcagc tgaggctcgt ggccatggag 60
 tgggggttctg agtcggctgc tgtgaggcgg caccgcgtcg gagtagagcg tcgagagggg 120
 gcggcggccg cgccaccgcc ggagaggag gcccgagcgc aggagcctct ggtggatggg 180
 tgcagcgcg gcgggaggac gcggaagagg agccccgggg gtagcgcgcg cgcgagcagg 240
 ggcgcgggga cggggtgtc tgaggtgcgc gccgcgtgg ggctcgcgt ctacctgatc 300
 gcgctgcgga cgctggtgca gctctcgtc cagcagctcg tgctacgcgg ggccgctgga 360
 caccgcgggg agttcgacgc gctccaagcc agggattatc ttgaacacat aacctccatt 420
 ggccccagga ctacaggaag tccagaaaat gaaattctga ccgtgcacta ctttttgaa 480
 cagattaaac tgattgaagt gcaaagcaac agccttcata agatttcagt agatgtacaa 540
 cggccacag gctcttttag cattgatttc ttgggaggtt ttacaagcta ttatgacaac 600

EX05-002patentin.txt

atcaccaatg ttgtggtaaa gctggaaccc agagatggag cccagcatgc tgtcttggct 660
aattgtcatt ttgactcagt agcaaactca ccaggtgcca gtgatgatgc agttagctgc 720
tcagtgatgc tggaaagtcct tcgctgtcttg tcaacatctt cagaagcctt gcatcatgct 780
gtcatatttc tctttaatgg tgctgaggaa aatgtcttgc aagccagtca tggtttcatt 840
actcagcacc cctgggctag cttgattcgt gcattcatta acctagaggc agcagggtgta 900
ggaggggaaag aacttgattt ccaaacaggt cctgaaaatc cttggttggt tcaagcttat 960
gtttcagcag ctaaaccacc ttttgcttct gtggtggctc aggagggttt tcagagtgga 1020
atcattcctt cagatactga ctttcgtatc tacagggatt ttgggaacat tccaggaata 1080
gacttagctt ttattgagaa tggatacatt tatcacacca agtatgacac agcggacaga 1140
attctaacag attccattca gagagcaggt gacaacattt tagcagttct taagcatcta 1200
gctacatctg atatgctggc tgctgcttct aagtatcgac atggaaacat ggtcttcttt 1260
gatgtgctgg gcctgtttgt cattgcctac ccctctcgta ttggctcaat cataaactac 1320
atggtggtaa tgggtgttgt tttgtacctg ggcaaaaaat ttttgcagcc caaacataag 1380
actggttaact acaagaagga cttcttgtgt ggacttgga tcactttgat cagctggttc 1440
actagccttg ttaccgttct cattatagca gtgttcatct ctcttattgg acagtctctc 1500
tcatggtata accacttcta tgtctccgtt tgtctgtatg gaactgcaac tgtagccaaa 1560
ataatactta tacatactct tgcgaaaaga ttttattaca tgaatgccag tgcccagtat 1620
ctgggagaag tttttttga catttcgctg tttgtccatt gctgttttct tgttaccctc 1680
acttaccaag gactttgctc ggcgtttatt agtgctgtct gggtagcatt cccattgctc 1740
acaaagctct gtgtgcataa ggacttcaag cagcatgggtg cccaaggaaa atttattgct 1800
ttttaccctt tggggatgtt tttccttat ctttatgcat tgtacctcat ctgggcagta 1860
tttgagatgt ttaccctat cctcgggaga agtgggtctg aaatcccacc tgatgttgtg 1920
ctggcatcca ttttggctgg ctgtacaatg attctctcgt cctattttat taacttcatt 1980
taccttgcca agagcacaaa aaaaaccatg ctaactttaa ctttggtatg tgcaattaca 2040
ttcctccttg tttgcagtgg aacatttttt ccatatagct ccaatcctgc taatccgaag 2100
ccaaagagag tgtttcttca gcatatgact agaacattcc atgacttgga aggaaatgca 2160
gttaaacggg actctggaat atggatcaat gggtttgatt atactggaat ttctcacata 2220
accctcaca ttcttgagat caatgatagt atccgagctc actgtgagga gaatgcacct 2280
ctttgtggtt ttccttggtg tcttccagtg cactttctga tcaggaaaaa ctggtatctt 2340
cctgccccag aagtttctcc aagaaatcct cctcatttcc gactcatatc caaagaacag 2400
acaccttggg attctataaa attgactttt gaagcaacag gaccaagcca tatgtccttc 2460
tatgttcgag cccacaaagg gtcaacactt tctcagtggc ctcttgga tggcacccca 2520
gtcacaagta aaggaggaga ctactttgtc ttttactccc atggactcca ggcctctgca 2580
tggcagttct ggatagaagt gcaggtttca gaagaacatc ctgaaggaat ggtcaccgtg 2640

EX05-002patentin.txt

gccattgctg cccactatct gtctggggaa gacaagagat cccctcaact ggatgctctg 2700
aaggaaaagt tcccagattg gacatttccc tctgcctggg tgtgcaccta cgatctcttt 2760
gtattttaat cttgtggatg agctctaagt acatgccag tggatactcc atgtgacatg 2820
gtttctccct atgttacgtg gatgtttgta acgtaagtca atgaatttta atgatcatat 2880
gttcaaagag ctttctgggt taacgctttt cagggccaag cactataagg gtttagctgt 2940
ggcgagtgat tgcattggcct gttgacactt gaaaatgcca gtcttttggc acttcagcac 3000
atgtgggtac tgccactaca cacacgtcat tttatatgac ctttaaggaca aagccaacaa 3060
tccacttcaa tagctgcccc tttaggatca agaaagatgt aactgtcag agcattgtta 3120
atgagacaaa agttgtttcc aatttaagcc caaaaccat ttgttgattt agtggatgg 3180
gggtaaaata tcattcactg aggtaatgat tccccttgag aatataactc tgtgtaggtc 3240
actggaaagt gattgccata gggctgggag agaagcattg cactcttgag gctgtagcct 3300
gtgtcaagct gtttcttcag gcagcctctc aaatgtgctt tgtctctctg tgctgaggcc 3360
tggaacctgt gctgagctgg tgactcactg tcctgacaag tggacacaca gatgcactgc 3420
tgtgtgctt tcctgaggtg gtttctatg cctgttttcc tctgaaacat gtctgttacc 3480
cctctccatc ttaccaagt gaaaagggga atatttgcc acatacccct ctggttttcg 3540
taggttcttt tggttcagaa tattgtttgt gccagtacat gaccttaact tccttcctca 3600
gagcactgag ctgccatctg ggctattctg gggtagaagg aaggctggga gtggtgggaa 3660
ttttataaat atttattctc ttttctttgt ttcataggag tcttggttta tacaaggtta 3720
gtccttcatg gtataatctt actgatgcac tgggcctatc tttttgtttt ccagccagtt 3780
gaatagatta gtttttctca gtaacttact atccagcaga ctggctttcc tgagacttga 3840
ggttggtgct tatactggaa tgagaccact gtacgtgtag gtggttcaga tcctgcgtaa 3900
tggaagcatg aggaactaaa aggtggtttt cattttgaag atggctatgt agcttgtaag 3960
gtgtatcaca gcagtacctc tcatggcttt ttggttccag cagtgagggc attggtgaga 4020
tcaatggtaa actgtgcaag ctttctttt atcattagga aatgtgaaac gttggacaaa 4080
ttttgagttt taacaaggac aaaaagttga aagaaaaggc acagttaaca aaaaagggtg 4140
gctagattta tcttgggtga tggaggaaat gagagaggaa tgctcttgaa aggtggtctg 4200
tggaatctgtc tgaatagaaa gagcacagta agtatgcatt gccggagaaa acgtccttga 4260
agctgcttgt ctcatgtgta tgatgtgctt tttaaactcat gcccctcggt gcctgcctaa 4320
tctgtgactc cctaaaaact aactgggccc atgtagatgg ggctgcaacc agagctgaat 4380
aacatgttag gctcacacat gcatcagcac tgcacactgg aatcattgct cttcctggac 4440
ttttagaaaa tcagtctcaa gtgcttcaag agtctggctc ctgctacttt tatctgtcag 4500
gtagcacata aggtttgcag ggtttatatt ttgtatagaa tcacagttgt ggagaaaaag 4560
taataatttc tcaatgaatt ttaaaaatgg gcctattttc tatccccgtg gttcatctga 4620
tataattagt gttccctgtg aattcccccc ctctatggga aggatgcctt tactctttat 4680

EX05-002patentin.txt

```

cagtaataaa ttatgactgt tttcatattg ccttaggggtt atttccctgt gtaaaccatt 4740
gtctttttgtt ttggttttct ttagcattat gaagctttgg tattgtacaa ggtcagtagt 4800
aagatgctca ctagtctcag ggcttgtgta atattctggg aggtcattta aatgccagaa 4860
atgggtcaagc aattatacac agtatttatg actctgttaa gcataccgtt tgtctgtcac 4920
attagtagat tctgagatta aaaaaaattt ttaaagagtg atcattttaa taatttctaa 4980
aagggtcttt tcaagctcta acaaagtcac taacaaatgc attattttct acagaattag 5040
atgttagtag tacagtactg catattcagg gaaaaagtgt gaggaattga tttcaaaata 5100
gttcgttctt gtgtttgacc taagaatgat tgctgcatga agtggtttgtt tttacagttt 5160
agcatatata aacaacatg ataggattcc ttaagatgtt accaccagg gggccacaag 5220
ccagcctgct gtctcaggaa gctgtagaag gagtgtttgt caatttcttg tctactggtt 5280
gctgacttac tgaggattaa ttgttgcctt acaatgttac tgaaataaac tgtttaatat 5340

```

```

<210> 8
<211> 3150
<212> DNA
<213> Homo sapiens

```

```

<400> 8
cccgaggct cggtgaatcg aacgttgagc agggcggtgg gtggtgtgga gtgccgagcg 60
gcctcacccc caaccgtcgg ccagtcgga cggttccgag gcgttgccgg gagccgggag 120
cggctctgtg tggactcggg gaaacgcggg gcgtctgcct gagcccgtt ttctacaaga 180
tgtggggatt tttgaagcgc cctgtagtgg tgacggctga catcaacttg agccttgtgg 240
ccctgactgg gatgggggta ctgagccggc tgtggcgact cacctaccgg cgggctgtgg 300
tttttgacga agtatattat gggcagtaca tctcttttta catgaaacaa atcttcttct 360
tggtatgacag tgggccgcca tttggccaca tgggtgctggc cttgggaggt tatttaggag 420
gattcgatgg caattttttg tggaacagaa ttggagcaga atacagtagc aacgtgcctg 480
tgtggtccct gcgcctgctg ccagcactcg cgggggcctt gtcggtcccc atggcctacc 540
agatagtgtt ggagctccac ttttctcatt gtgccgccat gggagctgct ctgttgatgc 600
ttatcaagaa tgctctcatc actcagtcaa ggctaattgct tttggaatca gtgttaatat 660
ttttcaatct attggccgtg ttgtcctacc tgaagtctt ccaactgccaa aagcacagcc 720
ctttttctct gagctgggtg ttctggctaa cactgacagg ggtcgcttgt tcctgtgcag 780
tgggcatcaa gtacatgggt gtgttcacgt acgtgctcgt gctgggtgtt gcagctgtcc 840
atgcctggca cctgcttgga gaccagactt tgtccaatgt aggtgctgat gtccagtgtc 900
gcatgaggcc ggcctgtatg gggcagatgc ggatgtcaca gggggctctgt gtgttctgtc 960
acttgctcgc ccgagcagtg gctttgctgg tcatcccggc cgtcctgtac ttactgttct 1020
tctacgtcca cttgattcta gtcttccgct ctgggccccg cgaccaaata atgtccagtg 1080
ccttcaggc cagcttagag ggaggactag ctcggatcac ccagggtcag ccaactggagg 1140

```

EX05-002patentin.txt

tggcctttgg	gtcccaggtc	actctgagga	acgtcttttg	gaaacctgtg	ccctgctggc	1200
ttcattccca	ccaggacacc	taccccatga	tatatgagaa	cggccgaggc	agctcccacc	1260
agcaacaggt	gacctgttac	cccttcaaag	acgtcaataa	ctggtggatt	gtaaaggatc	1320
ccaggaggca	ccagctggtg	gtgagcagcc	ctccgagacc	tgtgaggcac	ggggacatgg	1380
tgcagctggt	ccacggcatg	accacccgct	ccctgaacac	gcatgatgtt	gcagcccccc	1440
tgagccccca	ttcacaggag	gtctcctgct	acattgacta	taacatctcc	atgcccggcc	1500
agaacctctg	gagactggaa	attgtgaaca	gaggatctga	cacagacgtc	tggaagacca	1560
tcctctcaga	ggtccgcttt	gtgcacgtga	acacttccgc	tgtcttaaag	ctgagcgggg	1620
ctcacctccc	tgactggggg	tatcggaac	tggagatcgt	cggggagaag	ctgtcccggg	1680
gctaccacgg	gagcacggtg	tggaacgtgg	aggagcaccg	atacggcgcg	agccaggagc	1740
agagggagcg	ggaacgggag	ctgcactcac	ctgcgcaggt	ggacgtcagc	aggaacctca	1800
gcttcattgg	gagattctcg	gagctgcagt	ggaggatgct	ggcgctgaga	agtgatgact	1860
cggaaacaaa	gtacagctcc	agcccactgg	agtgggtcac	cctggacacc	aatattgcct	1920
actggctgca	ccccaggacc	agcgctcaga	tccacctact	tggaaacata	gtgatctggg	1980
tttcgggcag	cctcgctctg	gccatctacg	ccctgctgtc	cttggtggtac	ctgctccgac	2040
ggcgaagaaa	tgtccatgac	ctccctcagg	atgcctggct	gcgctgggtg	ctggctgggg	2100
cgctgtgtgc	cgggtggctgg	gcagtgaact	acctcccgtt	cttcctgatg	gagaagacac	2160
tcttcctcta	ccactacctg	ccgcactca	ccttccaaat	ccttctgctc	cctgtggtcc	2220
tgcagcacat	cagcgaccac	ctgtgcaggt	cccagctcca	gaggaattct	ttcagcgccc	2280
tggtggtggc	ctggtactcc	tccgcgtgcc	acgtgtccaa	cacgctgcgc	ccactcacct	2340
acggggacaa	gtcactctcg	ccacatgaac	tcaaggccct	tcgctggaaa	gacagctggg	2400
acatcttgat	ccgaaaacac	tagaacaaga	gtgtggcaaa	gaacacccgt	gctggggctg	2460
ggacgaggtt	gaagggtctt	ggtcaatgta	cgtaatgagc	aggggtgggccc	cacgctggga	2520
ggacacgggc	tgggctgagc	agggcctcta	gtggaacaca	ttgggggtct	cattgaaaag	2580
ctctctgatg	agcacctcct	tttgtgcaaa	gttaattttt	tctcgacaat	aaagatatct	2640
cgtgtcttca	cccctgaact	aagacacagg	gagtatttca	gaggccagcg	taggagtcac	2700
cgacaacgaa	aagccgagaa	cccagggccca	gcagtggaa	cctcaagcaa	gaccagggcc	2760
tggtccttgc	taattgctgc	aggggtggagt	ttgatctggc	agacccgatc	ctccttcctg	2820
aacacccagc	aacctgagca	agtcccggcc	ctgccctcag	cgagcccggc	aggcgtcccc	2880
ggacagctca	gtgttgagg	gccacctgaa	ccacgagcca	gggctggggc	ttgcatgtca	2940
ttgtctatga	cagcgtcaag	actgcccttg	gcaccgtgct	gtgtggaaac	cctccccctt	3000
gagactccac	tgagacgtgg	ctgagtgaac	tcttcctcgt	cagtgggtcaa	ggtgtgtcat	3060
ccatacagct	ccatgccttt	gtctttttta	aatgtaatta	aaaaaggaac	caactggcgt	3120
ttgtaaaaaa	aaaaaaaaaa	aaaaaaaaaa				3150

EX05-002patentin.txt

<210> 9
<211> 3649
<212> DNA
<213> Homo sapiens

<400> 9
gcggcaagcc ccgcctcagc ccctctggca ggctcccgcc agcgtcgctg cggctccggc 60
ccgggagcga gcgcccgag ctcggaaaga tgcggcgccc gcggcggcct gggggctctcg 120
ggggatccgg gggctctccg ctgctcctct gcctcctgct gctgagcagc cgcccggggg 180
gctgcagcgc cgtagtgcc cacggctgtc tatttgaccg caggctctgc tctcacctgg 240
aagtctgtat tcaggatggc ttgtttgggc agtgccaggt gggagtgggg caggcccggc 300
cccttttgca agtcacctcc ccagttctcc aacgcttaca aggtgtgctc cgacaactca 360
tgtccaagg attgtcctgg cacgatgacc tcaccagta tgtgatctct caggagatgg 420
agcgcatccc caggcttcgc ccccgagagc ccggtccaag ggacaggctt ggcttggcac 480
ccaagagacc tggctctgct ggagagctgc ttttacagga catccccact ggctccgccc 540
ctgctgcca gcatcggctt ccacaaccac cagtgggcaa aggtggagct ggggccagct 600
cctctctgtc ccctctgcag gctgagctgc tcccgctct cttggagcac ctgctgtgc 660
ccccacagcc tccccaccct tcaactgagtt acgaacctgc cttgctgcag ccctacctgt 720
tccaccagtt tggctcccgt gatggctcca gggcttcaga gggctcccca gggatggcca 780
gtgtcggccc cctgccaag gctgaagccc ctgccctctt cagcagaact gcctccaagg 840
gcatatttgg ggaccaccct ggccactcct acggggacct tccagggcct tcacctgccc 900
agctttttca agactctggg ctgctctatc tggcccagga gttgccagca ccagcaggg 960
ccagggtgcc aaggctgcca gagcaaggga gcagcagccg ggcagaggac tccccagagg 1020
gctatgagaa ggaaggacta ggggatcgtg gagagaagcc tgcttcccca gctgtgcagc 1080
cagatgctggc tctgcagagg ctggccgctg tgctggcggg ctatggggta gagctgcgtc 1140
agctgacccc tgagcagctc tccacactcc tgaccctgct gcagctactg cccaaggggtg 1200
caggaagaaa tccgggaggg gttgtaaag ttggagctga tatcaagaaa acaatggagg 1260
ggccggtgga gggcagagac acagcagagc ttccagcccc cacatcccc atgcctggac 1320
accccactgc cagccctacc tccagtgaag tccagcaggt gccaagccct gtctcctctg 1380
agcctcccaa agctgccaga cccctgtga cacctgtcct gctagagaag aaaagcccac 1440
tgggccagag ccagcccacg gtggcaggac agccctcagc ccgcccagca gcagaggaat 1500
atggctacat cgtcactgat cagaagcccc tgagcctggc tgcaggagtg aagctgctgg 1560
agatcctggc tgagcatgtg cacatgtcct caggcagctt catcaacatc agtgtggtgg 1620
gaccagccct caccttccgc atccggcaca atgagcagaa cctgtctttg gctgatgtga 1680
cccaacaagc agggctgggtg aagtctgaac tggaagcaca gacagggtc caaatcttgc 1740
agacaggagt gggacagagg gaggaggcag ctgcagtcct tccccaaact gcgcacagca 1800
cctcaccat gcgctcagtg ctgctcactc tgggtggccct ggcagggtgtg gctgggctgc 1860

EX05-002patentin.txt

```

tggtggctct ggctgtggct ctgtgtgtgc ggcagcatgc gcggcagcaa gacaaggagc 1920
gcctggcagc cctggggcct gagggggccc atggtgacac tacctttgag taccaggacc 1980
tgtgccgcca gcacatggcc acgaagtcct tgttcaaccg ggcagagggg ccaccggagc 2040
cttcacgggt gagcagtgtg tcctcccagt tcagcgacgc agcccaggcc agccccagct 2100
cccacagcag caccctgtcc tgggtgcgag agccggccca agccaacatg gacatctcca 2160
cgggacacat gattctggca tacatggagg atcacctgcg gaaccgggac cgccttgcca 2220
aggagtggca ggccctctgt gcctaccaag cagagccaaa cacctgtgcc accgcgagc 2280
gggagggcaa catcaaaaag aaccggcatc ctgacttcct gccctatgac catgcccgca 2340
taaaactgaa ggtggagagc agcccttctc ggagcgatta catcaacgcc agccccatta 2400
ttgagcatga ccctcggatg ccagcctaca tagccacgca gggcccgtg tcccatacca 2460
tcgcagactt ctggcagatg gtgtgggaga gcggctgcac cgtcatcgtc atgctgacct 2520
cgctgggtga ggatgggtgtc aagcagtgtg accgctactg gccagatgag ggtgcctccc 2580
tctaccacgt atatgaggtg aacctgggtg cggagcacat ctggtgcgag gactttctgg 2640
tgccggagctt ctacctgaag aacgtgcaga cccaggagac gcgcacgctc acgcagttcc 2700
acttcctcag ctggccggca gagggcacac cggcctccac gcggcccctg ctggacttcc 2760
gcaggaaggt gaacaagtgc taccggggcc gtcctgccc catcatcgtg cactgcagtg 2820
atggtgcggg gaggaccggc acctacatcc tcatcgacat ggtcctgaac cgcattggca 2880
aaggagtga ggagattgac atcgctgcca ccctggagca tgtccgtgac cagcggcctg 2940
gccttgtccg ctctaaggac cagtttgaat ttgccctgac agccgtggcg gaggaagtga 3000
atgccatcct caaggccctg cccagtgag accctggggc cccttggcg gacagcccagc 3060
ctctgtccct ctttgcctgt gtgagcatct ctgtgtaccc actcctcact gccccaccag 3120
ccacctcttg ggcatgctca gcccttccta gaagagtcag gaagggaaaag ccagaagggg 3180
cacgcctgcc cagcctcgca tgccagagcc tggggcatcc cagagcccag ggcattccat 3240
gggggtgctg cagccaggag gagaggaaa gacatgggta gcaattctac ccagagcctt 3300
ctcctgccta cattccctgg cctggctctc ctgtagctct cctgggggtt tgggagttcc 3360
ctgaacatct gtgtgtgtcc ccctatgtc cagtatggaa gaatgggggt gagggtcgcc 3420
acaccgggt cccctgctt ctacgccccg ggcctgcctc tgactcacac ttgggcgctc 3480
tgccctccct ggcctcacgc ccagcctcct cccaccaccc tcccaccatg cgtgtctcaa 3540
cctctctcct tctggcgcaa gagaacattt ctagaaaaaa ctacttttgt accagtgtga 3600
ataaagttag tgtgttgtct gtgcagctgc aaaaaaaaaa aaaaaaaaaa 3649

```

```

<210> 10
<211> 4767
<212> DNA
<213> Homo sapiens
<400> 10

```

EX05-002patentin.txt

gcctcccgcc	gcctcccgcg	cggccatgga	ctgagcgccg	cgggccaggc	cgcggggatg	60
gggcccgcgc	tcccgtgct	gctgctgcta	ctgctgctgc	tgccgccacg	cgctctgcct	120
gccgcccctt	cgcccgctccc	ccgcggcccg	cagctcccgg	ggcgtctggg	ctgcctgctc	180
gaggagggcc	tctgcggagc	gtccgaggcc	tgtgtgaacg	atggagtgtt	tggaagggtgc	240
cagaagggtc	cggcaatgga	cttttaccgc	tacgaggtgt	cgcccggtggc	cctgcagcgc	300
ctgcgcgtgg	cgttgacagaa	gctttccggc	acagggtttca	cgtggcagga	tgactatact	360
cagtatgtga	tggaccagga	acttgacagac	ctcccgaaaa	cctacctgag	gcgtcctgaa	420
gcatccagcc	cagccaggcc	ctcaaaacac	agcgttgga	gcgagaggag	gtacagtcgg	480
gagggcggtg	ctgccctggc	caacgccctc	cgacgccacc	tgcccttcct	ggaggccctg	540
tcccaggccc	cagcctcaga	cgtgctcgcc	aggaccata	cggcgcagga	cagaccccc	600
gctgaggggtg	atgaccgctt	ctccgagagc	atcctgacct	atgtggccca	cacgtctgcg	660
ctgacctacc	ctcccgggccc	ccggaccag	ctccgcgagg	acctcctgcc	gcggaccctc	720
ggccagctcc	agccagatga	gctcagccct	aagggtggaca	gtggtgtgga	cagacaccat	780
ctgatggcgg	ccctcagtgc	ctatgctgcc	cagaggcccc	cagctcccc	cggggagggc	840
agcctggagc	cacagtacct	tctgcgtgca	ccctcaagaa	tgcccaggcc	tttgctggca	900
ccagccgccc	cccagaagtg	gccttcacct	ctgggagatt	ccgaagacc	ctccagcaca	960
ggcgatggag	cacggattca	taccctcctg	aaggacctgc	agaggcagcc	ggctgaggtg	1020
aggggcctga	gtggcctgga	gctggacggc	atggctgagc	tgatggctgg	cctgatgcaa	1080
ggcgtggacc	atggagtagc	tcgaggcagc	cctgggagag	cggccctggg	agagtctgga	1140
gaacaggcgg	atggcccaa	ggccaccctc	cgtggagaca	gctttccaga	tgacggagtg	1200
caggacgacg	atgatagact	ttaccaagag	gtccatcgtc	tgagtgccac	actcgggggc	1260
ctcctgcagg	accacgggtc	tcgactctta	cctggagccc	tcccctttgc	aaggcccctc	1320
gacatggaga	ggaagaagtc	cgagcaccct	gagtcttccc	tgtcttcaga	agaggagact	1380
gccggagtgg	agaacgtcaa	gagccagacg	tattccaaag	atctgctggg	gcagcagccg	1440
cattcggagc	ccggggccgc	tgcgtttggg	gagctccaaa	accagatgcc	tgggccctcg	1500
aaggaggagc	agagccttcc	agcgggtgct	caggaggccc	tcagcgacgg	cctgcaattg	1560
gaggtccagc	cttccgagga	agaggcgcg	ggctacatcg	tgacagacag	agaccccctg	1620
cgccccgagg	aaggaaggcg	gctgggtggg	gacgtcgccc	gcctcctgca	ggtgcccagc	1680
agtgcgttcg	ctgacgtgga	ggttctcgga	ccagcagtga	ccttcaaagt	gagcgccaat	1740
gtccaaaacg	tgaccactga	ggatgtggag	aaggccacag	ttgacaacaa	agacaaactg	1800
gaggaaacct	ctggactgaa	aattcttcaa	accggagtcg	ggtcgaaaag	caaactcaag	1860
ttcctgcctc	ctcaggcgga	gcaagaagac	tccaccaagt	tcatcgcgct	caccctggtc	1920
tccctgcctc	gcatcctggg	cgctcctcctg	gcctctggcc	tcactctactg	cctccgccat	1980
agctctcagc	acaggctgaa	ggagaagctc	tcgggactag	ggggcgaccc	aggtgcagat	2040

EX05-002patentin.txt

gccactgccg cctaccagga gctgtgccgc cagcgtatgg ccacgcggcc accagaccga 2100
cctgagggcc cgcacacgtc acgcatcagc agcgtctcat cccagttcag cgacggggccg 2160
atccccagcc cctccgcacg cagcagcgcc tcatcctggt ccgaggagcc tgtgcagtcc 2220
aacatggaca tctccaccgg ccacatgata ctgtcctaca tggaggacca cctgaagaac 2280
aagaaccggc tggagaagga gtgggaagcg ctgtgcgctt accaggcgga gccaacacgc 2340
tcgttcgtgg cccagagggg ggagaacgtg cccaagaacc gctccctggc tgtgctgacc 2400
tatgaccact cccgggtcct gctgaaggcg gagaacagcc acagccactc agactacatc 2460
aacgctagcc ccatcatgga tcacgacccg aggaaccccg cgtacatcgc caccagggga 2520
ccgctgcccc ccaccgtggc tgacttttgg cagatggtgt gggagagcgg ctgctggtg 2580
atcgtcatgc tgacacccct cgcggagaac ggcgtccggc agtgctacca ctactggccg 2640
gatgaaggct ccaatctcta ccacatctat gaggtgaacc tggctctccg gcacatctgg 2700
tgtgaggact tcctggtgag gagcttctat ctgaagaacc tgcagaccaa cgagacgcgc 2760
accgtgacgc agttccactt cctgagttgg tatgaccgag gagtcccttc ctctcaagg 2820
tccctcctgg acttccgcag aaaagtaaac aagtgtctaca ggggccgttc ttgtccaata 2880
attgttcatt gcagtgcagg tgcaggccgg agcggcacct acgtcctgat cgacatggtt 2940
ctcaacaaga tggccaaagg tgctaaagag attgatatcg cagcgaccct ggagcacttg 3000
agggaccaga gacccggcat ggtccagacg aaggagcagt ttgagttcgc gctgacagcc 3060
gtggctgagg aggtgaacgc catcctcaag gcccttcccc agtgagcggc agcctcaggg 3120
gcctcagggg agccccacc ccacggatgt tgtcaggaat catgatctga ctttaattgt 3180
gtgtcttcta ttataactgc atagtaatag ggcccttagc tctcccgtag tcagcgcagt 3240
ttagcagtta aaagtgtatt ttgttttaat caaacaataa taaagagaga tttgtggaaa 3300
aatccagtta cgggtggagg ggaatcggtt catcaatttt cacttgctta aaaaaatac 3360
tttttcttaa agcaccctgt caccttcttg gttgaagttg tgtaacaat gcagtagcca 3420
gcacgttcga ggcggtttcc aggaagagtg tgcttgtcat ctgccacttt cgggaggggtg 3480
gatccactgt gcaggagtgg ccggggaagc tggcagcact cagtgaggcc gcccggcaca 3540
caaggcacgt ttggcatttc tctttgagag agtttatcat tgggagaagc cgcggggaca 3600
gaactgaacg tcctgcagct tcggggcaag tgagacaatc acagctcctc gctgcgtctc 3660
catcaacact gcgccgggta ccatggacgg ccccgtcagc cacacctgtc agccaagca 3720
gagtgattca ggggtctccc gggggcagac acctgtgcac cccatgagta gtgcccactt 3780
gaggctggca ctcccctgac ctacactttg caaagttaca gatgcacccc aacattgaga 3840
tgtgttttta atgttaaaat attgatttct acgttatgaa aacagatgcc cccgtgaatg 3900
cttacctgtg agataaccac aaccaggaag aacaaatctg ggcattgagc aagctatgag 3960
gggtccccggg agcacacgaa ccctgccagg cccccgtgg ctctccagg cacgtcccgg 4020
acctgtgggg cccagagag gggacatttc cctcctggga gagaaggaga tcagggcaac 4080

EX05-002patentin.txt

tcggagaggg	ctgcgagcat	ttccctccc	ggagaggaga	tcagggcgac	ctgcacgcac	4140
tgcgtagagc	ctggaaggga	agtgagaaac	cagccgaccg	gccctgcccc	tcttcccggg	4200
atcacttaat	gaaccacgtg	ttttgacatc	atgtaaacct	aagcacgtag	agatgattcg	4260
gatttgacaa	aataacattt	gagtatccga	ttcgccatca	ccccctaccc	cagaaatagg	4320
acaattcact	tcattgacca	ggatgatcac	atggaaggcg	gcgcagaggc	agctgtgtgg	4380
gctgcagatt	tcctgtgtgg	ggttcagcgt	agaaaacgca	cctccatccc	gcccttccca	4440
cagcattcct	ccatcttaga	tagatggtag	tctccaaagg	ccctaccaga	gggaacacgg	4500
cctactgagc	ggacagaatg	atgccaaaat	attgcttatg	tctctacatg	gtattgtaat	4560
gaatatctgc	tttaatatag	ctatcatttc	ttttccaaaa	ttactttctt	ctatctggaa	4620
tttaattaat	cgaaatgaat	ttatctgaat	ataggaagca	tatgcctact	tgtaatttct	4680
aactccttat	gtttgaagag	aaacctccgg	tgtgagatat	acaaatatat	ttaattgtgt	4740
catattaaac	ttctgattca	aaaaaaa				4767

<210> 11
 <211> 4781
 <212> DNA
 <213> Homo sapiens

<400> 11						
gaggaggagc	cggaggaaga	gggctgcctc	cgaagaaagg	agaatggcgt	tcagtaaagg	60
attccggatc	tatcacaaat	tggatcccc	acctttcagc	ctcatagtgg	aaactaggca	120
taaggaagaa	tgtctcatgt	tcgagtctgg	ggctgtcgct	gtgctctcat	ctgcagaaaa	180
agaggcaatc	aagggtacat	actccaaagt	actggatgca	tatggactct	taggtgttct	240
gcggttaaat	cttggtgata	ctatgttaca	ttatctgggc	ctagtactg	gatgtatgtc	300
tgttggaaaa	attcaagaat	ctgaagtttt	ccgagttact	tccactgagt	ttatatcact	360
gcgaatcgat	tcttcagatg	aggatcgcat	ttcagaagtg	cggaaagttt	tgaattcagg	420
aaacttttat	tttgcattgg	ctgcatctgg	catcagttta	gatttgagtc	ttaatgcgca	480
tcgtagcatg	caagaacaga	caactgataa	tagatttttc	tggaatcagt	ctttgcattt	540
gcatctcaaa	cactatggcg	tgaattgtga	tgactggtta	ttacgtctta	tgtgtggagg	600
agtagaaatc	agaacaattt	atgctgctca	taaacaggcg	aaggcttgcc	tcatttcaag	660
attaagctgt	gaacgagctg	ggaccagggt	taatgtccgg	ggaacaaatg	atgatggtca	720
tgttgccaat	tttgtagaaa	cagaacaggt	tgtgtactta	gatgactcag	tttcttcctt	780
catacaaatc	cgaggatctg	ttccattgtt	ctgggagcaa	ccagggttgc	aagtgggatc	840
tcatcgtgtc	cgtatgtcaa	ggggatttga	agccaatgca	cctgcttttg	acaggcattt	900
tagaacactt	aagaacttat	atggtagaca	aataatagta	aatttgcttg	gatctaagga	960
agggtgaacat	atgctaagta	aagctttcca	gagtcatttg	aaagcttctg	aacatgctgc	1020
tgatatccag	atggtgaatt	ttgactatca	tcaaattggt	aaggaggagg	aggcagaaaa	1080
attacatagt	gttcttaaac	ctcaagtcca	gaagtttcta	gattatggat	ttttttattt	1140

EX05-002patentin.txt

caatggaagt gaagttcaaa gatgccagag tggtagcatt cgaacaaact gcttggattg 1200
tcttgataga acaaatagtg tgcaggcatt tcttggctta gagatgctag ctaaacagtt 1260
ggaagctctt ggttttagctg aaaagcctca gttggtgact cgctttcaag aagtttttcg 1320
gtcaatgtgg tccgtgaatg gtgattcaat cagtaagata tatgcaggaa ctggagctct 1380
tgaagggaaa gcgaagttaa aagatggtgc tcgctctgtt acccgaacaa ttcagaataa 1440
cttctttgac agctccaagc aagaggccat tgatgttttg ctactgggaa atactctgaa 1500
tagtgattta gctgacaaag ctcgagcact tttactact ggaagtttgc gtgtttctga 1560
gcagacatta cagtcagcat cttctaaagt actaaagagc atgtgtgaga atttctacaa 1620
atattcaaa cctaagaaaa ttcgagtatg tgtcggaaac tggaatgtga atggtgggaa 1680
gcaatttcgc agcatagctt ttaagaatca gacactcact gactggcttc ttgatgcacc 1740
caagttagct ggcattccagg agtttcaaga taaaagaagt aagccaactg atatatattgc 1800
aattggtttt gaagaaatgg tagaattgaa tgctggaaac attgtgagt caagcacaac 1860
aaatcagaag ctctgggctg tagaacttca gaagacaatc tccagagaca acaagtatgt 1920
gctgctggct tctgaacagt tgggtggcgt ctgtttgttt gtttttatca gaccacagca 1980
tgctcctttt atcagggatg ttgcagttga tactgtgaag actggaatgg gaggtgcaac 2040
tggaataaag ggagcagttg caatccgaat gctcttccat acaaccagcc ttgcttcgt 2100
ctgtagccac ttgtctgcag ggcagtcaca agtcaaagaa agaaatgaag attttataga 2160
aatagcacga aaattgagtt ttcctatggg aaggatgcta ttttcccatg actatgtatt 2220
ttggtgtggt gatttcaact atcgaatcga tctccctaac gaagaagtta aagagctcat 2280
aagacagcaa aattgggatt ctcttatagc aggagatcaa cttatcaatc agaaaaatgc 2340
tggaacaggt ttttagaggat ttttagaagg aaaggtaacc ttgctccga catataagta 2400
tgacttgttt tctgacgact atgacaccag tgaaaagtgc cgcaccctg cctggacaga 2460
ccgtgtcctt tggagaagga ggaaatggcc ttttgataga tcagctgaag atctagatct 2520
tctaaatgct agttttcaag atgaaagcaa aattctgtac acgtggactc caggcacttt 2580
gctgcactat ggaagagctg agctgaagac ttctgaccac aggcctgtcg ttgccctgat 2640
tgatatagat atatttgaag ttgaagctga agagaggcaa aacatttata aagaagtaat 2700
tgcagttcag ggtccaccag atggtacagt attggtctca atcaaaagt ctttaccaga 2760
aaataatttt ttgatgatg ctttgattga tgagcttctg cagcagtttg caagttttgg 2820
tgaagttata cttataagat ttgtagaaga taaaatgtgg gttacatttt tggaggggaa 2880
ctctgccttg aatgttctga gcctaaatgg taaagagtta ttgaatcgga ctataactat 2940
tgctttaaaa agtccagact ggatcaaaaa tttggaagaa gaaatgagtt tagagaaaat 3000
tagcattgca ttgccatcat caacaagctc taccctgctt ggtgaagatg cagaggttgc 3060
agcagatttt gatatggaag gtgatgttga tgactatagt gctgaagtgg aggaacttct 3120
tcctcagcat ctccagccat cttcaagttc cggccttggg acttccccca gctcttcacc 3180

EX05-002patentin.txt

```

ccgaactagt ccctgccagt cacctacaat atcagagggg cctgtacctt cccttcccat 3240
cagaccaagc cgagcaccgt caagaactcc tgggcctccc agtgcacaga gttctcctat 3300
tgacgcgcag ccagcaacgc cgctgccgca gaaagacccc gccagccct tggagcccaa 3360
gcggccgccc ccgccccgcc cggtcgcccc tcccacacgc ccggctcccc cacagagacc 3420
tcctccgcct tcaggggcta ggagtcctgc acccactaga aaggaatttg gaggtattgg 3480
agccccctcc agtcctgggg tagctaggag agagatggaa gcacccaaaa gccctggaac 3540
aacaaggaaa gataatatag gacgcagtca gccttcacct caagcaggac ttgcaggccc 3600
aggacctgct ggatacagta cagccagacc gacgattcct cctcgtgctg gagttatcag 3660
tgccccacag agccacgcgc gggcatctgc tggaagactg actcctgaaa gccaaagcaa 3720
aacatcagaa acgtcgaaag gttcaacttt ccttcctgaa ccactgaagc ctcaggctgc 3780
ttttcctccg cagtcttctt tgccccgcc tgctcaaagg ttgcaagagc ctcttgctcc 3840
tgtggcagca cctatgcctc agtctggccc ccagccaaat ttggaaaccc caccacaacc 3900
accacctcga agcagggtcat cccatagctt gccttcagaa gcttcctcac aaccgcaagt 3960
aaaaacaaat ggaatctctg atggcaaaag agaatcacca ttaaagattg acccatttga 4020
agatctgtca tttaatctgc ttgctgtatc aaaggctcag ctatctgttc aaacgtcacc 4080
tgttcccacc ccagacccaa agaggttgat tcagttgcct tctgcaacgc aaagtaatgt 4140
taatactttg agttctgtaa gttgcatgcc aacaatgcct ccaattccag ctcggagtca 4200
atcccaggaa aatatgcgaa gttctccaaa cccatttatt actggcttga ccaggacaaa 4260
tcctttcagt gacaggactg ctgctcctgg aaaccattt agagccaagt ctgaagaatc 4320
agaggcaact tcatggttct ccaaagaaga gccggttact atcagtcctt tcccttctct 4380
gcagcctctt ggtcataaca aaagcagggc ttcattctca cttgatggct ttaaggacag 4440
ttttgatcta cagggccagt ctacattaaa aattagcaac ccgaaaggat gggtaacctt 4500
cgaggaagaa gaggattttg gtgtgaaagg gaagtcaaag tcagcttggt cagacttact 4560
gggtaatcag ccaagttcat tttctggctc caacctgaca ttgaatgatg actggaataa 4620
agggacaaat gtctccttct gtgtgttgcc gtcaagaaga cctcctccac ctctgtccc 4680
tctgctcccg cccggcacca gccctccagt agatcctttc acgaccttgg cctctaaggc 4740
ttcaccacac ctggacttta cagaaagata acgccagccc g 4781

```

<210> 12
 <211> 6746
 <212> DNA
 <213> Homo sapiens

```

<400> 12
ggcacgaggc ggggagctgt cgcgggcagc gcgccctcgg gaggacgtgg ccccgcccc 60
cgcccgcagt gggcccgacc ctcattggccc tgagcaaagg gctgcggctg ctggggcgcc 120
tgggggccga gggggactgt agcgtgctgc tggaggcgcg cggccgcgac gactgcctgc 180

```

EX05-002patentin.txt

tgttcgaggc	cggcacggtg	gccacgctgg	ctccagaaga	aaaggaagtc	attaaaggac	240
agtatggcaa	gctcacggac	gcgtacggct	gcctggggga	gctgaggctg	aaatctggtg	300
gcacgtctct	gagcttcctg	gtgttggtga	caggctgcac	atctgtgggc	agaattccag	360
atgctgaaat	ctacaaaatc	actgccactg	actttttacc	tcttcaggaa	gaggccaagg	420
aggaggaacg	cctcatagct	ttgaagaaaa	tcctcagctc	gggggtgttc	tattttctcat	480
ggccaaacga	tgggtctcgc	tttgacctga	ctgtccgcac	gcagaagcag	ggggatgaca	540
gctctgaatg	ggggaactcc	ttcttctgga	accagctggt	gcacgtgccc	ttgaggcagc	600
accaggtgag	ctgctgtgac	tggctgctga	agatcatctg	cggggtggtc	accatccgca	660
ccgtgtatgc	ctcccacaag	caggccaagg	cctgcctcgt	ctctcgcgtt	agctgtgagc	720
gcacaggcac	tcgcttcac	acccgtggcg	tgaacgacga	cggccatgtg	tccaacttcg	780
tggagacaga	gcagatgatt	tacatggacg	atggagtgtc	atcttttgtc	cagatcagag	840
gctccgttcc	gctgttctgg	gaacagccag	ggcttcagggt	tggctcccat	catctgagac	900
tccacagagg	cctggaagcc	aatgcccctg	ctttcgacag	gcacatggtg	cttctgaagg	960
agcagtacgg	gcagcaggtg	gtcgtgaacc	ttctgggaag	cagaggcggg	gaggaggtgc	1020
tcaacagagc	cttcaagaag	ctgctctggg	cttcttgcca	cgcgggcgac	acgcctatga	1080
tcaattttga	cttccatcag	tttgccaaag	gtgggaagct	agagaaattg	gagaccctct	1140
tgaggccaca	gttaaagctg	cactgggaag	acttcgatgt	gttcacaaag	ggggagaacg	1200
tcagtccacg	ttttcagaaa	ggcactttgc	ggatgaactg	tcttgactgc	ctggaccgaa	1260
ccaacactgt	gcagagcttc	atcgcgctcg	aggtcctgca	tctgcagctc	aagaccctgg	1320
ggctgagttc	aaaaccatc	gttgaccgct	ttgtggagtc	cttcaaagcc	atgtggtctc	1380
tgaatggcca	cagcctgagc	aagggtgtta	caggcagcag	agccctggaa	gggaaggcca	1440
aggtggggaa	gctgaaggat	ggagcccgtt	ccatgtctcg	aaccatccag	tccaacttct	1500
tcgacggggg	gaagcaggag	gccatcaagc	tgctgtggtt	tggggacgtc	tacggcgagg	1560
aggtggcaga	caaagggggc	atgctgctgg	acagcacggc	gctcctggtg	actcccagga	1620
tcctgaaagc	tatgactgag	cgtcagtccg	aattcacaaa	tttcaagcgg	atccggattg	1680
ctatggggac	ctggaacgtg	aacggaggaa	agcagttccg	gagcaacgtg	ctcaggacgg	1740
cggagctgac	agactggctg	ctcgactcgc	cccagctctc	gggagctacc	gactcccagg	1800
atgacagcag	cccagctgac	atatttgctg	tggggtttga	agagatggtg	gaattgagcg	1860
caggaatat	tgtcaatgcc	agtactacca	acaagaagat	gtggggtgaa	cagcttcaga	1920
aagccatctc	acgctctcat	agatacattc	tgttgacttc	ggcacagctg	gtgggcgtct	1980
gtctttatat	ctttgtacgt	ccataccatg	tcccgttcat	cagggacgta	gccatcgaca	2040
cagtgaagac	gggcatgggg	ggcaaggcgg	ggaacaaggg	cgccgtcggc	atccgcttcc	2100
agttccacag	caccagcttc	tgcttcatat	gtagtcacct	gacggccggg	cagtcccagg	2160
tgaaggagcg	gaatgaagac	tacaaggaga	tcaccagaa	actctgcttc	ccaatgggga	2220

EX05-002patentin.txt

gaaatgtttt	ttctcatgat	tatgtatttt	ggtgtggcga	tttcaactac	cgcattgatc	2280
ttacttatga	agaagtcttc	tatttttgta	aacgccaaga	ctggaagaaa	cttctggaat	2340
ttgatcaact	acagctacag	aatcaagtg	gaaaaatfff	taaggacttt	cacgaaggag	2400
ccattaactt	tggacccacc	tacaagtatg	acgttggctc	agccgcctac	gatacaagcg	2460
acaaatgccg	cacccccgcc	tggacagaca	gggtgctgtg	gtggaggaag	aaacatccct	2520
ttgataaaac	agctggagaa	ctcaaccttc	tagacagtga	tctagatggt	gacaccaaag	2580
tcagacacac	ctggtctcct	ggtgccctgc	agtattatgg	tcgtgaggag	ctacaagcgt	2640
ctgatcacag	acctgtgctg	gcgatcgtgg	aggtggaagt	tcaggaagtc	gatgtgggtg	2700
ctcgggagag	ggttttccag	gaagtgtcct	ccttccaggg	ccccctggat	gccactgttg	2760
tagtaaacct	tcaatcaccg	accttagaag	agaaaaacga	gtttccagag	gacctgcgta	2820
ctgagctcat	gcagaccttg	gggagttatg	ggacaattgt	tcttgtcagg	atcaaccaag	2880
ggcagatgct	ggtaactttt	gcagacagtc	actcggtctt	cagtgtcctg	gacgtggacg	2940
gtatgaaggt	gaaaggcaga	gcagtgaaga	ttagaccgaa	gaccaaggac	tggctgaaag	3000
gtttgcgaga	ggagatcatt	cggaaacgag	acagcatggc	ccccgtgtct	cccactgcca	3060
actcctgttt	gctggaggaa	aactttgact	tcacaagttt	ggactatgag	tcagaagggg	3120
atattcttga	agacgatgaa	gactacttgg	tggatgaatt	caatcagcct	ggagtctcgg	3180
acagtgaact	cgggggagac	gacctctctg	atgtccccgg	ccccacagca	ctggctcctc	3240
ccagcaagtc	acctgctctc	acaaaaaaga	agcagcatcc	aacgtacaaa	gatgacgcgg	3300
acctggtgga	gctcaagcgg	gagctggaag	ccgtcgggga	gttccgccac	cgttctccga	3360
gcaggtctct	gtcgggtccc	aaccggcctc	ggccacctca	acccccgcag	agaccccccc	3420
ctccaaccgg	tttaatggtg	aaaaagtcgg	cttcagatgc	gtccatctcc	tccggcacc	3480
atggacagta	ttcaattttg	cagacggcaa	gacttctacc	aggagcacct	cagcaacctc	3540
ccaaggctcg	gactggaata	agtaaacttt	ataatgtcaa	gcagatcaaa	accaccaatg	3600
cccaggaggc	agaagcagca	atccggtgtc	tcctggaagc	cagaggaggt	gcctccgaag	3660
aagccctaag	tgccgtggcc	ccaagggacc	ttgaagcatc	ctctgaacca	gagccacac	3720
cgggggcagc	caaaccagag	acccacaggg	cgccccact	ccttccccgt	cggccccac	3780
ccagagttcc	tgccatcaag	aagccaacct	tgagaaggac	aggaaagccc	ctgtcacccg	3840
aagaacagtt	tgagcaacag	actgtccatt	ttacaatcgg	gccccggag	acaagcgttg	3900
aggccctcc	tgtcgtgaca	gcccctcag	tccctcctgt	tcccaaacca	agaacatttc	3960
agcctgggaa	agctgcagag	aggccaagcc	acaggaagcc	agcatcagac	gaagcccctc	4020
ctggggcagg	agcctctgtg	ccaccacctc	tggaggcgcc	gcctcttggt	cccaaggtag	4080
ccccgaggag	gaagaagtca	gccccgcag	ccttccacct	gcaggtcctg	cagagcaaca	4140
gccagcttct	ccagggcctc	acttacaata	gcagtgcag	cccctctggg	caccacctg	4200
ccgcgggcac	cgtcttccca	caaggggact	ttctcagcac	ttcatctgct	acaagccccg	4260

EX05-002patentin.txt

acagcgatgg	caccaaagcg	atgaagccag	aggcagcccc	acttcttggt	gattatcagg	4320
accccttctg	gaaccttctt	caccacccta	aactgttgaa	taacacttgg	ctttctaaga	4380
gctcagaccc	tttggaactca	ggaaccagga	gccccaaaag	agatcccata	gaccagtggt	4440
cagctggcgc	ttcagctgcc	aaggcagagc	tgccaccaga	tcatgaacac	aaaaccttag	4500
gtcactgggt	gacaatcagt	gaccaagaaa	agaggacagc	actgcaggtg	tttgaccac	4560
tggaacaaac	atgactgagc	agctttgaag	gctgcagttc	tatagaatgc	ataccttctt	4620
ccctctagac	atccctccac	cagaagagac	atctatttaa	aggcacactg	gccaaaacgt	4680
ttgtgcatct	gtcactctcg	tgtagtttac	aaaaatcgtg	tctcttattc	agtaagatgg	4740
ttactcagcc	acaaaaatat	atttcactca	aggcttgtag	atctgaagtt	tgctcttcaa	4800
ggaatgggaa	ccttcctggt	aaattcgggtg	tatggatttt	aagaaaggaa	tctagccaat	4860
gaggtccaag	aagtcttcac	ccattgaatt	tttaaattggc	tgttcagttc	atgttgtagc	4920
tgatggagat	ttgtcttttg	ttttatttgc	attttacaga	tttggtataa	cattttgggg	4980
agccacctga	aggttgatgt	ataaagtaag	gattagagaa	agaggtcggt	gtgaccatta	5040
atagctgtcc	tggtccactt	aaacaagggt	acaaaaaatc	agagtcggaa	gcagccaaat	5100
aggtcaacct	aatgactaga	ctgtacattc	ccatgagcct	tcatgtttta	gtgtgtacat	5160
gtgcgttaac	cttgatgatg	cgtgaatccc	gagggagccg	gtggcataca	ccgttagctt	5220
aaccttagct	taaactagct	gaaggctcct	gtgccatgtc	ttagacattg	catgccctat	5280
caattactat	aatcctgagc	catggtgtgc	tactgaaacc	aatttttata	caccatctag	5340
tccttattaa	atgaaacctc	acggatcctt	tggtccgctt	atattccatg	cataccacat	5400
aaaagcacac	agtgcgaaaa	ctcttgctga	tacgcgatat	tgattctcat	tgttagaata	5460
tgagagtggt	ttcagcctcg	tctgtccggc	tgagagcttc	ggatggaaaag	tgctatgtgt	5520
ccctgcatat	aagaatcacc	aggccagtggt	ttctggggtt	gcttggtctat	atgtttgtct	5580
atattttttg	cctatacatt	tttccacgt	ttccaacagc	acttctcacc	tattcaataa	5640
ctgaaaaaga	cattaccata	gtgctttaca	tttttaaagt	aatgttacia	ggtctggaat	5700
ccatttgag	cagataccgt	gttttcgcta	tttaataaga	agttcagtag	tgaaatctta	5760
ctgtaccgcc	tggtgtatct	gggagcctcg	tacagaggct	cgcacagcag	tgatcaagtg	5820
tcatccctta	cgtgactggg	ggatgtctgt	cctaaaagct	gactgctagg	atagtaagga	5880
tcatcttgcc	tggtgtatgc	cactgtcttg	ttaccaatta	gacatctgga	atttcataat	5940
tagttttcat	tgctactgtc	aagatatatt	gcagattact	taaatatggc	catcaaaaca	6000
aaagttacia	cacgtatctc	ttttcatctg	aaaactaata	cctggaaaag	gataaaaaaa	6060
aaaaggaatc	cgtgaccac	agagctagac	agataagatg	catagttgac	cagtcataaa	6120
aggcgggtgt	taagtgatca	ggatgccgtt	gggtggcattt	acgtgcttta	tatgattttt	6180
acctctgtaa	caaacacaag	aaataaacag	aatggtcctt	aacagagttt	gggggagaga	6240
gcaagatggg	ttccttgag	aagctgattt	gccaagatgc	acatcgctat	taacagccag	6300

EX05-002patentin.txt

```

agtcataaat gaaatgaaat tgaagaattc attcaaatgc tcttttccct ataacctctt 6360
ttctcaccaa aaaggagata aatttgaaaa cagataaatg taacaaccag tcaaagaagc 6420
aggggaaaaag taagctcctc caaagttgct tgcagtgctg gaaatagatc tcatttttag 6480
gttttctctt cgttccagat accaaataaa tgggacagag aataaaaattt ttgttaaaat 6540
atgtgctcat ctctaagta gctcttcaga gtctgaccgt aagtaaaaac acacagaatt 6600
gtgttgactg ggggaggtga atcacaaaaa agttacgagg agtttaagag ttaaatatta 6660
tttgatcgtg gctgtcaaat ttagtgaaca acatagattg gatttgagat tggtagtaag 6720
tatggttctc ataccagaat tctctt 6746

```

<210> 13
 <211> 444
 <212> DNA
 <213> Homo sapiens

```

<400> 13
atggcgctga aacggattaa taaggaactt agtgatttgg cccgtgaccc tccagcacia 60
tgttctgcag gtccagtgg ggatgatatg tttcactggc aagccacaat tatgggacct 120
catgacagac catatcaagg cgggtgtattc ttttgacaa ttcgttttcc tacagactac 180
cccttcaaac catctaaggt tgcatttaca acaagaattt atcacccaaa tattaacagt 240
aatggcagca tttttcttga cattctaaga tcacagtggc cgcctgcttt aacactttct 300
aaagttcttt tatccatttg ttactgcta tgtgatccaa acccagatga tcccctagt 360
ccagagattg cacggatcta taaaacagac agagataagt acaacagaat atctcgggaa 420
tggtactcaga agtatgccat gtga 444

```

<210> 14
 <211> 1398
 <212> DNA
 <213> Homo sapiens

```

<400> 14
gtgcagcttg gtggcggctg agccggcagc gggccgcctc aggcagcccc ggccgggccc 60
cccgggtccc cggcagcggg gtaggatggc gctaaagcgg atccagaagg aattaaccga 120
cttgacagag gatcctcctg cccagtgttc tgcaggacct gtcggtgatg acttgttcca 180
ctggcaggcc accatcatgg gcccgaatga cagtccttac caaggagggtg ttttcttctt 240
gaccatccac tttcctacag attacccgtt caagcccca aagggttgctt tcacaaccaa 300
aatttatcac cctaatatca acagcaatgg cagcatctgc cttgatatcc tgcggtctca 360
gtggtctcca gcgttgactg tgtcaaaagt tctcttgcc atctgctgc tgccttgcga 420
ccccaacccc gatgacccc tgggtgccaga gatagcacac acctacaagg ccgacagaga 480
gaagtacaac agactagcaa gagagtggac acaaaaatat gctatgtaag tgccttggag 540
gttttacatg agacactgtc caagagaagc tggcagagag gtcttccctt aaaactttgg 600
gctgttggct gagccattca aagagcatca tctgttcttc aaacaaatgt tggtcaccca 660

```

EX05-002patentin.txt

```

ctctctccag ctgcagcatg ttggtgccat ttccagcaat tacggctttg acagtgccac 720
ctctttgatg ccaaatcagc aaccattgtt gttatgatct gcagtcttcc tggtgacact 780
ggaatctctc tctctgccgc ctcaagttgt ctgctggtct cttggggggc caggccctgc 840
acgtctctcc taccggcct caaatggtgc ttctgcccac gatggtacca caccagggcc 900
tcagcctggc ccctcaccac ataccctttg ccttttagaa ctcaagtcca tcctgggtgc 960
ccagggcaga gcaggctttg ttcgcacctc atctgctgca gaaccacatc ctgaggagtc 1020
tcagcttata ctggaggga ttgggaacag tgtcactggg aagtgaaggc ctagccctgt 1080
ggcttccacc agtctcctcc tgcagtcca cgtggtggca tttctgcct cacaccaaga 1140
agcagcaagt ggaaaatttc aggatacaaa gcacataaca ccccataaga gatgattatg 1200
tttttagaag caagagcaaa attatgaaac ctctagagat ttgggtcatg ttactccatt 1260
tgatgaagat tctcactacc gcccgctcct cccataggag cctacactaa gtccaagtgt 1320
gagccattca cagactagaa cacaaggagg gagagagact cttaaagta aataaaaatg 1380
caattcactc acaactct 1398

```

```

<210> 15
<211> 2715
<212> DNA
<213> Homo sapiens

```

```

<400> 15
gcttcgcagc gtcacgccct ccggggccgt ggcggcgacg gcggtgcgta gcttactcac 60
aggggcgggc cgtatccctc cgccgccggc gcggctcggc cctccctccc ctggcccggc 120
aatccccgcg cctcccgacc tgcccctcgg tcggggcccac cccgtgctcc gacggcccca 180
ccccggcggc gcagcccgcc cgcccgcgcg tccctcggtc cacctgcagc agggaggaaag 240
acaggcaatc cctccggctg tccgaccaag agaggccggc cgagcccgag gcttgggctt 300
ttgctttctg gcggagggat ctgcggcggt ttaggaggcg gcgctgatcc tgggaggaaag 360
aggcagctac ggcgggcgcg gcggtggcg ctaggcgggc ggcaataaaa ggggccgccg 420
ccgggtgatg cggtgaccgc tgcggcaggc ccaggagctg agtgggcccc ggccctcagc 480
ccgtcccgcg ggacccgctt tctcaactc tccatcttct cctgccgacc gagatcgccg 540
aggcggcctc aggtcccta gccccttccc cgtcccttcc ccgccccgt ccccgccccg 600
ggggccgccg ccacccgcct cccaccatgg ctctgaagag aatccacaag gaattgaatg 660
atctggcacg ggaccctcca gcacagtgtt cagcaggctc tgttgagat gatatgttcc 720
attggcaagc tacaataatg gggccaaatg acagtcccta tcagggtgga gtatttttct 780
tgacaattca tttcccaaca gattaccctt tcaaaccacc taagggtgca tttacaacaa 840
gaatttatca tccaaatatt aacagtaatg gcagcatttg tcttgatatt ctacgatcac 900
agtgtctcc agcactaact atttcaaaag tactcttgtc catctgttct ctgttggtg 960
atcccaatcc agatgatcct ttagtgctg agattgctcg gatctacaaa acagatagag 1020
aaaagtacaa cagaatagct cgggaatgga ctcagaagta tgcgatgtaa ttaaagaaat 1080

```

EX05-002patentin.txt

tattggataa cctctacaaa taaagatagg ggaactctga aagagaaagt ccttttgatt 1140
tccatttgac tgctttctat gagcccacgc ctcatcttcc cctgtgcaca tgtttacctg 1200
atacagcagt gctgcgtgtt gtacatactt ggaacaacaa actagaaata ctgtacttct 1260
gtaccaacat tgcctcctag cagagaagtg tgtgtgtgac aagccagttc tacaggcatt 1320
acctagggtg gagactaaaa gcttttctta ttgacttaaa tttggataac agcaagggtg 1380
gaggggggtg gtgggtatgg tgtgtgcttg gatgggaaag aaaaggctcc actcacctat 1440
aggagattat ttttaagtgg aatccattta aactcaaac agttatgaaa agcaagggtga 1500
agaacatgaa gctgtgtctg tattcatttt attccgaagg agctacgtct taggtgaaag 1560
ttatgaccaa ccagattaaa ctctaccac atcctgcatt ttaagggtcta agtttaactg 1620
gtcaacattt aaatggattg gagctattag tacatcaagt gtgatgggct ttgttcccaa 1680
ctcttttaca tctccctacc ccttcaacct ttggcctttc agcccttctt tctctcttcc 1740
atattccttg gtttgtatgt ggtttctcag ttaatacata gctaatagct cttatttttc 1800
ttatgttttt aaccgcttag gtctatttgg atgtaagggt gaaaattcat ttgatggaaa 1860
tacttgtgta tatttaaaga cccaattgct cctctggagc ttgtactttc aagaatgatt 1920
aatctgtgta ataaactggg tactacagtc attacatata attttgtgtg aataggcttt 1980
ttcattttta agaagtttgt ctagctgaga ttagtggtgg attttctccc acttctgaaa 2040
tgttcattta tactgggtgc attttaagat catgaaacaa ttccagttac attgtaaaaa 2100
ggatatctta cgagtaattt tattgaacaa gttagaggca taagcttaag agcatttcca 2160
tgaaacaaca catgcagcat tccaggaact tgattgttaa attcaataag aaatttgctt 2220
tattaatgaa actaagctgc atttcatcaa aaccttgtga cattcccttg gtacatagga 2280
cataaaacac agaggcattg ctatttggtg agttaagctt ctgtgattgt aattataaaa 2340
gagcaacatt gaccaaactt gggaaacaag agcacagtct tgtttggaga gtctacataa 2400
ttactttgca ctaacatttg caggatgttc acacaatttt aaattgtact gtatgtggct 2460
ttttgaagtc ttcccttgac cctagtaaaa tatagcttga aacttgtaaa caactgtgtt 2520
tgccagaaac atcattcatg tgaactaggc aagttacctt ttttcccccc ttcttttctt 2580
aattgtaaac taggccaacc tgaaagccat ggctgatgct ctagccatca ggttctttca 2640
aatgcatctt tacactcttg cacaaaagtt aaggaataaa tgtccactgc ttttggtttt 2700
aaaaaaaaaaaa 2715

<210> 16
<211> 2386
<212> DNA
<213> Homo sapiens

<400> 16
accaagtgag gaaactgggg gacgctgtgg ggaggggctg ggggctggat cgcgcagcgg 60
ctgcttcctt taccttcctc ccatggtctc cttccggttc tcgatgcttc tctgagccta 120

EX05-002patentin.txt

agggtttccg	ccactcgttc	accctcccc	cagctcatga	tcttctctcc	tccccgccc	180
tcctggtcca	atctccgata	tgttttagtaa	gaaggtgctg	ttccgagaag	gagaaggaaa	240
agggttgac	acgtattcac	tcggccccgg	acgtgggaag	caagccgtct	ggcttcggcc	300
tcacatcgg	cctgtgctcg	ggacggcggc	gttggcggac	tgatccgcgg	cggtgaagag	360
gcgcctgtgt	ctggcagagc	tgggtgtgaga	cgagacaatc	ctgccccgcc	gccgggataa	420
tcaagagttt	tggccggacc	tttgagcata	caccgagaga	gtgaggagcc	agacgacaag	480
cacacactat	ggcgtgaaa	cggattaata	aggaacttag	tgatttggcc	cgtgaccctc	540
cagcacaatg	ttctgcaggt	ccagttgggg	atgatatggt	tcattggcaa	gccacaatta	600
tgggacctaa	tgacagccca	tatcaaggcg	gtgtattctt	tttgacaatt	cattttccta	660
cagactaccc	cttcaaacca	cctaagggtg	catttacaac	aagaatttat	catccaaata	720
ttaacagtaa	tggcagcatt	tgtctcgata	ttctaagatc	acagtggctg	cctgctttaa	780
caattttctaa	agttctttta	tccatttgtt	ctctgctatg	tgatccaaac	ccagatgacc	840
ccctagtgcc	agagattgca	cggatctata	aaacagacag	agataagtac	aacagaatat	900
ctcgggaatg	gactcagaag	tatgccatgt	gatgctacct	taaagtcaga	ataacctgca	960
ttatagctgg	aataaacttt	aaattactgt	tccttttttg	attttcttat	ccggctgctc	1020
ccctatcaga	cctcatcttt	tttaatttta	ttttttgttt	acctccctcc	attcattcac	1080
atgctcatct	gagaagactt	aagtcttcc	agctttggac	aataactgct	tttagaaact	1140
gtaaagtagt	tacaagagaa	cagttgccc	agactcagaa	tttttaaaaa	aaaaaatgga	1200
gcatgtgtat	tatgtggcca	atgtcttcac	tctaacttgg	ttatgagact	aaaaccattc	1260
ctcactgctc	taacatgctg	aagaaatcat	ctgaggggga	gggagatgga	tgctcagttg	1320
tcacatcaaa	ggatacagca	ttattctagc	agcatccatt	cttgtttaag	ccttccactg	1380
ttagagattt	gaggttacat	gatatgcttt	atgctcataa	ctgatgtggc	tggagaattg	1440
gtattgaatt	tatagcatca	gcagaacaga	aaatgtgatg	tattttatgc	atgtcaataa	1500
aggaatgacc	tgttcttgtt	ctacagagaa	tggaaattgg	aagtcaaaca	ccctttgtat	1560
tccaaaatag	ggtctcaaac	attttgtaat	tttcatttaa	attgttagga	ggcttgagac	1620
tattagttaa	tctatcttcc	aatacactgt	ttaatatagc	actgaataaa	tgatgcaagt	1680
tgtcaatgga	tgagtgatca	actaatagct	ctgctagtaa	ttgatttatt	tttcttcaat	1740
aaagttgcat	aaaccaatga	gttagctgcc	tggattaatc	agtatgggaa	acaatctttt	1800
gtaaattgcaa	agctgttttt	tgtatatact	gttgggattt	gcttcattgt	ttgacatcaa	1860
atgatgatgt	aaagttcgaa	agagtgaata	ttttgccatg	ttcagttaaa	gtgcacagtc	1920
tgttacaggt	tgacacattg	cttgacctga	tttatgcaga	attaataagc	tatttgagata	1980
gtgtagcttt	aatgtgctgc	acatgatact	ggcagcccta	gagttcatag	atggactttt	2040
gggaccagc	agttttgaaa	tgtgtttatg	gagtttaaga	aattttat	ccagggtgcag	2100
cccctgtcta	actgaaattt	ctcttcacct	tgtacacttg	acagctgaaa	aaaaacaaca	2160

EX05-002patentin.txt

tgaggagtaaat aatgggtcaa aatttgcaaa ataaagtact gttttggtgt gggagttgtc	2220
atgaggctgt gttgaagtga cttatctatg tgggatattg agtatccatt gaaatggatt	2280
tgttcagcca ttacattaa tgagcattta aatgcaacag atatcatttc aggtgactta	2340
acatgaatga ataaaagtca atgctattgg aaaaaaaaaa aaaaaa	2386

<210> 17
 <211> 1356
 <212> DNA
 <213> Homo sapiens

<400> 17	
atggccccatg accttctctt caggcttttt ccacttttgg ccctgggagt ccccttataa	60
agcaaccgcc ttggccccac atctcgctg cgctattcca ggctcctaga tccttcta	120
gtcattttcc tgcgttgga ctttgacctt gaggtgaaa tcatcagttt tgagctccag	180
gtccgtacag ctggctgggt gggcttcggt gtcacaaatc gctacaccaa cgtgggaagt	240
gatctggttg ttggaggagt cttgccta atggcaatgtct atttctcgga tcagcacttg	300
gtggaggaag acactctgaa ggaggatggg agccaggatg ctgagctgct gggcctgacg	360
gaagatgctg tctacaccac catgcacttt tccaggccct tccgctcctg cgaccctcat	420
gacctggata ttacagcaa caccgtgagg gtgctggccg cctatggcct ggatgacact	480
ctgaagctgt atcgggagcg tacttttgtc aagtccatct ttctgtaca agtcgtccac	540
cctgacgatc tggatgtccc tgaggacacc atcatccatg acttggagat cactaatttc	600
ctcattccag aggatgacac cacgtatgcc tgcacctttc ttctctccc tattgtgagc	660
gagaagcatc acatttataa gtttgagcct aagttggtct accacaatga gacaacggtg	720
catcacatcc tgggtgtacgc ctgtggcaat gctagcgttc tccccacagg catcagcgac	780
tgctatgggg cggaccctgc cttctccctt tgctcacagg tcatcgtggg ctcggctgtc	840
gggggacacac tgtgcaaata cgacacggat gtcctccagc tgggcttctt cacgtttccc	900
atccacttca tcccccgagg cgctgagtc ttcattgtcct atgggctgtg taggacggag	960
aagtttgagg agatgaatgg agctcctatg cctgacatac aggtgtatgg ctacctgctg	1020
cacaccact tggctggacg ggctctgcaa gcagtgcatt acaggaatgg aacacaactt	1080
cgaaaaatct gtaaagacga ttcctatgac ttcaacctgc aggagactcg agatttgccc	1140
tctagagtgg agatcaagcc gggagatgaa ttgctggtag aatgtcacta ccagacactg	1200
gaccgtgact ccatgacatt tggaggcccc agcaccatta atgagatgtg cctcatcttc	1260
ctcttctact atccccaaaa taacatctcc agctgcatgg ggtaccctga cattatctac	1320
gtggccccacg agctagggga ggaggcatca gagtga	1356

<210> 18
 <211> 2960
 <212> DNA
 <213> Homo sapiens

<400> 18

EX05-002patentin.txt

```

tttccaagga aggaaaggca cacaatggta tcaaatgttc attcattcca tctcttgatg      60
ctctacgata ttatcagtct acactatgct ttccctgaaag gccagaagtt caaagatgga      120
ctagtttccc agggacctga ttccccagtt ggaataactcc agcccccttg aaattccccg      180
gatttataaa ataactctag acaacaagac tttgtcttta aaggctctat gaattctttt      240
ctctctgtat ttaggtatcc tgatttttct tttccatatt ttccacagga ttattttaca      300
aatgcaaata gagagttgaa aaaagatgct cagcaagatt accatctaga atatgccatg      360
gaaaatagca cacacacaat aattgaattt accagagagc tgcatacatg tgacataaat      420
gacaagagta taacggatag cactgtgaga gtgatctggg cctaccacca tgaagatgca      480
ggagaagctg gtcccaagta ccatgactcc aataggggca ccaagagttt gcggttattg      540
aatcctgaga aaactagtgt gctatctaca gccttaccat actttgatct ggtaaatacag      600
gacgtcccca tcccaaacaa agatacaaca tattggtgcc aaatgtttaa gattcctgtg      660
ttccaagaaa agcatcatgt aataaagggt gagccagtga tacagagagg ccatgagagt      720
ctggtgcacc acatcctgct ctatcagtgc agcaacaact ttaacgacag cgttctggag      780
tccggccacg agtgctatca cccaacatg cccgatgcat tcctcacctg tgaaactgtg      840
atTTTTgcct gggctattgg tggagagggc ttttcttatt cacctcatgt tggattatcc      900
cttggcactc cattagatcc gcattatgtg ctctagaag tccattatga taatcccact      960
tatgaggaag gcttaataga taattctgga ctgaggttat tttacacaat ggatataagg      1020
aaatatgatg ctggggtgat tgaggctggc ctctgggtga gcctcttcca taccatccct      1080
ccagggatgc ctgagttcca gtctgagggt cactgcactt tggagtgctt ggaagaggct      1140
ctggaagccg aaaagccaag tggaattcat gtgtttgctg ttcttctcca tgctcacctg      1200
gctggcagag gcatcaggct gcgtcatttt cgaaaaggga aggaaatgaa attacttgcc      1260
tatgatgatg attttgactt caatttccag gagtttcagt atctaaagga agaacaaaca      1320
atcttaccag gagataacct aattactgag tgtcgctaca acacgaaaga tagagctgag      1380
atgacttggg gaggactaag caccaggagt gaaatgtgtc tctcatacct tctttattac      1440
ccaagaatta atcttactcg atgtgcaagt attccagaca ttatggaaca acttcagttc      1500
attggggtta aggagatcta cagaccagtc acgacctggc ctttcattat caaaagtctc      1560
aagcaatata aaaacctttc tttcatggat gctatgaata agtttaaatg gactaaaaag      1620
gaaggctctt cttcaacaa gctggtcctc agcctgccag tgaatgtgag atgttccaag      1680
acagacaatg ctgagtggtc gattcaagga atgacagcat tacctccaga tatagaaaga      1740
ccctataaag cagaaccttt ggtgtgtggc acgtcttctt cctcttccct gcacagagat      1800
ttctccatca acttgcttgt ttgccttctg ctactcagct gcacgctgag caccaagagc      1860
ttgtgatcaa aattctgttg gacttgacaa tgttttctat gatctgaacc tgtcatttga      1920
agtacagggt aaagactgtg tccactttgg gcatgaagag tgtggagact tttcttcccc      1980
attttccctc cctccttttt ctttccatg ttacatgaga gacatcaatc aggttctctt      2040

```


EX05-002patentin.txt

ctcttttctta gaaatatctg atgttatata tacatggtca ataaaaataaa actggcctga 2100
 cttaagataa ccatttttaa aaattgggct gtcattgtgg aataaaagaa ttctttcttt 2160
 cctactacat tctgttttat ttaaatactc attgttgcta tttcactttt tgacttgact 2220
 tttatatattc tttaaaaaat tccttccttt taaaaaatat aaaagggact actgttcatt 2280
 ccagttttct tcttctttgt tgttcttcta gtgtgacttt tcaagtgtaa cagccattct 2340
 tcctgacttt aatattgtcc agttctggtc ttttctgtga attaccactg ggccccttac 2400
 ctcaatgctt tttgttgatg cccactctgg ttcccttggt tatctgagtc tgttggtacc 2460
 ccaaagacc ccacacccat yttaaagtac tttttttcac cttccctggt tagtactggc 2520
 cagatgagtt ttttctagag ctctgtcact atctgaaaag aaagaggcta tgggaaacat 2580
 agaaatggta tgtattaata actgatcata ggctgaggag aaaaaatgta gctggctgca 2640
 aaccagtg cgtgagggtga cttatatgag gttccagatc aaagacaggc cgtgtgagcc 2700
 agtccaggag ggtgtaagtt ctgaatggtt ccttgctgac tttgggtgac acatgtacca 2760
 catactggct cagtttaagt catggttcta ttgtagattt atttttatat tagttaataa 2820
 atgactttaa attgtcacca attgaaaatc ttgtcactct tttgggtttt tttatatagc 2880
 tcagccaaat ctctgtttta tgtcctgtcc tcatctctta agctaaatct gtttgatca 2940
 tattaataaa cctcgtgccg 2960

<210> 19
 <211> 3421
 <212> DNA
 <213> Homo sapiens

<400> 19
 aaaaagaaga aaccaggca gacaggcagt tggacacact gaggaagacc cccacgagt 60
 gggaaccccc tggaaggaa acaccggccc cggccccag gaaggagca caatggaggc 120
 cgctcatgct aaaaccacgg aggaatgttt ggctattttt ggggtgagtg agaccacggg 180
 cctcacccc gaccaagtta agcggaatct ggagaaatac ggctcaatg agctccctgc 240
 tgaggaagg aagaccctgt gggagctggt gatagagcag tttgaagacc tcctggtgcg 300
 gattctcctc ctggccgcat gcatttcctt cgtgctggcc tggtttgagg aaggtgaaga 360
 gaccatcact gcctttgttg aaccctttgt catcctcttg atcctcattg ccaatgccat 420
 cgtgggggtt tggcaggagc ggaacgcaga gaacgccatc gaggccctga aggagtatga 480
 gccagagatg gggaaggctt accgggctga ccgcaagtca gtgcaaagga tcaaggctcg 540
 ggacatcgtc cctggggaca tcgtggaggt ggctgtgggg gacaaagtcc ctgcagacat 600
 ccgaatcctc gccatcaa atccaccgct gcgggttgac cagtccatcc tgacaggcga 660
 gtctgtatct gtcacaaac acacggagcc cgttcctgac ccccgagctg tcaaccagga 720
 caagaagaac atgcttttct cgggcaccaa cattgcagcc ggcaaggcct tgggcatcgt 780
 ggccaccacc ggtgtgggca ccgagattgg gaagatccga gaccaaagtg ctgccacaga 840
 acaggacaag acccccttgc agcagaagct ggatgagttt ggggagcagc tctccaaggt 900

EX05-002patentin.txt

catctccctc atctgtgtgg ctgtctggct tatcaacatt ggccacttca acgaccccgt	960
ccatgggggc tcctggttcc gcggggccat ctactacttt aagattgccg tggccttggc	1020
tgtggctgcc atccccgaag gtcttcctgc agtcatcacc acctgcctgg ccctgggtac	1080
ccgtcggatg gcaaagaaga atgccattgt aagaagcttg ccctccgtag agaccctggg	1140
ctgcacctct gtcattctgtt ccgacaagac aggcaccctc accaccaacc agatgtctgt	1200
ctgcaagatg tttatcattg acaagggtgga tggggacatc tgcctcctga atgagttctc	1260
catcaccggc tccacttacg ctccagaggg agagggtcttg aagaatgata agccagtccg	1320
gccagggcag tatgacgggc tgggtggagct ggccaccatc tgtgccctct gcaatgactc	1380
ctccttgga c ttcaacgagg ccaaagggtgt ctatgagaag gtcggcgagg ccaccgagac	1440
agcactcacc accctggtgg agaagatgaa tgtgttcaac acggatgtga gaagcctctc	1500
gaagggtggag agagccaacg cctgcaactc ggtgatccgc cagctaata gaaggaatt	1560
caccctggag ttctcccgag acagaaagtc catgtctgtc tattgctccc cagccaaatc	1620
ttcccggtg gctgtgggca acaagatgtt tgtcaagggt gccctgagg gcgtcatcga	1680
ccgctgtaac tatgtgcgag ttggcaccac ccgggtgcc a ctgacggggc cggatgaagga	1740
aaagatcatg gcggtgatca aggagtgggg cactggccgg gacaccctgc gctgcttggc	1800
cctggccacc cgggacaccc ccccgaagcg agaggaaatg gtcctggatg actctgccag	1860
gttcctggag tatgagacgg acctgacatt cgtgggtgta gtgggcatgc tggaccctcc	1920
gcgcaaggag gtcacgggct ccatccagct gtgccgtgac gccgggatcc gggatgatcat	1980
gatcactggg gacaacaagg gcacagccat tgccatctgc cggcgaattg gcatctttgg	2040
ggagaacgag gaggtggccg atcgcgccta cacggggcca gagttcgacg acctgcccct	2100
ggctgaacag cgggaagcct gccgacgtgc ctgctgcttc gccctgtgtg agccctcgca	2160
caagtccaag attgtggagt acctgcagtc ctacgatgag atcacagcca tgacaggatga	2220
tggcgtcaat gacgcccctg ccctgaagaa ggctgagatt ggcattgcca tgggatctgg	2280
cactgccgtg gccaagactg cctctgagat ggtgctggct gacgacaact tctccaccat	2340
cgtagctgct gtggaggagg gccgcgccat ctacaacaac atgaagcagt tcatccgcta	2400
cctcatttcc tccaacgtgg gcgaggtgggt ctgtatcttc ctgaccgtg ccctggggct	2460
gcctgaggcc ctgatcccgg tgcagctgct atgggtgaac ttggtgaccg acgggctccc	2520
agccacagcc ctgggcttca acccaccaga cctggacatc atggaccgcc cccccggag	2580
ccccaaggag cccctcatca gtggctggct cttcttccgc tacatggcaa tcgggggcta	2640
tgtgggtgca gccaccgtgg gagcagctgc ctgggtgggt ctgtacgtg aggatgggccc	2700
tcatgtcaac tacagccagc tgactcactt catgcagtgc accgaggaca acaccactt	2760
tgagggcata gactgtgagg tcttcgaggc ccccgagccc atgaccatgg ccctgtccgt	2820
gctggtgacc atcgagatgt gcaatgcact gaacagcctg tccgagaacc agtccctgct	2880
gcggatgcca ccctgggtga acatctggct gctgggctcc atctgcctct ccatgtccct	2940

EX05-002patentin.txt

```

gcacttcctc atcctctatg ttgacccccct gccgatgata ttcaagctcc gggccctgga 3000
cctcaccagc tggctcatgg tcctcaagat ctactgcca gtcattgggc tcgacgaaat 3060
cctcaagtgc gttgctcgga actacctaga gggataactg ttccccctcc tccatctctg 3120
agcccgtgtc acagatccag aagatgaaag aaggaagtga gcatcctttt gctctgtcct 3180
ccccaccccg atagtgcac atcttcaggc agagctgtgg cacagacccc cgtcctgtcc 3240
cccacacccg tgtcatgtgt ctgtttataa acatgtcccc ttccctttcc ttccccctcg 3300
gccacccgcc tccctctcaa ccttgtaa at tccccctccc aaccccgagg ggcttgacagg 3360
gacaaggcga ccgactgcgc tgagctgctt atttattgaa aataaacgac ggaaaagtct 3420
g 3421

```

```

<210> 20
<211> 3942
<212> DNA
<213> Homo sapiens

```

```

<400> 20
gggtgattca ggcggcgaggc aggcggaagc ggccgcaaga ggaggagggg agagcccgtc 60
cgcgccctggg ctcccggggg ggcacgagcc cgcgcccgga gtgcgaggcg gaggcgagga 120
ggccgcggggg acgggaggcg aggcgggccc ggcccccgaa gccatggaga acgcgcacac 180
caagacgggtg gaggagggtg tgggccactt cgcgctcaac gagagtacgg ggctgagcct 240
ggaacagggtc aagaagctta aggagagatg gggctccaac gagttaccgg ctgaagaagg 300
aaaaaccttg ctggaacttg tgattgagca gtttgaagac ttgctagtta ggattttatt 360
actggcagca tgtatatctt ttgttttggc ttggtttgaa gaagggtgaag aaacaattac 420
agcctttgta gaaccttttg taattttact catattagta gccaatgcaa ttgtgggtgt 480
atggcaggaa agaaatgctg aaaatgccat cgaagccctt aaggaatatg agcctgaaat 540
gggcaaagtg tatcgacagg acagaaagag tgtgcagcgg attaaagcta aagacatagt 600
tcctgggtgat attgtagaaa ttgctgttgg tgacaaagtt cctgctgata taaggttaac 660
ttccatcaaa tctaccacac taagagttga ccagtcaatt ctacaggtg aatctgtctc 720
tgtcatcaag cactatgat ccgtccctga cccacgagct gtcaaccaag ataaaaagaa 780
catgctgttt tctggtacaa acattgctgc tgggaaagct atgggagtgg tggtagcaac 840
tggagttaac accgaaattg gcaagatccg ggatgaaatg gtggcaacag aacaggagag 900
aacacccctt cagcaaaaac tagatgaatt tggggaacag ctttccaaag tcatctccct 960
tatttgcatg gcagtctgga tcataaatat tgggcacttc aatgaccggt ttcatggagg 1020
gtcctggatc agagggtgcta ttactactt taaaattgca gtggccctgg ctgtagcagc 1080
cattcctgaa ggtctgcctg cagtcacac cacctgcctg gctcttgga ctcgcagaat 1140
ggcaaagaaa aatgccattg ttcgaagcct cccgtctgtg gaaacccttg gttgtacttc 1200
tgttatctgc tcagacaaga ctggtacact tacaacaaac cagatgtcag tctgcaggat 1260

```

EX05-002patentin.txt

gttcattctg gacagagtgg aaggtgatac ttgttccctt aatgagttta ccataactgg 1320
 atcaacttat gcacctattg gagaagtgca taaagatgat aaaccagtga attgtcacca 1380
 gtatgatggt ctggtagaat tagcaacaat ttgtgctctt tgtaatgact ctgctttgga 1440
 ttacaatgag gcaaagggtg tgtatgaaaa agttggagaa gctacagaga ctgctctcac 1500
 ttgcctagta gagaagatga atgtatttga taccgaattg aagggtcttt ctaaaataga 1560
 acgtgcaaat gcctgcaact cagtcattaa acagctgatg aaaaaggaat tcaactctaga 1620
 gttttcacgt gacagaaagt caatgtcggg ttactgtaca ccaaataaac caagcaggac 1680
 atcaatgagc aagatgtttg tgaagggtgc tcctgaagggt gtcattgaca ggtgcaccca 1740
 cattcgagtt ggaagtacta aggttcctat gacctctgga gtcaaacaga agatcatgtc 1800
 tgtcattcga gagtggggta gtggcagcga cactctgcga tgcctggccc tggccactca 1860
 tgacaacca ctgagaagag aagaaatgca ccttgaggac tctgccaact ttattaaata 1920
 tgagaccaat ctgaccttcg ttggctgctg gggcatgctg gatcctccga gaatcgaggt 1980
 ggcctcctcc gtgaagctgt gccggcaagc aggcattccg gtcattcatga tcaactggga 2040
 caacaagggc actgctgtgg ccatctgtcg ccgcatcggc atcttcgggc aggatgagga 2100
 cgtgacgtca aaagctttca caggccggga gtttgatgaa ctcaaccctt ccgccagcg 2160
 agacgcctgc ctgaacgccc gctgttttgc tcgagttgaa ccctcccaca agtctaaaat 2220
 cgtagaattt cttcagtctt ttgatgagat tacagctatg actggcgatg gcgtgaacga 2280
 tgctcctgct ctgaagaaag ccgagattgg cattgctatg ggctctggca ctgcggtggc 2340
 taaaaccgcc tctgagatgg tcctggcgga tgacaacttc tccaccattg tggctgccgt 2400
 tgaggagggg cgggcaatct acaacaacat gaaacagttc atccgctacc tcatctcgtc 2460
 caacgtcggg gaagtgtgtc gtattttcct gacagcagcc cttggatttc ccgaggcttt 2520
 gattcctgtt cagctgtctt ggggtcaatct ggtgacagat ggctgcctg ccaactgcact 2580
 ggggttcaac cctctgatc tggacatcat gaataaacct ccccggaacc caaaggaacc 2640
 attgatcagc ggggtggctt ttttccgtta cttggctatt ggctgttacg tcggcgctgc 2700
 taccgtgggt gctgctgcat ggtggttcat tgctgctgac ggtggtccaa gagtgtcctt 2760
 ctaccagctg agtcatttcc tacagtgtaa agaggacaac ccggactttg aaggcgtgga 2820
 ttgtgcaatc tttgaatccc catacccgat gacaatggcg ctctctgttc tagtaactat 2880
 agaaatgtgt aacgccctca acagcttgct cgaaaaccag tccttgctga ggatgcccc 2940
 ctgggagaac atctggctcg tgggctccat ctgcctgtcc atgtcactcc acttcctgat 3000
 cctctatgtc gaacccttgc cactcatctt ccagatcaca ccgctgaacg tgaccagtg 3060
 gctgatggtg ctgaaaatct cttgcccgt gattctcatg gatgagacgc tcaagtttgt 3120
 ggcccgaac tacctggaac ctgcaatact ggagtaaccg cttcctaaac cttttgcag 3180
 aaatgtaagg gtgttcggtt gcgtgcatgt gcgttttttag caacacatct accaaccctg 3240
 tgcagtactg atgttgggga aaaagaaaag taaaaaactt cccaactcac tttgtgttat 3300

EX05-002patentin.txt

gtggaggaaa tgtgtattac caatgggggtt gttagctttt aaatcaaaat actgattaca 3360
gatgtacaat ttagcttaat cagaaagcct ctccagagaa gtttggtttc tttgctgcaa 3420
gaggaatgag gctctgtaac cttatctaag aacttggaag ccgtcagcca agtcgccaca 3480
tttctctgca aaatgtcata gcttatataa atgtacagta ttcaattgta atgcatgcct 3540
tcggttgtaa gtagccagat ccctctccag tgacattgga acatgctact ttttaattgg 3600
ccctgtacag tttgcttatt tataaattca ttaaaaacac tacagggtgtt gaatgggttaa 3660
aatgtaggcc tccagttcat tttcagttat tttctgagtg tgcagacagc tatttcgcac 3720
tgtattaaat gtaacttatt taatgaaatc agaagcagta gacagatgtt ggtgcaatac 3780
aaatattgtg atgcatttat ctttaataaaa tgctaaatgt caatttatca ctgcgcatgt 3840
ttgactttag actgtaaata gagatcagtt tgtttctttc tgtgctggta acaatgagcg 3900
tcgcacagac atgggtttcag gtaaataaat ctattctatg at 3942

<210> 21
<211> 4698
<212> DNA
<213> Homo sapiens

<400> 21
ccgccgccac tgccgtcggg taagggtccca gcacggacat ggcctcgcgc ggcgcccgcc 60
cgggcccag tccccgcgc cccgctttgt agccccccgg cggagaggcg gcctcgacgg 120
tgccgacggc gcagacggcc gggcgggcgg catggaggcg gcgcatctgc tcccgccgc 180
cgacgtgctg cgccacttct cggtgacagc cgagggcggc ctgagcccgg cgcagggtgac 240
cggcgcgcgg gagcgctacg gcccacga gctcccagat gaggaaggga agtccctgtg 300
ggagctgggt ctggaacagt ttgaggacct cctggtgcgc atcctgctgc tggctgcctt 360
tgtctccttt gtcctggcct gggtcgagga gggcgaggag accacgaccg ccttcgtgga 420
gcccctggtc atcatgctga tcctcgtagc caacgccatt gtgggcgtgt ggcaggaacg 480
caacgccgag agtgccatcg aggccctgaa ggagtatgag cctgagatgg gcaagggtgat 540
ccgctcggac cgcaaggcg tgacagggat ccgtgcccgg gacatcgtcc caggggacat 600
tgtagaagtg gcagtggggg acaaagtgcc tgctgacctc cgcctcatcg agatcaagtc 660
caccacgctg cgagtggacc agtccatcct gacgggtgaa tctgtgtccg tgaccaagca 720
cacagaggcc atcccagacc ccagagctgt gaaccaggac aagaagaaca tgctgttttc 780
tggcaccaat atcacatcgg gcaaagcggg ggggtgtggc gtggccaccg gcctgcacac 840
ggagctgggc aagatccgga gccagatggc ggagtcgag cccgagcggg cgcgctgca 900
gcgcaagctg gacgagtttg gacggcagct gtcccacgcc atctctgtga tctgcgtggc 960
cgtgtgggtc atcaacatcg gccacttcgc cgaccggcc cacgggtggc cctggctgcg 1020
tggcgtgtc tactacttca agatcgccgt ggccctggcg gtggcgcca tccccaggg 1080
cctcccggt gtcactacta catgcctggc actgggcacg cggcgcatgg cagcaagaa 1140
cgccatcgtg cgaagcctgc cgtccgtgga gaccctgggc tgcacctcag tcattctgctc 1200

EX05-002patentin.txt

cgacaagacg	ggcacgctca	ccaccaatca	gatgtctgtc	tgccgcatgt	tcgtggtagc	1260
cgaggccgat	gcgggctcct	gccttttgca	cgagttcacc	atctcgggta	ccacgtatac	1320
ccccgagggc	gaagtgcggc	agggggatca	gcctgtgcgc	tgcggccagt	tcgacgggct	1380
ggtggagctg	gcgaccatct	gcgccctgtg	caacgactcg	gctctggact	acaacgagggc	1440
caaggggtgtg	tatgagaagg	tgggagaggg	cacggagaca	gctctgactt	gcctgggtgga	1500
gaagatgaac	gtgttcgaca	ccgacctgca	ggctctgtcc	cgggtggagc	gagctggcgc	1560
ctgtaacacg	gtcatcaagc	agctgatgcg	gaaggagtcc	accctggagt	tctcccgaga	1620
ccggaaatcc	atgtccgtgt	actgcacgcc	caccgcctct	caccctactg	gccagggcag	1680
caagatgttt	gtgaaggggg	ctcctgagag	tgtgatcgag	cgctgtagct	cagtccgcgt	1740
ggggagccgc	acagcacccc	tgacccccac	ctccagggag	cagatcctgg	caaagatccg	1800
ggattggggc	tcaggctcag	acacgctgcg	ctgcctggca	ctggccaccc	gggacgcgcc	1860
cccaaggaag	gaggacatgg	agctggacga	ctgcagcaag	tttgtgcagt	acgagacgga	1920
cctgaccttc	gtgggctgcg	taggcatgct	ggacccgccg	cgacctgagg	tggctgcctg	1980
catcacacgc	tgctaccagg	cgggcatccg	cgtggtcatg	atcacggggg	ataacaaagg	2040
cactgccgtg	gccatctgcc	gcaggcttgg	catctttggg	gacacggaag	acgtggcggg	2100
caaggcctac	acgggcccgc	agtttgatga	cctcagcccc	gagcagcagc	gccaggcctg	2160
ccgcaccgcc	cgctgcttcg	cccgcgtgga	gcccgcacac	aagtcccgcg	tcgtggagaa	2220
cctgcagtcc	tttaacgaga	tcactgctat	gactggcgat	ggagtgaacg	acgcaccagc	2280
cctgaagaaa	gcagagatcg	gcatcgccat	gggctcaggc	acggccgtgg	ccaagtcggc	2340
ggcagagatg	gtgctgtcag	atgacaactt	tgcttccatc	gtggctgcgg	tggaggaggg	2400
ccgggccatc	tacagcaaca	tgaagcaatt	catccgctac	ctcatctcct	ccaatgttgg	2460
cgaggctgct	tgcatcttcc	tcacggcaat	tctgggcctg	cccgaagccc	tgatccctgt	2520
gcagctgctc	tgggtgaacc	tgggtgacaga	cggcctacct	gccacggctc	tgggcttcaa	2580
cccgcagac	ctggacatca	tggagaagct	gccccggagc	ccccgagaag	ccctcatcag	2640
tggctggctc	ttcttccgat	acctggctat	cggagtgtac	gtaggcctgg	ccacagtggc	2700
tgccgccacc	tgggtggttg	tgtatgacgc	cgagggacct	cacatcaact	tctaccagct	2760
gaggaaactc	ctgaagtgtc	ccgaagacaa	cccgtctttt	gccggcatcg	actgtgaggt	2820
gttcgagtca	cgcttcccc	ccaccatggc	cttgtccgtg	ctcgtgacca	ttgaaatgtg	2880
caatgccctc	aacagcgtct	cggagaacca	gtcgtgtctg	cggatgccgc	cctggatgaa	2940
cccctggctg	ctggtggctg	tggccatgtc	catggccctg	cacttcctca	tcctgtcgtg	3000
gccgccccctg	cctctcatth	tccaggtgac	cccactgagc	gggcgccagt	gggtgggtgg	3060
gctccagata	tctctgcctg	tcacctgtct	ggatgaggcc	ctcaagtacc	tgtcccggaa	3120
ccacatgcac	gaagaaatga	gccagaagtg	agcgtgggga	acagagtggg	gtctccgggtg	3180
tgtacctcag	actgatgggtg	cccatgtgtt	cgcctccgcc	ccccaccctt	gccaccacac	3240

EX05-002patentin.txt

```

tcgcccactt gccacccggg tcccgcggga taaatgacag gcccgaggtc agaatggcca 3300
tccccggggc ccgtcctggg gtctctgtcc ccacttcctt ctggcctggg aggtctgtaa 3360
ttcctgtctc ctggactctc ctgggaagtt ccctgctctg cagctctggc ccaggagctg 3420
caggctggga gggggcagcc aagaagccgg agctggcagc ataccagag atccggggcc 3480
ccccacccc caaatcacga gtgcagctgg agcttgctcc cccttgttcg gaagctggac 3540
gttcacttgg tgactggtgc ctctgcactg acggaggact ctgggggtcc ttcttaccgg 3600
ctctgacctc tctcttcgtg cctgggtctgg gactgggtca gccctggggg atcagaaggg 3660
gccatctggg ccagctgtg tacagcgagg gtgggcagcc ccctccactc cactctgctt 3720
ccacaaagtc ggctcccag agctcgaggc tgcttctgtt tatatgtgca gggcccgggc 3780
gggtgaaggg tcagagagac ggacacaagg agccggcagg agggcggagc gaggatgtcc 3840
tttcccggga gacaagtcgg gaaagcctgg ctggactgcc tcagccccgc gcgcctcctg 3900
gactcagggg tccccgtcct gagctcggga gatgttcaga gtcacactgc cgcccgggtct 3960
gccacgcaga ggtccaactt gccacccgcg tccctggtac ctgagaccac cgacatcctc 4020
aggttcctga ccgtggcgcc cttctacca gccagtggtg cgcccgccgc gctgtctgca 4080
cagctggggg cctctgagcc tgggtgggctt cctggactct tggcctcact ccttgcccc 4140
tccccacgac acccatgagc cgaaaggatg tactaagga tggctgattc cccaagggca 4200
cccgctctcc ctccctccct gctggaggaa cacgtcatat cagatgagag gaagatggcc 4260
tctgatggac agaatttttc tcttaactca gcttttgcta ctttgcaaaa aactagcgag 4320
gggtagcaga aacctgcacc aaggattgtc cctatgtctt ggccactcct agagcgtgtg 4380
cagactgatg attttatatg taaatcaaga ctacatccc tttcctagtc cccacatcc 4440
aaagccccctc agcctgcctt gcagaccaat gggctccatg ttctgtagcc ccctccccta 4500
cgcctcacc ctcctccctc tcacagggtc tgggcggcca gtgagagaaa cgagtgggg 4560
gaggcagga gtctggtgcc tgcagagatt ctctgcttct ttcctggggg gaggtgggga 4620
ggtcttagca ggagcgggcc ctgtaccac ctgctgacct gctgtttggt agagaaataa 4680
aggttgtgtg actggggg 4698

```

```

<210> 22
<211> 2867
<212> DNA
<213> Homo sapiens

```

```

<400> 22
aaggctagcc tctctcagt ggtgactgag ctgtcttcag tggaagccc aggcagatgc 60
cacgcaattc tggagctgga tacggctgcc cacacgggga cccagcatg ctggacagca 120
gagagacccc acaggagagc cggcaggaca tgattgtgag gaccaccaa gaaaaattga 180
aaaccagctc actgactgac aggcagccac tctccaaaga gtcctgaac catgctctcg 240
agctctcagt gccagagaag gtgaataatg ccagtgggga tgctccagag gaggcgctgt 300

```

EX05-002patentin.txt

ggacgactcg	ggccgatggg	cgggtgccc	tgcgcataga	ccccagctgc	ccacagcttc	360
cctacactgt	gcatcggatg	ttctacgagg	ccctggataa	gtatggggac	ctcatcgctt	420
tgggcttcaa	gcgccaggac	aagtgggaac	acatctccta	ctcccaatac	tacctgctcg	480
cccgcagagc	cgccaagggc	ttcctgaagc	tcggcctgaa	gcaggcccac	agtgtggcca	540
tcctcggctt	caactccccg	gagtggttct	tctcggcagt	gggcacagta	tttgaggtg	600
gcatcgtcac	tggcatctac	accaccagct	ccccagaggc	ctgccagtac	atcgcttatg	660
actgctgcgc	caatgtcatc	atggtcgaca	cgcagaagca	gctggaaaag	atcctgaaga	720
tctggaaaca	gttgccacat	ctaaaggcag	tcgtgatata	taaagaacct	cctccaaaca	780
agatggccaa	tgtgtacacg	atggaggaat	tcatggagct	ggggaatgaa	gtgcctgagg	840
aagccctgga	cgccatcatt	gacaccagc	agcccaacca	gtgctgtgtg	ctagtctaca	900
cttccggcac	cactgggaac	ccaagggcg	tgatgctgag	tcaagacaat	atcacgtgga	960
cggcacggta	cggcagccag	gccggtgaca	tccggccggc	agaagtccag	caggaggtgg	1020
tagtcagcta	cctgcccctc	agccatattg	ccgcccagat	ctacgacctg	tggacaggca	1080
tccagtgggg	ggcccaggtt	tgctttgccg	aaccgcagc	cctgaagggg	agcctggtga	1140
acacgctgcg	ggaggtggag	cccacatcac	acatgggggt	gccccgggta	tgggagaaga	1200
tcatggagcg	catccaggag	gtggcggctc	agtctggctt	catccggcga	aagatgctgc	1260
tgtgggcat	gtcggtgacc	ttggagcaga	acctcacctg	ccccggcagc	gacctgaagc	1320
ccttcacaac	cagactggca	gattacctgg	tgctagccaa	ggttcgccag	gcactgggat	1380
ttgccaagtg	tcaaaagaac	ttctatggag	cggcccccac	gatggcagag	acacagcact	1440
tcttcctggg	tctcaacatc	cgcttgatg	cgggctacgg	cctcagttag	acctcaggcc	1500
cccacttcat	gtccagtccc	tacaactacc	ggctgtacag	ctcaggcaag	ttggtgcccg	1560
gctgtcgggt	gaagctggtg	aaccaggacg	cagagggcat	tggcgagatc	tgctgtggg	1620
gccgcaccat	attcatgggc	tacctgaaca	tggaggacaa	gacttgtgag	gccatcgacg	1680
aggaaggctg	gctgcacacg	ggtgatgctg	gccgcctgga	cgccgatggc	ttcctctaca	1740
tactgggcg	cctcaaagaa	ttaatcatca	cagctggtgg	ggagaatgtg	ccccctgtgc	1800
ccatcgagga	ggccgtgaag	atggagctgc	ccatcatcag	caacgccatg	ctcattgggg	1860
accagaggaa	gttcctgtcc	atgctgctca	ccttgaagtg	cactctggac	ccagacacct	1920
ctgaccagac	tgataatctg	actgaacaag	ctatggagtt	ctgccagagg	gtgggcagca	1980
gagccaccac	agtgtccgag	atcatagaga	agaaggatga	ggccgtgtac	caggccatcg	2040
aagaggggat	ccggaggggc	aacatgaacg	cggcgcccg	gccctaccac	atccagaagt	2100
gggccattct	cgagagagac	ttctccattt	cgggtggaga	gttgggtccc	acgatgaaac	2160
tgaacggct	cacagttttg	gagaagtaca	aaggatcat	tgactccttt	taccaagagc	2220
aaaaaatgta	atcagggcct	atgcctgcag	tttctataga	atagagggca	ggcgttccga	2280
gcctcttcct	gagccccagg	tctcttcagt	ctgggcacag	gcatttctgc	caagtctgtt	2340

EX05-002patentin.txt

agatctccag gtcagggcac agcactggct ctacatttac caggtcttac gccacaata	2400
gctgacaatt ccaagaagct tcacgtgtgg gtagttttta ttcagtttaa gtattgcttt	2460
ttgttcaggt gacaaatgag atcagctctc cttccagaac gaaagggctg ataatttttg	2520
gccttagttc caggtagatt aaaaagctgc tagctcacat acaggacagc cagcagtagg	2580
ctgtggagcg ggtaggagag agatggctga tactgctcac gtgcgctgca ggaaaagcaa	2640
tcagtcacaa ctcacctagc gacctgactt actctggaat cttggcgggc atcgccgacc	2700
ctattattcc attaccaggc actccgccac ccacatgcca actgacttga tgcttaataa	2760
aactgctgct gcctgtttga ttctatttaa tgtataattt gaatattaaa ctttttaaca	2820
gaactgtcaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa	2867

<210> 23
 <211> 2717
 <212> DNA
 <213> Homo sapiens

<400> 23	
gtcgagagcg gtatggggta gaaggcctgt tgtggagggga aaccacccat cctcctgcct	60
cccaccacca ccatcatcct ggctggacgg agaggggtgac gggggctggg aaggggcagc	120
tcatgttcag gtttccagga ggggctacct gttgactgtc tttgcaggaa gaagaaaaca	180
cctgagtgc cagatgtccc agctccagtg ctgtggagca tggtttctgc acacctggaa	240
tgactggaac cccaaagact caagaaggag ctaaagatct tgaagtagac atgaataaaa	300
cagaagttac tcccaggctg tggaccacct gtcgagatgg agaagtcctt ctgaggctat	360
ccaaacacgg accaggccat gagaccccga tgaccatccc tgaatttttt cgagagtcag	420
tcaaccgatt tggaaacttat ccagccctcg catccaagaa tggcaaaaag tgggaaattc	480
tgaatttcaa ccagtactat gaggcttgtc ggaaggctgc aaaatccttg atcaagctgg	540
gtttggagcg tttccacgga gttggtatcc tggggtttaa ctctgcagag tggtttatca	600
ctgctgttgg tgccatccta gccgggggtc tttgtgttgg tatttatgcc accaactctg	660
ccgaggcttg tcaatatgtc atcactcatg ccaaagtga catcttgctg gttgagaatg	720
atcaacagtt acagaaaatc ctttcgattc cacagagcag cctagagccc ctaaaagcga	780
tcatccagta cagactgcca atgaagaaga acaacaactt gtactcttgg gatgatttca	840
tggaaacttg cagaagtatc cctgacaccc aactggagca ggtcatcgag agccagaagg	900
cgaatcaatg cgagtgctc atctacactt caggggaccac aggcataccc aagggagtga	960
tgctcagtca tgacaacatc acgtggattg caggagcagt gacaaaggac tttaaactga	1020
cagacaagca tgagacggtg gttagctacc tcccactcag ccatattgca gcacagatga	1080
tggacatctg ggtaccata aagattgggg cgctcacata ctttgctcaa gcagatgctc	1140
tcaagggcac cttggtaagt actctaaagg aggtaaaacc tactgtcttc attggagtgc	1200
ctcaaatttg ggagaagata catgagatgg tgaagaaaaa tagtgccaag tccatgggct	1260
tgaagaagaa ggcattcgtg tgggcaagaa acattggctt caagggtcaac tcaaaaaaga	1320

EX05-002patentin.txt

tgttggggaa atataatact cccgtgagct accgcatggc taagactctc gtgttcagca	1380
aagtcaagac atcccttggc ttggatcact gtcactcttt tatcagtggg actgcgcccc	1440
tcaaccaaga gactgccgag ttcttttctaa gcttggacat acctataggc gagttgtatg	1500
ggttgagtga aagctcggga ccccacacga tatccaacca gaataactac aggccttctaa	1560
gctgtggcaa gatcttgact ggggtgaaga atatgctgtt ccagcagaac aaggatggca	1620
ttggggagat ctgcctctgg ggtaggcaca tcttcatggg ctatctggaa agtgagactg	1680
aaactacaga ggccatcgat gatgaaggct ggctacactc tggggatctg ggccagctgg	1740
acggtctggg tttcctctat gtcaccggcc acatcaaaga aatccttatc actgctgggtg	1800
gtgaaaatgt gccccccatt cctgttgaga ccttggttaa gaagaagatc cccatcatca	1860
gtaacgccat gttagtagga gataaactga agtttctgag catgttgctg acgctgaagt	1920
gtgagatgaa tcagatgagc ggagaacctc tggacaagct gaactttgag gccatcaact	1980
tctgtcggga tctggacagc caggcatcca ccgtgactga gattgtgaag cagcaagacc	2040
ccctggtcta caaggccatc cagcaaggca tcaatgctgt gaaccaggaa gccatgaaca	2100
atgcacagaa gattcaaaag tgggtcatct tggagaagga cttttccatc tatggtggag	2160
agctaggtcc aatgatgaaa cttagagac attttgtagc ccagaaatac aaaaaacaaa	2220
ttgatcacat gtaccactga ctgctttgat ggagctgctc tcagctgttc tgatgccttc	2280
agcaggaaga cctcattgca ataagtgaag tgctgctcta ggtagaagct ctccctgctg	2340
tttttaagaa gccacattcc tcattggtca gtttcttgat tgttcgtctg ttggagaggt	2400
gctccctaga agaacctgcc atacgtttca aagcaataaa atcactgtat atctttctaa	2460
ggaccttcaa gtcatgactc cagggaagcc tattgggaag tctactaaaa actgcctgat	2520
ttacaagaaa gacctgaact tgtgggctcc catttgattt ttttctctc aggggactca	2580
gacattagaa agaaaaagcc tcacagattt gaagaactgg acccccaaat caactcacct	2640
gcctggaagc aactgggaaa cccttccaat aagtcctgat aataaagcac ttcagggtcc	2700
caaaaaaaaa aaaaaaa	2717

<210> 24
 <211> 1068
 <212> DNA
 <213> Homo sapiens

<400> 24	
cgccggagga gttctgcgtc tcgggggtgg gactgggtcc agaattggctt cggattcggg	60
gaaccagggg accctctgca cgttggagtt cgcggtgcag atgacctgtc agagctgtgt	120
ggacgcggtg cgcaaattccc tgcaaggggt ggcagggtgtc caggatgtgg aggtgcactt	180
ggaggaccag atgggtcttg tacacaccac tctaccagc caggaggtgc aggctctcct	240
ggaaggcacg gggcggcagg cggtactcaa gggcatgggc agcggccagt tgcagaatct	300
gggggcagca gtggccatcc tggggggggc tggcaccgtg caggggggtg tgcgcttcct	360

EX05-002patentin.txt

```

acagctgacc cctgagcgct gcctcatcga gggaactatt gacggcctgg agcctgggct 420
gcatggactc cacgtccatc agtacgggga cttacaaac aactgcaaca gctgtgggaa 480
tcactttaac cctgatggag catctcatgg gggcccccag gactctgacc ggcaccgcgg 540
agacctgggc aatgtccgtg ctgatgctga cggccgcgcc atcttcagaa tggaggatga 600
gcagctgaag gtgtgggatg tgattggccg cagcctgatt attgatgagg gagaagatga 660
cctgggccgg ggaggccatc cttatccaa gatcacaggg aactccgggg agaggttggc 720
ctgtggcatc attgcacgct ccgctggcct tttccagaac cccaagcaga tctgctcttg 780
cgatggcctc accatctggg aggagcgagg cggcccatc gctggcaagg gccgaaagga 840
gtcagcgag cccctgccc acctttgagc aggacctcac cttggctctg ttgctgtcct 900
ccagggcgag cactttccac ttccagaggg ggccagaggg actttgcctg cccagtcttt 960
ggagagctca gtacagggca ggagctgctg tgggtttccc ttggcaaatg aaagttttat 1020
tttcgtttgg gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1068

```

```

<210> 25
<211> 3031
<212> DNA
<213> Homo sapiens

```

```

<400> 25
ccgcaccccc ggctcggggc tgtgagcggc tcggggccgg ggggtgggcg cggctgcggcg 60
ggcggccgac gtcctcttc ggcggcggcg gcggcggcg cccatgcgtg gggcggcgcg 120
gctggggcg cggggccgga gttgcctccc gggggccgcg ctgagggccg ccgccgcgcc 180
cgccctgctg cttgctcggt gcgctgttgc cgctgctgcc ggcctgcgtg ccgccgccc 240
tccgcggccc ccggagctgc agtcggcttc cgcggggccc agcgtgagtc tctacctgag 300
cgaggacgag gtgcgccggc tgatcgggtc tgatgcagaa ctttattatg tgagaaatga 360
ccttattagt cactacgctc tatcctttaa tctgttagta cccagtgaga caaatttcc 420
gcacttcacc tggcatgcga agtccaaggt tgaatataag ctgggattcc aagtggacaa 480
tgttttggca atggatatgc cccagggtcaa catttctgtt cagggggaag ttccacgcac 540
tttatcagtg tttcgggtag agctttcctg tactggcaaa gtagattctg aagttatgat 600
actaatgcag ctcaacttga cagtaaattc ttcaaaaaat tttaccgtct taaattttaa 660
acgaaggaaa atgtgctaca aaaaacttga agaagtaaaa acttcagcct tggacaaaaa 720
cactagcaga actatttatg atcctgtaca tgcagctcca accacttcta cgctgtgtgt 780
ttatattagt gtaggggttt gttgtgcagt aatatttctc gtagcaataa tattagctgt 840
tttgacctt cataatatga aaaggattga actggatgac agcattagtg ccagcagtag 900
ttcccaaggg ctgtctcagc catccacca gacgactcag tatctgagag cagacacgcc 960
caacaatgca actcctatca ccagttatcc taccttgcg atagagaaga acgacttgag 1020
aagtgtcact cttttggagg ccaaaggcaa ggtgaaggat atagcaatat ccagagagag 1080
gataactcta aaagatgtac tccaagaagg tacttttggg cgtattttcc atgggatttt 1140

```

EX05-002patentin.txt

aatagatgaa aaagatccaa ataaagaaaa acaagcattt gtcaaaacag ttaaagatca	1200
agcttctgaa attcaggtga caatgatgct cactgaaagt tgtaagctgc gaggtcttca	1260
tcacagaaat cttcttccta ttactcatgt gtgtatagaa gaaggagaaa agcccatggt	1320
gatattgcct tacatgaatt gggggaatct taaattgttt ttacgacagt gcaagttagt	1380
agaggccaat aatccacagg caatttctca gcaagacctg gtacacatgg ctattcagat	1440
tgctgtgga atgagctacc tggccagaag ggaagtcac cacaagacc tggctgccag	1500
gaactgtgtc attgatgaca cacttcaagt taagatcaca gacaatgccc tctccagaga	1560
cttgttcccc atggactatc actgtctggg ggacaatgaa aacaggccag ttcgttggat	1620
ggctcttgaa agtctggta ataacgagtt ctctagcgct agtgatgtgt gggcctttgg	1680
agtgacgctg tgggaactca tgactctggg ccagactccc tacgtggaca ttgaccctt	1740
cgagatggcc gcatacctga aagatgggta ccgaatagcc cagccaatca actgtcctga	1800
tgaattatth gctgtgatgg cctgttgctg ggccttagat ccagaggaga ggcccaagtt	1860
tcagcagctg gtacagtgcc taacagagtt tcatgcagcc ctgggggcct acgtctgact	1920
cctctccaat cccacaccat caggaagaag gtgcctgtcg gggctcactt gaagcctgtc	1980
agggatgctt tgtatctaac acaacgccaa cagaagcaca tttgtcttcc agaacaccgt	2040
gccttagaaa tgcttttagaa tctgaacttt ttaagacaga ctttaataatg tggcatatth	2100
tctagatatc acttttatta ggttgaactg aaagggtttt tgtaaatttt ttggccaaaa	2160
ttttttaaaa catacttact ttggactagg ggtacattct tacaaaataa ataaacagtt	2220
tttaaaattg ttttagacaca gatatttgga attagctatc ttagggccaa ctgcttttta	2280
tttttttact tcatcaaggt gatgtaagtg actttgttta gacacagata tttggaatta	2340
gcctatctta gtgccaaactg ctttttattt ttttccttca tcaaggtgat gtaagtgact	2400
caccttttaa gtttttttag tgttattttt tatcactact ctgggaaatg gtttgtcttc	2460
aagatgcaat acttttctta gataaggaaa aacagcataa aaagatacct ggtctgcctt	2520
gtacaagaaa accgaatatt agaggaagaa aatttaaaga aaagctagag aaaaaaaaaa	2580
ttttttaaaa aatacttatt agaagcaaac tgcccttgca tggaaaactg tttatttttt	2640
tcagtgaaaa aggaattctg ctttcgtgtt tttgggaaag caggaactga gttcattaca	2700
tctttaattt ggcagaaatt agcctttctg tgaaccagat gtggtttggg gcagatctgt	2760
agtaaacaaat ggtgatthta tttattttta ctctctggaa aaggagataa tacaattcca	2820
gaaagtgaac tcatatttct aaggtaagat cccttttatg cacctagaat atgctatgca	2880
cagagcgggt gcttgagttg ttgtcgthtt ttgtttgttt tttaaatgta aactggtaaa	2940
ttttgtgctt atcttcaagg ctggcttaag tataaaattg ttttttaaac acttgaaaaa	3000
ttaaaggatt tgthttatat taaaaaaaaa a	3031

<210> 26
 <211> 2940

EX05-002patentin.txt

<212> DNA

<213> Homo sapiens

<400> 26

```
ctaacttcag cggtggcacc gggatcggtt gccttgagcc tgaaatatga ccaccccagg      60
aaaagagaac tttcgctga aaagttacaa gaacaaatct ctgaatcccg atgagatgcg      120
caggaggagg gaggaagaag gactgcagtt acgaaagcag aaaagagaag agcagttatt      180
caagcggaga aatgttgcta cagcagaaga agaaacagaa gaagaagtta tgtcagatgg      240
aggctttcat gaggtcaga ttagtaacat ggagatggca ccagggtggtg tcatcacttc      300
tgacatgatt gagatgatat tttccaaaag cccagagcaa cagctttcag caacacagaa      360
attcaggaag ctgctttcaa aagaacctaa ccttcctatt gatgaagtta tcagcacacc      420
aggagtagtg gccaggtttg tggagttcct caaacgaaaa gagaattgtt cactgcagtt      480
tgaatcagct tgggtactga caaatattgc ttcaggaaat tctcttcaga cccgaattgt      540
gattcaggca agagctgtgc ccatcttcat agagttgctc agctcagagt ttgaagatgt      600
ccaggaacag gcagtctggg ctcttggaac cattgctgga gatagtacca tgtgcagggg      660
ctatgtctta gactgcaata tccttcccc tcttttgagc ttattttcaa agcaaaaccg      720
cctgaccatg acccggaatg cagtatgggc tttgtctaata ctctgtagag ggaaaagtcc      780
acctccagaa tttgcaaagg tttctccatg tctgaatgtg ctttcctggg tgctgtttgt      840
cagtgcact gatgtactgg ctgatgcctg ctgggccctc tcatatctat cagatggacc      900
caatgataaa attcaagcgg tcatcgatgc gggagtatgt aggagacttg tggaactgct      960
gatgcataat gattataaag tggtttctcc tgctttgcga gctgtgggaa acattgtcac     1020
aggggatgat attcagacac aggtaattct gaattgctca gctctgcaga gtttattgca     1080
tttgctgagt agcccaaagg aatctatcaa aaaggaagca tggtggacga tatctaatat     1140
tacagctgga aatagggcac agatccagac tgtgatagat gccaacattt tcccagccct     1200
cattagtatt ttacaaactg ctgaatttcg gacaagaaaa gaagcagctt gggccatcac     1260
aaatgcaact tctggaggat cagctgaaca gatcaagtac ctagtagaac tgggttgtat     1320
caagccgctc tgtgatctcc tcacggtcat ggactctaag attgtacagg ttgccctaaa     1380
tggcttggaa aatatcctga ggcttggaga acaggaagcc aaaaggaacg gcactggcat     1440
taacccttac tgtgctttga ttgaagaagc ttatggtctg gataaaattg agttcttaca     1500
gagtcatgaa aaccaggaga tctacaaaaa ggcctttgat cttattgagc attacttcgg     1560
gaccgaagat gaagacagca gcattgcacc ccaggttgac cttaccagc agcagtacat     1620
cttccaacag tgtgaggctc ctatggaagg tttccagctt tgaagcaata ctctgctttc     1680
acgtacctgt gctcagacca ggctacccag tcgagtcctc ttgtggagcc cacagtcctc     1740
atggagctaa cttctcaaat gttttccata atactgtttg cgctcatttg cttgccttgc     1800
gcacctgctc tcttacacac atctggaaaa cctccggctc tctgtggtgg gatacccttc     1860
taataaaaagg gtaaccagaa cggccctc tcttttacgg aaaaatccct aggctttgga     1920
```

EX05-002patentin.txt

gatccgcact tacattagag ttatgggaat atacacatat taatgtggct ccctttttct 1980
 tgtgggggaa taaaagagga ctctctctca ttccctttaa catgggggaa aaaactgaca 2040
 ttaaaagatg agactaaatc tttatcttga attttacaca actacttacg acaagggaga 2100
 tgtttagacc tgttggtata cttcagagta cttttcatga gttcttcac agtgaaccct 2160
 tggattacct ggtggctttt tctagccaga ttgcattaat cttactgag attggatggt 2220
 tttctttcct ctattggcgc cattcttcag atattaaagt taaaccatcc actccctcac 2280
 cttcagcctt cagtgaatgt gctttctagt tgtcaggaat gctgaagaat taacactttg 2340
 actcctaaat gtgatactgg tgggtaagag cagggcacat ttaatttggt cgcttttgct 2400
 tctctttggt ctgggcacat ttaatttggt cgcttttgct tctctttggt cttttcgaat 2460
 acttagtaat cgaaaacat atcctgtaat ttaataaaaa aaactaagga cgaaaaaacc 2520
 cctccaattt tcccaaatgc aatcagtgtg actaggggct gtgtttctgc attaaaaataa 2580
 atgtttcagg ctttggtgct ctgatcaagg tcctcattaa aaaattggag ttcaccctag 2640
 gcttttcccc tctgtgactg gcagataaca catacttttg aaagtaactt tgggattttt 2700
 tttcttaggt gcagctcgat tctaattctt tcatgctgca cacgattcct ttaatcgata 2760
 gcatccttat ctgaaagaaa taaccatctt ctcaacatga cctgcttaac ccaaataaga 2820
 acagtgatct tataacctca ttgtttccta atctatttta tttcatctcc tgctagtact 2880
 gtgccgcttc cccctcccc cacacaaaat aaaaacagta tctcgcttct ggctcatttt 2940

<210> 27
 <211> 2172
 <212> DNA
 <213> Homo sapiens

<400> 27
 ggccgcatc ttggattgag aactgggtcg ctacgcttca cgccaggggc ggagtggcgg 60
 cccttctgtt acccgccaca cacgtcgccg ctggggactg ggaaatcagg gcatcggaga 120
 gtgccacatt aatggatgcc atggctagtc cagggaaaga taactataga atgaaaagtt 180
 ataagaataa agccctaaat cctcaagaga tgcgtagacg aagagaagaa gaaggaatac 240
 agcttagaaa acaaaaaaga gaagaacagt tgttcaaacg cagaaatgtc tatttgccca 300
 gaaatgatga atctatgctt gaaagtccta tacaggatcc agatattagt tccactgtac 360
 ccattccaga ggaagaagtt gttactacag atatggttca gatgattttt tctaataatg 420
 ctgatcaaca gctaacagca acacagaaat ttagaaagct gctttctaaa gaacctaatc 480
 caccaataga tcaagttata cagaaaccag gagttgtaca gagattttgtg aaatttcttg 540
 aaagaaatga aaattgcact ttacaatttg aagctgcatg ggcattaaca aatatagcat 600
 ctggaacttt tctgcatacc aaggtagtga ttgaaactgg ggctgttccg atttttatca 660
 aacttcttaa ttctgaacat gaagatgttc aggaacaggc tgtttgggca cttggtaata 720
 ttgctggtga caatgcagaa tgcagagatt ttgttttgaa ttgtgaaata cttccacctc 780
 ttttagagtt attaacaaat tcaaacagac tcacaacaac aagaaatgcc gtgtgggccc 840

EX05-002patentin.txt

```

tctcaaattt atgtagaggc aaaaaccctc ctccaaactt tagtaagggt tcaccttgct 900
taaagtgcct gtcacgactg ttgttttagca gtgaccaga tgtgttagca gacgtgtgtt 960
gggccctttc ttatctctcc gatggacca atgataaaat tcaagcagtc attgattctg 1020
gagtctgtcg aagattggtg gaacttttga tgcacaatga ttataaagtt gtatcacctg 1080
cattaagggc agttggtaat attgtgactg gtgatgatat tcaaacacag gtaattttga 1140
attgttctgc attaccctgt ctcttacatt tattgagtag ccaaaggag tcaattagaa 1200
aagaagcctg ctggactgtt tctaacaatca ctgctggaaa tagagctcag attcaggctg 1260
ttatagatgc aaatattttt cctgttttga ttgagattct tcagaaagca gagtttcgta 1320
ccagaaaaga agcagcttgg gctataacta atgcaacatc aggaggtact ccagagcaaa 1380
taaggatatt ggtagcttta ggctgcatta aaccactttg tgatcttttg actgttatgg 1440
actccaaaat agtccaagtg gctttaaatg gacttgaaaa tattttacgt cttggagaac 1500
aagaatctaa gcagaatgga ataggcatta atccatactg tgctctcatt gaagaagcat 1560
atggtctgga taaaattgag tttttgcaaa gccatgaaaa tcaggaaatt taccagaagg 1620
catttgatct gattgaacat tactttggtg tagaagaaga tgacccagc attgtacctc 1680
agggtgatga aaaccaacaa cagtttatat ttcagcagca ggaagcacca atggatggat 1740
ttcaacttta acttactgga ggaaaaaaaa tttatggcta aaaagggtag cttcagaaat 1800
gacagacttt ttcattgaat gatgaggaca cagcagccat attatgccaa gaggaaaaat 1860
atcatgatca tattgaaaga tcaagcatga gcttccatgg tgaagtcttc tgtaccaatg 1920
caccagagaa tgcctaccat ccaaaaaagc agtcagctga tggaaaagaa gattattaaa 1980
cctttgttct gggatttact gttaaaaaac aaacaaaaaa caacaaaaaa gcggtgacag 2040
gaaacagtta aggaaatgat ttaactgaag ggaagcaaga tttttttaa gcattgttct 2100
taatcccat gactgtcctt cagtcacaat tccagaataa aagaatctac tttgtgtaaa 2160
aaaaaaaaaa aa 2172

```

```

<210> 28
<211> 3984
<212> DNA
<213> Homo sapiens

```

```

<400> 28
atattgtcta ctgaaagctg ccgctgaagc tgccgccgtt gcctccgccg ccaagagtga 60
gcgagcggac ccgcatgga gaccatggcg agcccaggga aagacaatta tcgaatgaag 120
agctataaga acaatgctct aaaccctgaa gaaatgagac gaagaagaga ggaagagggc 180
attcagctcc ggaagcagaa gcgagagcaa caacttttta aacggagaaa tgtggagctg 240
attaatgaag aagctgccat gttcgatagt cttctcatgg actcttatgt gagctctacc 300
actggggaga gtgtgacac aagagagatg gtggagatgc tcttttctga tgattctgac 360
ctgcagttag caaccacaca gaaattccgg aaactgctct ccaaagagcc tagtcctcca 420

```

EX05-002patentin.txt

atagatgaag ttatcaacac tccaagagtg gtggatcggg tcgtggagtt tctgaagagg	480
aatgagaatt gtacattaca gtttgaagct gcctgggctc taacgaatat tgcctctgga	540
acctctcagc agacaaaaat tgtcattgaa gcaggggctg tccccatttt tatagagctg	600
cttaattcag actttgagga tgttcaggaa caggcagtct gggcactggg aaacatagct	660
ggagatagct ctgtttgccg agattacgtc ttgaactgtt ccattcctta tcctttgtta	720
acactcctta ccaagtccac acgactgacg atgacacgga atgcagtctg ggccctgtca	780
aatctctgcc gagggaaaaa cccacccccca gagtttgcaa aggtctctcc ttgtttgcct	840
gtactgtctc gcctactctt cagcagcgac tcggacttgc tggcagatgc ttgctgggcc	900
ctttcttatt tgtctgatgg ccccaatgag aagatccagg cagtcataga ctccggagtc	960
tgccggagat tggtagagct gctgatgcac aatgattaca aagtggcttc tcctgccctg	1020
agagccgtgg gtaacatcgt cactggggat gacatccaga cccagggtcat tcttaactgt	1080
tcagccctac ctgaccttct ccacttggtg agcagtccca aggagtcaat ccggaaggaa	1140
gcttgctgga ctatttcaaa tattactgct ggcaacaggg ctcaaataca ggctgttata	1200
gatgcaaata tcttccctgt gttgatcgaa atccttcaga aagcagagtt tcgtacaagg	1260
aaagaggcag cctgggccat caccaatgcc acatcaggag gaaccctga gcagatcagg	1320
tacctggtct cactgggctg catcaaacc ctatgtgact tgctgactgt aatggattcg	1380
aagattgtgc aagtggccct caatggactg gagaacatcc tgcggttgg agagcaagag	1440
ggcaagcgca gtggctcagg ggtcaatcct tattgtggcc tcatagagga agcctatggc	1500
ttggataaaa ttgagtttct ccagagccac gagaaccagg agatctacca gaaggccttc	1560
gacctcattg agcactactt tgggtgtaga gacgatgata gcagcctggc tccccagtc	1620
gatgaaacgc aacagcagtt catcttcag cagcctgagg ccccatgga gggcttcag	1680
ctataatatc tgcctccagg gaggggaggg gatgggaagc accaccagcc agcggaagag	1740
cagccctctg gtggcgagg aaccagtgtc cccaccatca gccaccacac acctctgctg	1800
ccctggagac tgtgctcttg acctgctccg ccccttccc tggagggagc acctctgga	1860
cagacagaac catctgaggc tcacctttgg gttttgtgac aagaagggga cgtgttgggt	1920
ttttcttctt tacactatat tttggctgca cacatgtctt taaccagga gccagggggt	1980
agacaaagga ggactaagg aatcaatttg cacctttttt tttttttatt tttttcttt	2040
ttttcttcag tgggtgactt cttcccttta tcttttttca ttcttcccgg tcctctgccc	2100
tgatctgtgt aactcttatt ttgggtactt gagcagacgg tatattccag aggtgggagg	2160
tgggagggga agggagaaat ccaaaacaaa gtgttcttgc tctgacagaa tattaatctt	2220
gtacgcttgg attgagttat ttaatttttt tttcttttgc acatttttct tgtattaaga	2280
ttgctcttcc caagagccac aagttcctgg ttttagtaaa cccagctgcc tgcattgcct	2340
gggactagag gctggggagg ctaccatgaa acaaaggctc ctccctccct ctgactcttt	2400
gccagacct ctttagtttg ggggatcctc ctactctcc tgaagtgtct caagtatacc	2460

EX05-002patentin.txt

```

agtgggagtg caggggagga gcacaggcct tcagatgggg cttcccacgt gtagctactg 2520
atcccatatt tcctactcac cttccaaatg gtgcgaccca acttcatttg tttacttgaa 2580
aattccccct cgagggttgag agaacctctg aggtggctgt attttctcct aagcttgaga 2640
tagggggctg tggtccttcc tttctcctga ggagaaagtc cttgctctgg tgacctgtaa 2700
gttgagagg aggggtggagt gagagtgtca tgtattggga tagtcaggga tccctgcctt 2760
tggcctttct tcttcttctt cttcctcttc catagtggga tcatgtatat tttacttcta 2820
aaggagagaa tgtcaaaaag ttctgtatgt ttttatattc tatatattag gtaggtcaat 2880
cttaattggt ctcaagagga agaactgtct gtcatttcgg taagtaggat actgtgagga 2940
agaccaaaaa gagatatgga tgcttcctcg ctcaggaggc ctgagcttgg tcttttctct 3000
ctctgcttgg attctggacc accacctggg accaaccttc agctctggaa ccttcataaa 3060
gcaggtcagc gtggcctgat tgtcccagga cctgaaggga gcaaggatgg cctcaggggc 3120
tgggtgaagtc tgctactctg tccttactgc tgaacatcct gcttgtatca ggaaactcag 3180
aagcagtttg ccttgtcaaa ttcaatctca atggccattg tccacataac tgatcaccca 3240
tggctgcctc tcctattatc tattatcact gaaacttagt agcctgcttt tttttttttt 3300
tttttttagag ctattgcgta tcttccctgt ttgggatcct tgtacctggg ttgggttttc 3360
ccttccttgt gacaattata atccagatgc ctcttctttc tgtttgaatt acggtagtgc 3420
attgccttag tggcttgcct gtgcctctgg gtggattaca tatgatagta aagcccacct 3480
gtttggatgg gagtagagga agttggtgta gaccagctgt ggagctgaag gcacagtctg 3540
ccccacccc acctccccac tgtggttagt cagaggcatc ctgctccaag ctctgctttt 3600
ccttcctctg aaacaatgcc attcttgctt ctattgctac acatctcctt ctggctcagg 3660
tgaaatccat gcccttctgc ttatagacct aaagttcagg tacttattat tggccattga 3720
tcttgaattt gccctctcct agtgctgcag tcccacttca aagccatttt ctgaggagga 3780
tggtttaggt ctggcaattg tccttgaaaa atccccacca tgttgtacca ccttgggtgag 3840
tcatatgcca ctcatcagct tgggaatgat ggctgccaac tcccaatctc ccaggaaggc 3900
agggggcaga atcttttttt cacttggcct gctacctcca ttaaaaaacc attctcttac 3960
agtttaaaaa aaaaaaaaaa aaaa 3984

```

<210> 29
 <211> 2409
 <212> DNA
 <213> Homo sapiens

```

<400> 29
atgcggggcg tgtggccgcc cccggtgtcc gccctgctgt cggcgctggg gatgtcgacg 60
tacaagcggg ccacgtgga cgaggaggac ctgggtggact cgctctccga gggcgacgca 120
taccccaacg gcctgcaggt gaacttccac agcccccgga gtggccagag gtgctgggct 180
gcacggaccc aggtggagaa gcggctggtg gtgttggtgg tacttctggc ggcaggactg 240
gtggcctgct tggcagcact gggcatccag taccagacaa gatccccctc tgtgtgcctg 300

```

EX05-002patentin.txt

agcgaagctt gtgtctcagt gaccagctcc atcttgagct ccatggaccc cacagtggac 360
 ccctgccatg acttcttcag ctacgcctgt gggggctgga tcaaggccaa cccagtccct 420
 gatggccact cacgctgggg gaccttcagc aacctctggg aacacaacca agcaatcatc 480
 aagcacctcc tcgaaaactc cacggccagc gtgagcgagg cagagagaaa ggcgcaagta 540
 tactaccgtg cgtgcatgaa cgagaccagg atcgaggagc tcagggccaa acctctaattg 600
 gagttgattg agaggctcgg gggctggaac atcacaggct cctgggccaa ggacaacttc 660
 caggacaccc tgcaggtggt caccgcccac taccgcacct cacccttctt ctctgtctat 720
 gtcagtgccg attccaagaa ctccaacagc aacgtgatcc aggtggacca gtctggcctg 780
 ggcttgcct cgagagacta ttacctgaac aaaactgaaa acgagaaggt gctgaccgga 840
 tatctgaact acatgggtcca gctggggaag ctgctgggcg gcggggacga ggaggccatc 900
 cggccccaga tgcagcagat cttggacttt gagacggcac tggccaacat caccatccca 960
 caggagaagc gccgtgatga ggagctcatc taccacaaag tgacggcagc cgagctgcag 1020
 accttggcac ccgccatcaa ctggttgctt tttctcaaca ccatcttcta ccccgaggag 1080
 atcaatgaat ccgagcctat tgtggtctat gacaaggaat accttgagca gatctccact 1140
 ctcatcaaca ccaccgacag atgcctgctc aacaactaca tgatctggaa cctggtgctg 1200
 aaaacaagct ccttccttga ccagcgcttt caggacgccg atgagaagtt catggaagtc 1260
 atgtacggga ccaagaagac ctgtcttcct cgctggaagt tttgcgtgag tgacacagaa 1320
 aacaacctgg gctttgcgtt gggcccatg tttgtcaaag caaccttcgc cgaggacagc 1380
 aagagcatag ccaccgagat catcctggag attaagaagg catttgagga aagcctgagc 1440
 accctgaagt ggatggatga ggaaacctga aaatcagcca aggaaaaggc cgatgccatc 1500
 tacaacatga taggataccc caacttcac atggatccca aggagctgga caaagtgttt 1560
 aatgactaca ctgcagttcc agacctctac tttgaaaatg ccatgcggtt tttcaacttc 1620
 tcatggaggg tcatgcccga tcagctcagg aaagccccca acagagatca gtggagcatg 1680
 accccgccc tggtgaacgc ctactactcg cccaccaaga atgagattgt gtttccggcc 1740
 gggatcctgc aggcaccatt ctacacacgc tcctcaccca aggccttaaa ctttggtggc 1800
 ataggtgtcg tcgtgggcca tgagctgact catgcttttg atgatcaagg acgggagtat 1860
 gacaaggacg ggaacctccg gccatggtgg aagaactcat ccgtggaggc cttcaagcgt 1920
 cagaccgagt gcatggtaga gcagtacagc aactacagcg tgaacgggga gccggtgaac 1980
 gggcggcaca ccctggggga gaacatcgcc gacaacgggg gtctcaaggc ggcctatcgg 2040
 gcttaccaga actgggtgaa gaagaacggg gctgagcact cgctccccac cctgggcctc 2100
 accaataacc agctcttctt cctgggcttt gcacagggtc ggtgctccgt ccgcacacct 2160
 gagagctccc acgaaggcct catcaccgat cccacagcc cctctcgctt ccgggtcatc 2220
 ggctccctct ccaattccaa ggagttctca gaacacttcc gctgccacc tggctcacc 2280
 atgaacctgc ctcacaagtg cgaagtctgg taaggacgaa gcggagagag ccaagacgga 2340

EX05-002patentin.txt

ggaggggaag gggctgagga cgagaccccc atccagcctc cagggcattg ctcagcccgc 2400
 ttggccacc 2409

<210> 30
 <211> 3410
 <212> DNA
 <213> Homo sapiens

<400> 30
 agttaccgga gcggaactgc gggtagccgc aagtcgagta ctgggatcag cgctaccaag 60
 gcgcagccga ttctgcccc tacgattggt tcggggactt ctcctccttc cgtgccctcc 120
 tagagccgga gctgcggccc gaggaccgta tccttggtgct aggttgctggg aacagtgtccc 180
 tgagctacga gctgttcctc ggaggcttcc ctaatgtgac cagtgtggac tactcatcag 240
 tcgtggtggc tgccatgcag gctcgccatg cccatgtgcc gcagctgcgc tgggagacca 300
 tggatgtgct gaagctggac ttccccagt cttcttttga tgtggtgctc gagaagggca 360
 cgctggatgc cctgctggct ggggaacgag atccctggac cgtgtcctct gaagggtgtcc 420
 aactgtgga ccaggtgttg agtgagggtg gattccagaa ggggacaaga cagtgttag 480
 gctcacgcac gcagctggag ctggtcttag caggtgcctc tctactgctg gctgcactgc 540
 ttctgggctg ccttggtggc ctaggggtcc agtaccacag agacccatcc cacagcacct 600
 gccttacaga ggcctgcatt cgagtggctg gaaaaatcct ggagtccctg gaccgagggg 660
 tgagccccctg tgaggacttt taccagttct cctgtggggg ctggattcgg aggaaccccc 720
 tgcccgatgg gcgttctcgc tggaacacct tcaacagcct ctgggaccaa aaccaggcca 780
 tactgaagca cctgcttgaa aacaccacct tcaactccag cagtgaagct gagcagaaga 840
 cacagcgctt ctacctatct tgcctacagg tggagcgcag tgaggagctg ggagcccagc 900
 cactgagaga cctcattgag aagattggtg gttggaacat tacggggccc tgggaccagg 960
 acaactttat ggaggtgttg aaggcagtag caggaccta cagggccacc ccattcttca 1020
 ccgtctacat cagtgtgac tctaagagtt ccaacagcaa tggtatccag gtggaccagt 1080
 ctgggctctt tctgccctct cgggattact acttaaagag aactgccaat gagaaagtgc 1140
 tcaactgcta tctggattac atggaggaa tggggatgct gctgggtggg cggccacact 1200
 ccacgagggg gcagatgcag caggtgctgg agttggagat acagctggcc aacatcacag 1260
 tgccccagga ccagcggcgc gacgaggaga agatctacca caagatgagc atttcggagc 1320
 tgcaggctct ggcgccctcc atggactggc ttgagttcct gtctttcttg ctgtcaccat 1380
 tggagttgag tgactctgag cctgtggtgg tgtatgggat ggattatttg cagcaggtgt 1440
 cagagctcat caaccgcag gaaccaagca tcctgaacaa ttacctgatc tggaacctgg 1500
 tgcaaaagac aacctcaagc ctggaccgac gctttgagtc tgcacaagag aagctgctgg 1560
 agaccctcta tggcactaag aagtcctgtg tgccgaggtg gcagacctgc atctccaaca 1620
 cggatgacgc ccttggtctt gctttggggt ccctcttcgt gaaggccacg tttgaccggc 1680

EX05-002patentin.txt

```

aaagcaaaga aattgcagag gggatgatca gcgaaatccg gaccgcattt gaggaggccc 1740
tgggacagct ggtttggatg gatgagaaga cccgccaggc agccaaggag aaagcagatg 1800
ccatctatga tatgattggt ttcccagact ttatcctgga gcccaaagag ctggatgatg 1860
tttatgacgg gtacgaaatt tctgaagatt ctttcttcca aaacatgttg aatttgtaca 1920
acttctctgc caaggttatg gctgaccagc tccgcaagcc tcccagccga gaccagtgga 1980
gcatgacccc ccagacagtg aatgcctact accttccaac taagaatgag atcgtcttcc 2040
ccgctggcat cctgcaggcc cccttctatg cccgcaacca cccaaggcc ctgaacttcg 2100
gtggcatcgg tgtggtcatg ggccatgagt tgacgcatgc ctttgatgac caagggcgcg 2160
agtatgacaa agaagggaac ctgcgccctt ggtggcagaa tgagtccttg gcagccttcc 2220
ggaaccacac ggcctgcatg gaggaacagt acaatcaata ccagggtcaat ggggagaggc 2280
tcaacggccg ccagacgctg ggggagaaca ttgctgacaa cggggggctg aaggctgcct 2340
acaatgctta caaagcatgg ctgagaaagc atggggagga gcagcaactg ccagccgtgg 2400
ggctcaccaa ccaccagctc ttcttcgtgg gatttgccca ggtgtggtgc tcggtccgca 2460
caccagagag ctctcacgag gggctggtga ccgaccccca cagccctgcc cgcttccgcg 2520
tgctgggcac tctctccaac tcccgtgact tctgcggca cttcggctgc cctgtcggct 2580
cccccataaa cccagggcag ctgtgtgagg tgtggtagac ctggatcagg ggagaaatgc 2640
ccagctgtca ccagacctgg ggcagctctc ctgacaaagc tgtttgctct tgggttggga 2700
ggaagcaaat gcaagctggg ctgggtctag tccctcccc ccacagggtga catgagtaca 2760
gaccctctc aatcaccaca ttgtgcctct gctttggggg tgcccctgcc tccagcagag 2820
ccccaccat tactgtgac atctttccgt gtcaccctgc ctggaagagg tctgggtggg 2880
gaggccagtt cccataggaa ggagtctgcc tcttctgtcc ccaggctcac tcagcctggc 2940
ggccatgggg cctgccgtgc ctgccccact gtgaccaca ggcctgggtg gtgtacctcc 3000
tggacttctc cccaggctca ctcagtgcgc acttaggggt ggactcagct ctgtctggct 3060
caccctcacg ggctaccccc acctcaccct gtgctccttg tgccactgct cccagtgtg 3120
ctgctgacct tactgacag ctctagtgg aagcccaagg gcctctgaaa gcctcctgct 3180
gcccactgtt tccctgggct gagaggggaa gtgcatatgt gtagcgggta ctggttcctg 3240
tgtcttaggg cacaagcctt agcaaatgat tgattctccc tggacaaagc aggaaagcag 3300
atagagcagg gaaaagggaag aacagagttt atttttacag aaaagagggt gggagggtgt 3360
ggtcttgccc cttataggac cctgtgcaa taaacagaca tgcattccgtc 3410

```

<210> 31
 <211> 2872
 <212> DNA
 <213> Homo sapiens

```

<400> 31
cggcgctggg agacaccgga cgcccgctcg gctgcgctgc ggctcaggcc cccgctcggg 60
cccgacccgc tcggtcaccg ccggctcggg cgcgcacctg ccggctgcgg cccaggggcc 120

```

EX05-002patentin.txt

atgcggaggc	ccacgaggag	gccggcggcc	acgcgcatcc	cgtagcccag	gtggcccagg	180
tctgcaccgc	ggcggcctcg	gcgccatgga	gccccgtat	tcgctgacgg	cgactacga	240
tgagttccaa	gaggtcaagt	acgtgagccg	ctgcggcgcg	gggggcgcg	gcggggcctc	300
cctgcccccg	ggcttcccgt	tgggcgctgc	gcgcagcgcc	accggggccc	ggtccgggct	360
gccgcgctgg	aaccggcgcg	aggtgtgcct	gctgtcgggg	ctggtgttcg	ccgccggcct	420
ctgcgccatt	ctggcggcta	tgctggccct	caagtacctg	ggcccggtcg	cgccggcgcg	480
cggcgccctgt	cccgagggct	gccctgagcg	caaggccttc	gcgcgcgccg	ctcgcttcct	540
ggccgccaac	ctggacgcca	gcatcgaccc	atgccaggac	ttctactcgt	tcgcctgcgg	600
cggttggctg	cggcgccacg	ccatccccga	cgacaagctc	acctatggca	ccatcgcggc	660
catcggcgag	caaaacgagg	agcgccctacg	gcgcctgctg	gcgcggccccg	ggggtgggcc	720
tggcggcgcg	gcccagcgca	aggtgcgcgc	cttcttccgc	tcgtgcctcg	acatgcgcga	780
gatcgagcga	ctggggcccg	gacccatgct	agaggtcatc	gaggactgcg	ggggctggga	840
cctgggcggc	gcggaggagc	gtccgggggt	cgcggcgcga	tgggacctca	accggctgct	900
gtacaaggcg	cagggcggtg	acagcgccgc	cgcgctcttc	tcgctcacgg	tcagcctgga	960
cgacaggaac	tcctcgcgct	acgtcatccg	cattgaccag	gatgggctca	ccctgccaga	1020
gaggaccctg	tacctcgctc	aggatgagga	cagtgagaag	gtcctggcag	catacagggg	1080
gttcatggag	cgagtgtca	gcctcctggg	tgcagacgct	gtggaacaga	aggcccaaga	1140
gatcctgcaa	gtggagcagc	agctggccaa	catcactgtg	tcagagtatg	acgacctacg	1200
gcgagatgtc	agctccatgt	acaacaagg	gacgctgggg	cagctgcaga	agatcacccc	1260
ccacttgccg	tggaaagtgg	tgctagacca	gatcttccag	gaggacttct	cagaggaaga	1320
ggaggtggtg	ctgctggcga	cagactacat	gcagcaggtg	tcgcagctca	tccgctccac	1380
acccaccagg	gtcctgcaca	actacctgg	gtggcgcgctg	gtggtggtcc	tgagtgaaca	1440
cctgtccccg	ccattccgtg	aggcactgca	cgagctggca	caggagatgg	agggcagcga	1500
caagccacag	gagctggccc	gggtctgctt	gggccaggcc	aatcgccact	ttggcatggc	1560
gcttggcgcc	ctctttgtac	atgagcactt	ctcagctgcc	agcaaagcca	aggtgcagca	1620
gctagtggaa	gacatcaagt	acatcctggg	ccagcgccctg	gaggagctgg	actggatgga	1680
cgccgagacc	agggtgctg	ctcgggccaa	gctccagtac	atgatggtga	tggtcggcta	1740
cccgacttc	ctgctgaaac	ccgatgctgt	ggacaaggag	tatgagtttg	aggtccatga	1800
gaagacctac	ttcaagaaca	tcttgaacag	catccgcttc	agcatccagc	tctcagttaa	1860
gaagattcgg	caggaggtgg	acaagtccac	gtggctgctc	ccccacagg	cgctcaatgc	1920
ctactatcta	cccaacaaga	accagatgg	gttccccgcg	ggcatcctgc	agcccaccct	1980
gtacgaccct	gacttcccac	agtctctcaa	ctacgggggc	atcggcacca	tcattggaca	2040
tgagctgacc	cacggctacg	acgactgggg	gggccagtat	gaccgctcag	ggaacctgct	2100
gcactggtgg	acggaggcct	cctacagccg	cttcctgcga	aaggctgagt	gcatcgctccg	2160

EX05-002patentin.txt

tctctatgac aacttcactg tctacaacca gcggtgaac gggaaacaca cgcttgggga	2220
gaacatcgca gatatgggcg gcctcaagct ggcctaccac gcctatcaga agtgggtgcg	2280
ggagcacggc ccagagcacc cacttccccg gctcaagtag acacatgacc agctcttctt	2340
cattgccttt gcccagaact ggtgcatcaa gcggcggtcg cagtccatct acctgcaggt	2400
gctgactgac aagcatgccc ctgagcacta cagggtgctg ggcagtgtgt cccagtttga	2460
ggagtttggc cgggttttac actgtccaaa ggtctcacc atgaaccctg cccacaagt	2520
ttccgtgtgg tgagcctggc tgcccgctg cagccccca ctgccccgc acgaatcacc	2580
tcctgctggc taccggggca ggcattgcacc cgggtgccagc cccgctctgg gcaccacctg	2640
ccttccagcc cctccaggac ccggtcccc tgctgcccct cacttcagga ggggcctgga	2700
gcagggtag gctggacttt ggggggctgt gagggaaata tactggggtc cccagattct	2760
gctctaaggg ggccagaccc tctgccaggc tggattgtac gggccccacc ttcgctgtgt	2820
tcttgctgca aagtctggc aataaatcac tgcactgtta aaaaaaaaaa aa	2872

<210> 32
 <211> 2562
 <212> DNA
 <213> Homo sapiens

<400> 32	
gggaggagaa gcctgggtgc cccccactga taagcaggct ccacccagag gccagtcctg	60
tgtgtctggg gacaaggcga aagagcagca gaagtgcctt ttctccagga tcaaggaact	120
ggggcggggg gtgtttcctg gaccccagtc ctccgaatca gctcctagag tggaaccagg	180
aaggattctg gagccacaga agatagacag atggaagggtg gggaccaaag tgaggaagag	240
ccgagggaa gcagccaggc aggtggaatg ggaactctct ggagccaaga gagcactcca	300
gaagagaggc tgcccgtgga agggagcagg ccatgggcag tggccaggcg ggtgctgaca	360
gctatcctga ttttgggcct gctcctttgt ttttctgtgc ttttgttcta caacttcag	420
aactgtggcc ctgccccctg tgagacatct gtgtgtttgg atctccggga tcattacctg	480
gcctctggga acacaagtgt gggccccctgc accgacttct tcagctttgc ctgtggaagg	540
gccaaagaga ccaataattc ttttcaggag cttgccaca agaacaaaaa ccgacttcg	600
agaatactgg aggtccagaa ttcctggcac ccaggctctg gggaggagaa agccttcag	660
ttctacaact cctgcatgga tacacttgcc attgaagctg cagggactgg tcccctcaga	720
caagttattg aggagcttg aggctggcgc atctctggta aatggacttc cttaaacttt	780
aaccgaacgc tgagacttct gatgagtcag tatggccatt tccctttctt cagagcctac	840
ctaggacctc atcctgcctc tccacacaca ccagtcattc agatagacca gccagagttt	900
gatgttcccc tcaagcaaga tcaagaacag aagatctatg cccagatctt tcgggaatac	960
ctgacttacc tgaatcagct gggaaacctg ctgggaggag acccaagcaa ggtgcaagaa	1020
cactcttctt tgtcaatctc catcacttca cggctgttcc agtttctgag gcccttgag	1080

EX05-002patentin.txt

cagcggcggg cacagggcaa gctcttccag atgggtcacta tcgaccagct caaggaaatg 1140
 gcccccgcca tcgactgggtt gtcctgcttg caagcgacat tcacaccgat gtccctgagc 1200
 ccttctcagt ccctcgtggt ccatgacgtg gaatatattga aaaacatgtc acaactgggtg 1260
 gaggagatgc tgctaaagca gagggacttt ctgcagagcc acatgatctt agggctgggtg 1320
 gtgacccttt ctccagccct ggacagtcaa ttccaggagg cacgcagaaa gctcagccag 1380
 aaactgcggg aactgacaga gcaaccaccc atgcctgccc gccacgatg gatgaagtgc 1440
 gtggaggaga caggcacgtt cttcgagccc acgctggcgg ctttgtttgt tcgtgaggcc 1500
 tttggcccga gcacccgaag tgctgccatg aaattattca ctgcgatccg ggatgccctc 1560
 atcactcgcc tcagaaacct tccctggatg aatgaggaga ccagaaacat ggcccaggac 1620
 aaggttgctc aactgcaggt ggagatgggg gcttcagaat gggccctgaa gccagagctg 1680
 gcccgacaag aatacaacga tatacagctt ggatcgagct tcctgcagtc tgtcctgagc 1740
 tgtgtccggt ccctccgagc tagaattgtc cagagcttct tgcagcctca ccccaacac 1800
 aggtggaagg tgtccccctt ggacgtcaat gcttactatt cggatatctga ccatgtggta 1860
 gtctttccag ctggactcct ccaacccccca ttcttccacc ctggctatcc cagagccgtg 1920
 aactttggcg ctgctggcag catcatggcc cagcagctgt tgcacatctt ctaccagctc 1980
 ttactgcctg ggggctgcct cgctgtgac aaccatgccc tccaggaagc tcacctgtgc 2040
 ctgaagcgcc attatgctgc ctttccatta cctagcagaa cctccttcaa tgactccctc 2100
 acattcttag agaatgctgc agacgttggg gggctagcca tcgcgctgca ggcatacagc 2160
 aagaggctgt tacggcacca tggggagact gtcctgccc gcctggacct cagccccag 2220
 cagatcttct ttcgaagcta tgcccagggt atgtgtagga agcccagccc ccaggactct 2280
 cacgacactc acagccctcc acacctccga gtccacgggc ccctcagcag cccccagcc 2340
 tttgccagggt atttccgctg tgcacgtggt gctctcttga acccctccag ccgctgccag 2400
 ctctggtaac ttggttacca aagatgccac agcacagaaa tatcgaccaa cacctccctg 2460
 gtcacatcca tggaatcaga gcaagatttc ctttctgctt ctgttccaaa aataaaagct 2520
 ggcacttggc ttccgcttgt ctcttaaaaa aaaaaaaaaa aa 2562

<210> 33
 <211> 5595
 <212> DNA
 <213> Homo sapiens

<400> 33
 gcggagatgt gcaagtggcg aagcttgacc gagagcaggc tggagcagcc gccaactcc 60
 tggcgcggga tctgctgagg ggtcacggat tttagggtgat gggcaagtca gaaagtcaga 120
 tggatataac tgatatcaac actccaaagc caaagaagaa acagcgatgg actcgactgg 180
 agatcagcct ctcggtcctt gtcctgtccc tcaccatcat agctgtgaga atgatcgac 240
 tctatgcaac ctacgatgat ggtatttgca agtcatcaga ctgcataaaa tcagctgctc 300
 gactgatcca aaacatggat gccaccactg agccttgtag agactttttc aaatatgctt 360

EX05-002patentin.txt

gcggaggctg gttgaaacgt aatgtcattc ccgagaccag ctcccgttac ggcaactttg 420
acattttaag agatgaacta gaagtcgttt tgaaagatgt ccttcaagaa cccaaaactg 480
aagatatagt agcagtgcag aaagcaaaag cattgtacag gtcttgata aatgaatctg 540
ctattgatag cagaggtgga gaacctctac tcaaactggt accagacata tatgggtggc 600
cagtagcaac agaaaactgg gagcaaaaat atggtgcttc ttggacagct gaaaaagcta 660
ttgcacaact gaattctaaa tatgggaaaa aggtccttat taatttggtt gttggcactg 720
atgataagaa ttctgtgaat catgtaattc atattgacca acctcgactt ggcctccctt 780
ctagagatta ctatgaatgc actggaatct ataaagaggc ttgtacagca tatgtggatt 840
ttatgatattc tgtggccaga ttgattcgtc aggaagaaag attgcccac gatgaaaacc 900
agcttgcttt ggaaatgaat aaagttatgg aattggaaaa agaaattgcc aatgctacgg 960
ctaaacctga agatcgaaat gatccaatgc ttctgtataa caagatgaga ttggcccaga 1020
tccaaaataa cttttcacta gagatcaatg ggaagccatt cagctggttg aatttcacaa 1080
atgaaatcat gtcaactgtg aatattagta ttacaaatga ggaagatgtg gttgtttatg 1140
ctccagaata tttaaccaa cttaagccca ttcttaccaa atattctgcc agagatcttc 1200
aaaatttaat gtcctggaga ttcataatgg atcttgtaag cagcctcagc cgaacctaca 1260
aggagtccag aaatgctttc cgcaaggccc tttatggtac aacctcagaa acagcaactt 1320
ggagacgttg tgcaaactat gtcaatggga atatggaaaa tgctgtgggg aggctttatg 1380
tggaagcagc atttgctgga gagagtaaac atgtggtcga ggatttgatt gcacagatcc 1440
gagaagtttt tattcagact ttagatgacc tcacttggat ggatgccgag acaaaaaaga 1500
gagctgaaga aaaggcctta gcaattaaag aaaggatcgg ctatcctgat gacattgttt 1560
caaatgataa caaactgaat aatgagtacc tcgagttgaa ctacaaagaa gatgaatact 1620
tcgagaacat aattcaaaaat ttgaaattca gccaaagtaa acaactgaag aagctccgag 1680
aaaagtgga caaagatgag tggataagtg gagcagctgt agtcaatgca ttttactctt 1740
caggaagaaa tcagatagtc ttcccagccg gcattctgca gcccccttc tttagtgcc 1800
agcagtccaa ctcatgaac tatgggggca tcggcatggt cataggacac gaaatcacc 1860
atggcttcga tgacaatggc agaaacttta acaagatgg agacctcgtt gactggtgga 1920
ctcaacagtc tgcaagtaac tttaaggagc aatcccagtg catggtgtat cagtatggaa 1980
acttttcctg ggacctggca ggtggacagc accttaatgg aattaataca ctgggagaaa 2040
acattgctga taatggaggt cttggtcaag catacagagc ctatcagaat tatattaaaa 2100
agaatggcga agaaaaatta cttcctggac ttgacctaaa tcacaaacaa ctatttttct 2160
tgaactttgc acaggtgtgg tgtggaacct ataggccaga gtatgctggt aactccatta 2220
aaacagatgt gcacagtcca ggcaatttca ggattattgg gactttgcag aactctgcag 2280
agttttcaga agcctttcac tgccgcaaga attcatacat gaatccagaa aagaagtgcc 2340
gggtttggtg atcttcaaaa gaagcattgc agcccttggc tagacttgcc aacaccacag 2400

EX05-002patentin.txt

aaatggggaa	ttctctaadc	gaaagaaaat	gggccctagg	ggtcactgta	ctgacttgag	2460
ggtgattaac	agagagggca	ccatcacaaat	acagataaca	ttaggttggtc	ctagaaaggg	2520
tgtggaggga	ggaagggggt	ctaagggtcta	tcaagtcaat	catttctcac	tgtgtacata	2580
atgcttaatt	tctaaagata	atattactgt	ttatttctgt	ttctcatatg	gtctaccagt	2640
ttgctgatgt	ccctagaaaa	caatgcaaaa	cctttgaggt	agaccaggat	ttctaataca	2700
aagggaag	aagatgttga	agaatagagt	taggcaccag	aagaagagta	ggtgacacta	2760
tagtttaaaa	cacattgcct	aactactagt	ttttactttt	atttgcaaca	tttacagtcc	2820
ttcaaaatcc	ttccaaagaa	ttcttataca	cattggggcc	ttggagctta	catagtttta	2880
aactcatttt	tgccatacat	cagttattca	ttctgtgatc	atttatttta	agcactctta	2940
aagcaaaaaa	tgaatgtcta	aaattgtttt	ttgttggtacc	tgctttgact	gatgctgaga	3000
ttcttcaggc	ttcctgcaat	tttctaagca	atttcttgct	ctatctctca	aaacttggtta	3060
tttttcagag	atttatataa	atgtaaaaat	aataattttt	atatttaatt	attaactaca	3120
tttatgagta	actattatta	taggtaatca	atgaatattg	aagtttcagc	ttaaaataaa	3180
cagttgtgaa	ccaagatcta	taaagcgata	tacagatgaa	aatttgagac	tatttaaact	3240
tataaatcat	attgatgaaa	agatttaagc	acaaacttta	gggtaaaaat	tgcgattgga	3300
cagttgtcta	gagatatata	tacttggtgt	tttcaaattg	gactttcaaa	attaaatctg	3360
tccctgagag	tgtctctgat	aaaagggcaa	atctgcacct	atgtagctct	gcatctcctg	3420
tcttttcagg	tttgtcatca	gatggaaata	ttttgataat	aaattgaaat	tgtgaactca	3480
ttgtcccta	agactgtgac	aactgtctaa	ctttagaagt	gcatttctga	atagaaatgg	3540
gaggcctctg	atggaccttc	tagaattata	agtcacaaag	agttctggaa	aagaactgtt	3600
tactgcttga	taggaattca	tcttttgagg	cttctgttcc	tctcttttcc	tgttgatttg	3660
actattttcg	ttcattactt	gattaagatt	ttacaaaaga	ggagcacttc	caaaattctt	3720
atttttccta	acaaaagatg	aaagcaggga	atttctatct	aatgatgag	tattagttcc	3780
ctgtctcttg	aaaaatgccc	atttgccttt	aaaaaaaaaa	gttacagaaa	tactataaca	3840
tatgtacata	aattgcataa	agcataagta	tacagttcaa	taaacttaac	tttaactgaa	3900
caatggccct	gtagccagca	cctgtaagaa	acagagcagt	accagcgctc	taaaagcacc	3960
tccttgctac	tttattactc	ccagaacaac	aactatcctg	acttctaata	tcattcacta	4020
gctttgctg	gttttgctt	ttatgcagat	agaatcaatc	agtatgtatt	cttttggtcc	4080
tggcttcttt	ctctcagcct	tacatttggt	agattcctct	gtattgtgct	gattgtggat	4140
cttttcattc	tcattgcaga	ataatgttct	attgtgggac	ttattacaat	ttgttcattc	4200
tattgttgat	gggcacttga	gaactttcca	ttttggcgct	attacaaata	gtgcaactat	4260
gaatgtactg	catgttacca	tcttacttga	gcctttaatg	gacttatttc	ttcaaatcct	4320
tccaaaaatt	attataagca	ttgaaattat	agtttcaagc	caactgtgga	tacccttacc	4380
ctttcctcct	ttatcacaa	caccgttaca	agtatactta	tatttcctta	aaatacattt	4440

EX05-002patentin.txt

```

aaaacttacc taagtgacat ttgtagttgg agtaatagga gcttccagct ctaataaaac 4500
agctgtctct aacttatattt atttccatca tgtcagagca ggtgaagagc cagaagtgaa 4560
gagtgactag tacaaattat aaaaagccac tagactcttc actgttagct ttttaaaaca 4620
ttaggctccc atccctatgg aggaacaact ctccagtgcc tggatcccct ctgtctacaa 4680
atataagatt ttctgggcct aaaggataga tcaaagtcaa aaatagcaat gcctccctat 4740
ccctcacaca tccagacatc atgaatttta catggtactc ttgttgagtt ctatagagcc 4800
ttctgatgtc tctaaagcac taccgattct ttggagttgt cacatcagat aagacatatc 4860
tctaattcca tccataaatc cagttctact atggctgagt tctggtcaaa gaaagaaagt 4920
ttagaagctg agacacaaag ggttgggagc tgatgaaact cacaatgat ggtaggaaga 4980
agctctcgac aatacccggt ggcaaggagt ctgcctccat gctgcagtgt tcgagtggat 5040
tgtaggtgca agatggaaaag gattgtaggt gcaagctgtc cagagaaaag agtccttggt 5100
ccagccctat tctgccactc ctgacagggt gaccttgggt atttgcaata ttcctttggg 5160
cctctgcttc tctcacctaa aaaaagagaa ttagattata ttggtggttc tcagcaagag 5220
aaggagtatg tgtccaatgc tgccttccca tgaatctgtc tcccagttat gaatcagtgg 5280
gcaggataaa ctgaaaactc ccatttaagt gtctgaatcg agtgagacaa aatttttagtc 5340
caaataacaa gtaccaaagt tttatcaagt ttgggtctgt gctgctgtta ctgttaacca 5400
tttaagtggg gcaaaacctt gctaattttc tcaaaagcat ttatcattct tgttgccaca 5460
gctggagctc tcaaactaaa agacatttgt tattttggaa agaagaaaga ctctattctc 5520
aaagtttcct aatcagaaat ttttatcagt ttccagtctc aaaaatacaa aataaaaaca 5580
aacgttttta atact 5595

```

```

<210> 34
<211> 2784
<212> DNA
<213> Homo sapiens

```

```

<400> 34
aaaggttcct gcggtgctct cccgtccaga gccctgctga tggggaagtc cgaaggccgt 60
ggggatggtg gagagcgccg gccgtgcagg gcagaagcgc ccgggggtcc tggagggggg 120
gctgctgctg ctgctgctgc tggtgaccgc tgccctggtg gccttgggtg tcctctacgc 180
cgaccgcaga gggaagcagc tgccacgcct tgctagccgg ctgtgcttct tacaggagga 240
gaggaccttt gtaaaacgaa aaccccgagg gatcccagag gcccaagagg tgagcgaggt 300
ctgcaccacc cctggctgctg tgatagcagc cgccaggatc ctccagaaca tggacccgac 360
cacggaaccg tgtgacgact tctaccagtt tgcattgcga ggctggctgc ggcgccacgt 420
gatccctgag accaactcaa gatacagcat ctttgacgtc ctccgcgacg agctggaggt 480
catcctcaaa gcggtgctgg agaattcgac tgccaaggac cggccggctg tggagaaggc 540
caggacgctg taccgctcct gcatgaacca gagtgatgata gagaagcgag gctctcagcc 600

```

EX05-002patentin.txt

cctgctggac	atcttgagg	tggtgggagg	ctggccggtg	gcgatggaca	ggtggaacga	660
gaccgtagga	ctcgagtggg	agctggagcg	gcagctggcg	ctgatgaact	cacagttcaa	720
caggcgcgtc	ctcatcgacc	tcttcatctg	gaacgacgac	cagaactcca	gccggcacat	780
catctacata	gaccagccca	ccttgggcat	gccctcccga	gagtactact	tcaacggcgg	840
cagcaaccgg	aaggtgcggg	aagcctacct	gcagttcatg	gtgtcagtgg	ccacgttgct	900
gcgggaggat	gcaaacctgc	ccagggacag	ctgcctggtg	caggaggaca	tggtgcaggt	960
tctggagctg	gagacacagc	tggccaaggc	cacggtaccc	caggaggaga	gacacgacgt	1020
catcgccttg	taccaccgga	tgggactgga	ggagctgcaa	agccagtttg	gcctgaaggg	1080
atttaactgg	actctgttca	tacaaactgt	gctatcctct	gtcaaaatca	agctgctgcc	1140
agatgaggaa	gtggtggtct	atggcatccc	ctacctgcag	aaccttgaaa	acatcatcga	1200
cacctactca	gccaggacca	tacagaacta	cctggtctgg	cgcttggtgc	tggaccgcat	1260
tggtagccta	agccagagat	tcaaggacac	acgagtgaac	taccgcaagg	cgctgtttgg	1320
cacaatggtg	gaggaggtgc	gctggcgtga	atgtgtgggc	tacgtcaaca	gcaacatgga	1380
gaacgccgtg	ggctcccctct	acgtcaggga	ggcgttccct	ggagacagca	agagcatggt	1440
cagagaactc	attgacaagg	tgcggacagt	gtttgtggag	acgctggacg	agctgggctg	1500
gatggacgag	gagtccaaga	agaaggcgca	ggagaaggcc	atgagcatcc	gggagcagat	1560
cgggcaccct	gactacatcc	tggaggagat	gaacaggcgc	ctggacgagg	agtactccaa	1620
tctgaacttc	tcagaggacc	tgtactttga	gaacagtctg	cagaacctca	aggtgggcgc	1680
ccagcggagc	ctcaggaagc	ttcgggaaaa	ggtggaccca	aatctctgga	tcatcggggc	1740
ggcgttggtc	aatgcgttct	actccccaaa	ccgaaaccag	attgtattcc	ctgccgggat	1800
cctccagccc	cccttcttca	gcaaggagca	gccacaggcc	ttgaactttg	gaggcattgg	1860
gatggtgatc	gggcacgaga	tcacgcacgg	ctttgacgac	aatggccgga	acttcgacaa	1920
gaatggcaac	atgatggatt	ggtggagtaa	cttctccacc	cagcacttcc	gggagcagtc	1980
agagtgcag	atctaccagt	acggcaacta	ctcctgggac	ctggcagacg	aacagaacgt	2040
gaacggattc	aacacccttg	gggaaaacat	tgctgacaac	ggaggggtgc	ggcaagccta	2100
taaggcctac	ctcaagtgga	tggcagaggg	tggcaaggac	cagcagctgc	ccggcctgga	2160
tctcaccat	gagcagctct	tcttcatcaa	ctatgccag	gtgtggtgcg	ggtcctaccg	2220
gcccagagttc	gccatccaat	ccatcaagac	agacgtccac	agtcccctga	agtacaggg	2280
actggggctg	ctgcagaacc	tggccgcctt	cgcagacacg	ttccactgtg	cccggggcac	2340
ccccatgcac	ccaaggagc	gatgccgcgt	gtggtagcca	aggccctgcc	gcgctgtgcg	2400
gcccacgccc	acccgctgct	cggaggcatc	tgtgcgaagg	tgcagctagc	ggcgacccag	2460
tgtacgtccc	gccccggcca	accatgccaa	gcctgcctgc	caggcctctg	cgcttggcct	2520
agggtgcagc	cacctgcctg	acacccaggg	atgagcagtg	tccagtgag	tacctggacc	2580
ggagccccct	tcacagacac	ccgcggggct	cagtgcccc	gtcacaactc	tgtagagaca	2640

EX05-002patentin.txt

atcaactgtg	tcctgcccac	ccttcaaggt	gcattgtcct	ccagtatcta	cagcttcaga	2700
acttgagcta	agtaaagtct	ttcaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	2760
aaaaaaaaaa	aaaaaaaaaa	aaaa				2784

<210> 35
 <211> 3130
 <212> DNA
 <213> Homo sapiens

<400> 35						
gatccactag	taacggccgc	cagtgtggtg	gaattcaagg	gactcacaca	ctgaaagaat	60
atctttgatg	aagacaattc	aggcaagcag	aatgattcct	gcaacagaat	tacatgatta	120
attgagatct	tgaagtgggt	ccggtgaatc	ctggccacct	aacttatcat	gatttggggg	180
agtttcacga	gaatccagtt	ttgataaaac	aattgttttt	ttcctcccca	agtgactata	240
catttaaata	gctaaaacat	ctgttcagca	acatagtaaa	acatatatac	tcggaacgct	300
tgagagaaga	gcctgccaaa	cagggaacttt	gctgagggag	agcaccaaga	taaagcaaca	360
ctgtttgttt	tgtctagtca	gggggggaaag	ccaaggcaac	caatattttg	gtttttataa	420
ttttcatttg	tgaagaatta	tttgagaaaag	ggttggcgag	gggagatttc	ctgacggcag	480
tttcttaagc	tgtccattag	tagaagagca	agagagcctt	ggatgtcaac	gcctcgctct	540
tgagaccagc	caccaaacca	cgaaaagtga	ctttcttctc	gtgtgctctc	tacggccctt	600
ctgatggaag	cagaaacagg	gagcagcgtg	gagactggaa	agaaggccaa	cagaggcact	660
cgaattgccc	tggtcgtgtt	tgtcggtggt	accctagttc	tgggcacgat	cctctttcta	720
gtgagtcaag	gtctcttaag	tctccaagct	aaacaggagt	actgcctgaa	gccagaatgc	780
atcgaagcgg	ctgctgccat	cttaagtaaa	gtaaatctgt	ctgtggatcc	ttgtgataat	840
ttcttccggt	tcgcttgtga	tggctggata	agcaataatc	caattcccga	agatatgcca	900
agctatgggg	tttatccttg	gctgagacat	aatggtgacc	tcaagttgaa	ggaacttttg	960
gagaaatcaa	tcagtagaag	gcgggacacc	gaagccatac	agaaagccaa	aatcctttat	1020
tcatcctgca	tgaatgagaa	agcgattgaa	aaagcagatg	ccaagccact	gctacacatc	1080
ctacggcatt	cacctttccg	ctggcccgtg	cttgaatcta	atattggccc	tgaaggggtt	1140
tggtcagaga	gaaagttcag	ccttctgcag	acacttgcaa	cgtttcgtgg	tcaatacagc	1200
aattctgtgt	tcatccgttt	gtatgtgtcc	cctgatgaca	aagcatccaa	tgaacatatc	1260
ttgaagctgg	accaagcaac	actctccctg	gccgtgaggg	aagactacct	tgataacagt	1320
acagaagcca	agtcttatcg	ggatgccctt	tacaagttca	tggtggatac	tgccgtgctt	1380
ttaggagcta	acagttccag	agcagagcat	gacatgaagt	cagtgtcag	attggaaatt	1440
aagatagctg	agataatgat	tccacatgaa	aaccgaacca	gcgaggccat	gtacaacaaa	1500
atgaacattt	ctgaactgag	tgctatgatt	ccccagttcg	actggctggg	ctacatcaag	1560
aaggtcattg	acaccagact	ctaccccat	ctgaaagaca	tcagcccctc	cgagaatgtg	1620
gtgggtccgcg	tcccgcagta	ctttaaagat	ttgttttagga	tattaggggtc	tgagagaaaag	1680

EX05-002patentin.txt

```

aagaccattg ccaactatTTT ggtgtggaga atggtttatt ccagaattcc aaaccttagc 1740
aggcgctttc agtatagatg gctggaattc tcaagggtaa tccaggggac cacaactttg 1800
ctgcctcaat gggacaaatg tgtaaaacttt attgaaagtg ccctccctta tgttggttga 1860
aagatgtttg tagatgtgta cttccaggaa gataagaagg aaatgatgga ggaattgggt 1920
gagggcgttc gctgggcctt tattgacatg ctagagaaag aaaatgagtg gatggatgca 1980
ggaacgaaaa ggaaagccaa agaaaaggcg agagctgttt tggcaaaagt tggctatcca 2040
gagtttataa tgaatgatac tcatgttaat gaagacctca aagctatcaa gttttcagaa 2100
gccgactact ttggcaacgt cctacaaact cgcaagtatt tagcacagtc tgatttcttc 2160
tggctaagaa aagccgttcc aaaaacagag tggtttaca atccgacgac tgtcaatgcc 2220
ttctacagtg catccaccaa ccagatccga tttccagcag gagagctcca gaagcctttc 2280
ttttggggaa cagaatatcc tcgatctctg agttatggtg ctataggagt aattgtcgga 2340
catgaattta cacatggatt tgataataat ggtagaaaat atgataaaaa tggaaacctg 2400
gatccttggg ggtctactga atcagaagaa aagtttaagg aaaaaacaaa atgcatgatt 2460
aaccagtata gcaactatta ttggaagaaa gctggcttaa atgtcaaggg gaagaggacc 2520
ctgggagaaa atattgctga taatggaggc ctgcgggaag cttttagggc ttacaggaaa 2580
tgataaatg acagaaggca gggacttgag gagcctcttc taccaggcat cacattcacc 2640
aacaaccagc tcttcttcct gagttatgct catgtgaggt gcaattccta cagaccagaa 2700
gctgcccag aacaagtcca aattggtgct cacagtcccc ctgagtttag ggtcaatggt 2760
gcaattagta actctgaaga attccagaaa gcttttaact gtccacccaa ttccacgatg 2820
aacagaggca tggactcctg ccgactctgg tagctgggac gctgggttat ggcacctga 2880
gacagttgca cagtgccagc ggaggctgca ctgagccttc atcgcccatt gctttaggcc 2940
tggaggagct ttcattttta gtgcattttc attatttggg taggtgacct gcttggatct 3000
agacagcatc tgttcaaagt tgtagggctt ataaagtgga atataagaag aactaagtat 3060
gtttcttttag aaaatcaaac caacaaaaat aaatccctag gctacttttg ttaaaaaaaa 3120
aaaaaaaaa 3130

```

```

<210> 36
<211> 6099
<212> DNA
<213> Homo sapiens

```

```

<400> 36
ccggcggccg agcgttctga gtcacccggg actggaggta ggaaccagc catggtgaac 60
gaagccagag gaaacagcag cctcaacccc tgcttgagg gcaagtgccag cagtggcagt 120
gagagctcca aagatagttc gagatgttcc accccgggcc tggaccctga gcggcatgag 180
agactccggg agaagatgag gcggcgattg gaatctggtg acaagtgggt ctccctggaa 240
ttcttccctc ctcgaactgc tgaggagct gtcaatctca tctcaagggt tgaccggatg 300

```

EX05-002patentin.txt

gcagcaggtg gccccctcta catagacgtg acctggcacc cagcaggtga ccctgggtca 360
gacaaggaga cctcctccat gatgatcgcc agcaccgccg tgaactactg tggcctggag 420
accatcctgc acatgacctg ctgccgtcag cgcctggagg agatcacggg ccatctgcac 480
aaagctaagc agctgggcct gaagaacatc atggcgctgc ggggagaccc aataggtgac 540
cagtgggaag aggaggagg aggcttcaac tacgcagtgg acctggtgaa gcacatccga 600
agtgagtttg gtgactactt tgacatctgt gtggcagggt accccaaagg ccaccccgaa 660
gcaggagact ttgaggctga cctgaagcac ttgaaggaga aggtgtctgc gggagccgat 720
ttcatcatca cgcagctttt ctttgaggct gacacattct tccgctttgt gaaggcatgc 780
accgacatgg gcatcacttg ccccatcgtc cccgggatct tcccatcca gggctaccac 840
tcccttcggc agcttgtgaa gctgtccaag ctggagggtgc cacaggagat caaggacgtg 900
attgagccaa tcaaagacaa cgatgctgcc atccgcaact atggcatcga gctggccgtg 960
agcctgtgcc aggagcttct ggccagtggc ttggtgccag gcctccactt ctacaccctc 1020
aaccgcgaga tggctaccac agagggtgctg aagcgcttg ggatgtggac tgaggacccc 1080
aggcgtcccc taccctgggc tctcagtgcc caccccaagc gccgagagga agatgtacgt 1140
cccattctct gggcctccag accaaagagt tacatctacc gtaccagga gtgggacgag 1200
ttccctaacg gccgctgggg caattcctct tcccctgcct ttggggagct gaaggactac 1260
tacctcttct acctgaagag caagtcccc aaggaggagc tgctgaagat gtggggggag 1320
gagctgacca gtgaagcaag tgtctttgaa gtctttgttc ttacctctc gggagaacca 1380
aaccggaatg gtcacaaagt gacttgctg ccctggaacg atgagcccct ggcggctgag 1440
accagcctgc tgaaggagga gctgctgcgg gtgaaccgcc agggcatcct caccatcaac 1500
tcacagccca acatcaacgg gaagccgtcc tccgaccca tcgtgggctg gggccccagc 1560
gggggctatg tcttcagaa ggcctactta gagtttttca cttcccgcga gacagcgaa 1620
gcattctgc aagtgtgaa gaagtacgag ctccgggtta attaccacct tgtcaatgtg 1680
aagggtgaaa acatcaccaa tgcccctgaa ctgcagccga atgctgtcac ttggggcatc 1740
ttccctgggc gagagatcat ccagcccacc gtagtggatc ccgtcagctt catgttctg 1800
aaggacgagg ctttgccct gtggattgag cagtggggaa agctgtatga ggaggagtcc 1860
ccgtcccga ccatcatcca gtacatccac gacaactact tcctggtcaa cctggtggac 1920
aatgacttcc cactggacaa ctgcctctgg cagggtgggtg aagacacatt ggagcttctc 1980
aacaggccca ccagaatgc gagagaaacg gaggtccat gaccctgcgt cctgacgccc 2040
tgcgttgag ccactcctgt cccgccttc tcctccacag tgctgcttct cttgggaact 2100
ccactctct tcgtgtctct cccaccccg cctccactcc cccacctgac aatggcagct 2160
agactggagt gaggcttcca ggctcttct ggacctgagt cggccccaca tgggaacct 2220
gtactctctg ctctagccag gagtctgtgc tcttttggtg gggagcactt gcgtcctgca 2280
gaggaccaca gtgggtggca cctcctgaga aggcgaggag agtggttgtt gccactaag 2340

EX05-002patentin.txt

ccctcgaacc	aaggcagcct	ccagagccag	cctgggactc	ccagtgaact	tacacttgga	2400
gcccgtgcag	tacaggcaaa	acacgcaagg	gcatcaggca	ctggtggcat	cgtagaagag	2460
atgtggcaaa	gtgctgtacc	cttccacctc	ctagaggtgg	gcagctgggc	cccacctact	2520
tgtgactgaa	ggggcacacc	actgccctgc	ctgcccactt	agccgtccat	ggcaccagcc	2580
ccctggatgg	gcattgggct	gacacctacc	atgctgcttt	ttggcacagt	tgtctattct	2640
gagccttgag	agaaaaagtg	ccccttaagg	gttgaaggca	gtctgaaccc	ttgtgcttgg	2700
tggggctcgt	ggccttcccc	ttttgcctgg	ctgtggaggc	ctgatgctgc	cccgttccct	2760
gtcagaggct	aagatgagat	ttgccagcac	aggggccccca	gatctgcctg	ggcctgtgca	2820
gcagcccagc	ttcctgggtg	atttttcagg	tagggccctt	tcctgccagc	tgcttccctc	2880
atccccctcg	cctgtcccag	aggttatctg	cctggcctgg	ctccccacga	gtcacctgca	2940
agccccaggg	cctgggggca	gtgactggca	ggtgcagatg	ggctgtttcg	tgtagtggaa	3000
gagcagcctg	atggccaagg	gggtggacgc	aattgtggga	tgtcctcttt	actcccttcc	3060
tggcctcact	ggctggggca	gaggggcagc	cgctaggaga	gactgaaagc	agcagctagg	3120
actgaggagt	gggttttatt	gtccttcaga	gctcttcaag	ctgtcccctc	tgtcatcact	3180
ccctggatgt	gtggggcatg	gttccttccc	tgggaaggct	aagttcagtt	ctgtttttta	3240
ttctatgaga	acaagtcaca	gctgcagctg	ggccccatgc	tctgccccaa	gcccccaacc	3300
ccgcggtgct	ccggcggctt	cctgtccact	ctcggggccc	ttggggcctg	gcttgctcca	3360
gggtcttggg	ctactggcag	ctcctctcct	tgggctcctg	gctgccaggc	gttggtgcca	3420
cttcttaaag	gcctggaacc	agggaggaga	ggaaatgcta	ttgttggtgg	ctttctccgg	3480
ggtctgtgct	gtgcctgcta	gagcaacccc	tgtaccagc	tccttttgtc	cccaggggcc	3540
ctccctctgc	cccaagcagc	cagccagtct	tgccataggc	aaatgcacaa	gctcagaata	3600
gatctgatgg	tgagctggga	agctgtactc	agagcagagc	aaatgaggga	gggggcgctc	3660
aggaccaggg	ccctccatgg	gctagtgtga	gtggcagcca	tgccctatgc	cacaccttct	3720
tcgcaaactg	atggaccggg	tgggcctggc	ctgagctggg	gccacaaatc	aaagcaaggg	3780
ctccagtatc	cagcctgtgt	gttctgtaat	ggaactgacc	ccctcccctg	aaaacgaagg	3840
ggccccgggg	ctggcaagca	gggaaagctc	cacggtgcgc	ggctgtggca	cagacttctg	3900
gaaggctggc	tgagtggaat	gcagggaaga	gggcagtacc	tgggaaagga	cccaccatc	3960
ttcctgctgc	tgtaactgct	gagccactcg	cagtcgcagg	atccgctgcc	accacgtctg	4020
ccaggcccat	ctcaggtgcc	actccctgag	ctttggggac	agttggcaga	gaaggcctct	4080
tgtgctcacg	ctcccccgca	gtccccagcc	cttctgcctt	tctccccga	cactgctgca	4140
ccagagtgaa	agggctatgg	caaggggggtg	tcacttgagg	agtattaaga	atgcagattc	4200
ctgggcctgt	cccccaaggt	tttggagtca	gtaggtccaa	gggccatact	tttgagaggg	4260
gtttgggtta	agtatgaggt	gaaatgggag	atggtcagtg	tggagagggg	tgcaccact	4320
caccagggtc	cgcaccagct	gctctgcccc	ttgggcatcc	acccagtgtg	gccatgccac	4380

EX05-002patentin.txt

tgccaggcac	ctggcctgct	gggaacccccg	cagcccgtga	agcagtgccct	cgaggcaccg	4440
gcgctgcagg	tacttcctcc	tgatggccaa	gagcatcgtg	acccttcagg	gccagaagga	4500
gggcagagcc	atgggcctgg	gcctgctttt	ccaggatcct	gcaggaacga	gacttgacca	4560
gagagggccc	agctgtagcc	atggctcagg	caagcccctc	agcccttgcc	cccatccctc	4620
ggaccaccca	aactgcacac	acagctcctc	ttaccgtagc	ctccgtttat	gggccttgct	4680
ttgggctttg	gaggctctgg	gctcagggct	ggagtgcgct	cttgggtccct	ggccctcgt	4740
ccacaggggc	aggcctggga	cccagctact	ctgtccaggc	cactgtggcc	agagctggaa	4800
ggcagggcag	agggaaatgtt	ccctgcaccc	tggaaagggg	agttgagtca	caagagttta	4860
aggtgggtcc	aggaaggcag	ctgctcttag	tgcccgtta	ggagttgagt	acagtgagga	4920
gggtggagga	aggtgctgag	cttagccttg	tgccctgccc	ccatctcccc	aggcctccag	4980
cctctcacgg	ctgcctgccg	cccaaagaga	aatcacaggg	gcggggcagg	aatgcaaagt	5040
gttttctcag	aacagctgaa	acattccgaa	gagggaaatgg	atggggagaa	tggtcaatac	5100
acataagacc	gtgtcccaag	gagctgattt	ccaggcccct	gaggactgga	gaccgcttca	5160
cccctgcact	tcagacaccg	tttgtcccc	ggggcaagggt	ctccttactc	tgagcccagg	5220
ccgttcccc	tggcttcctc	cgccaccca	ggctgcactg	cagtgatggc	gcgggaggca	5280
ccagctctgt	ggcctgtgtc	cagcagctgt	gggtctgaag	gaatagccag	agaggagcac	5340
ctgaacccca	tgggcttgga	cttcctgggg	ccccgctggg	atttcttcgc	tgctctagct	5400
ggcaggacac	atcccggcct	cttcaccca	ttcccccatg	tggctgaaga	cattccaaca	5460
atgggggtggg	cccataatag	ttagccctca	gtcagttccc	ggagcacagc	cctgggaggg	5520
ggctattttct	ctccccactg	aaaacatttc	aaagctgagt	tacttgctcg	aggcctcatc	5580
cctcggaagc	cgtctgactc	cagagtctga	gccccgggt	agtaccctat	agagaggggg	5640
ctctccaaag	gggctgctgg	ggcatgtgtg	cctgtggcag	aaaagaggag	accctggaat	5700
tcagcaccct	gggtgccatt	cccagcgttt	agtttctaga	ggcctcagtt	tctccatcag	5760
cttatgggat	ccttgtcttt	actgacaaga	atggaataga	aatgtaaaag	tactctgaaa	5820
agcaattgcc	ctgtaactta	tctagaaaga	aaagaccctg	agactccaga	atctgctggt	5880
gccatagccc	catatgtgtg	aattctgcaa	ctagccaagg	ctagttcctt	tcaattccat	5940
ttaaaaaaca	aaaaccagca	ggtgtggtgg	ctcatggcgt	aatgggcctg	cccaatgctt	6000
tgggaggcca	aggcagatag	atcgcttgag	cccaggagtt	tgagacaagc	cctggcaaca	6060
tagtgagatc	ccatttctac	aaaaaaaaa	aaaaaaaaa			6099

<210> 37
 <211> 1350
 <212> DNA
 <213> Homo sapiens

<400> 37	
aggttaatct	taaaagccca
ggttaccgcg	ggaaatttat
gctgtccggt	caccgtgaca
	60
atgcagctga	ggaaccaga
actacatctg	ggctgcgcgc
ttgcgcttcg	cttcctggcc
	120

EX05-002patentin.txt

```

ctcgtttcct gggacatccc tggggctaga gcactggaca atggattggc aaggacgcct 180
accatgggct ggctgcactg ggagcgcttc atgtgcaacc ttgactgcca ggaagagcca 240
gattcctgca tcagtgagaa gctcttcatt gagatggcag agctcatggg ctgagaaggc 300
tggaaggatg caggttatga gtacctctgc attgatgact gttggatggc tccccaaaga 360
gattcagaag gcagacttca ggcagaccct cagcgctttc ctcattggat tcgccagcta 420
gctaattatg ttcacagcaa aggactgaag ctagggaatt atgcagatgt tggaaataaa 480
acctgcgcag gcttccttgg gagttttgga tactacgaca ttgatgcca gacctttgct 540
gactggggag tagatctgct aaaatttgat ggttggtact gtgacagttt ggaaaatttg 600
gcagatgggt ataagcacat gtccttggcc ctgaatagga ctggcagaag cattgtgtac 660
tcctgtgagt ggcctcttta tatgtggccc tttcaaaagc ccaattatac agaaatccga 720
cagtactgca atcactggcg aaattttgct gacattgatg attcctggaa aagtataaag 780
agtatcttgg actggacatc ttttaaccag gagagaattg ttgatgttgc tggaccaggg 840
ggttggaatg acccagatat gttagtattg ggcaactttg gcctcagctg gaatcagcaa 900
gtaactcaga tggccctctg ggctatcatg gctgctcctt tattcatgtc taatgacctc 960
cgacacatca gccctcaagc caaagctctc cttcaggata aggacgtaat tgccatcaat 1020
caggaccctt tgggcaagca agggtagcag cttagacagg gagacaactt tgaagtgtgg 1080
gaacgacctc tctcaggctt agcctgggct gtagctatga taaaccggca ggagattggg 1140
ggacctcgct cttataccat cgcagttgct tccctgggta aaggagtggc ctgtaatcct 1200
gcctgcttca tcacacagct cctccctgtg aaaaggaagc tagggttcta tgaatggact 1260
tcaaggtaa gaagtcacat aaatcccaca ggcactgttt tgcttcagct agaaaataca 1320
atgcagatgt cattaaaaga cttactttaa 1350

```

<210> 38
<211> 3598
<212> DNA
<213> Homo sapiens

```

<400> 38
cgcttcggta gcataagtgc ggtgggaggg ggctctgcgg ttttggggac ccagggcggg 60
aaccggacc cggctggaag tccggagcct gccgcagccc cggccctccg ctctttcttg 120
gtgaccttaa gccagtggct gcctttttct gagcccgggc ggggcccgaag gcgcccgtag 180
gccctcggga ctcccagcac tgcagagggg gtgaggtctg acatccaaga cacgttgttt 240
cgtatttctg aaggaagaac tcaagctccg ggaagtgatg gctggggatg gggcgggcaa 300
cttggggacc gagtgtacga tccacgccta aggttgaggg cggccgagct agccaggcag 360
ccgtgacccc agtgcttttc agacgtttct tagcttccag agcccaacac atacagctga 420
tacacgcaga ccagatctgg tcaggctcctc ggaagctgag tccagagcga tgctgctgaa 480
gacagtgtct ttgctgggac atgtggccca ggtgctgatg ctggacaatg ggctcctgca 540

```

EX05-002patentin.txt

gacaccaccc atgggctggc tggcctggga acgcttccgc tgcaacatta actgtgatga	600
ggacccaaag aactgcataa gtgaacagct cttcatggag atggctgacc ggatggcaca	660
ggatggatgg cgggacatgg gctacacata cctaaacatt gatgactgct ggatcggcgg	720
tcgcgatgcc agtggccgcc tgatgccaga tccaagcgc tccctcatg gcattccttt	780
cctggctgac tacgttcact ccctgggcct gaagtgggt atctacgcgg acatgggcaa	840
cttcacctgc atgggttacc caggcaccac actggacaag gtggtccagg atgctcagac	900
cttcgccgag tggaaggtag acatgctcaa gctggatggc tgcttctcca ccccgagga	960
gcgggcccag gggtaaccca agatggctgc tgccctgaat gccacaggcc gcccacgc	1020
cttctcctgc agctggccag cctatgaagg cggcctcccc ccaagggtga actacagtct	1080
gctggcggac atctgcaacc tctggcgtaa ctatgatgac atccaggact cctggtggag	1140
cgtgctctcc atcctgaatt gggtcgtgga gcaccaggac atactgcagc cagtggccgg	1200
ccctgggcac tggaatgacc ctgacatgct gctcattggg aactttggtc tcagcttaga	1260
gcaatcccgg gccagatgg ccctgtggac ggtgctggca gccccctct tgatgtccac	1320
agacctgct accatctccg ccagaacat ggacattctg cagaatccac tcatgatcaa	1380
aatcaaccag gatcccttag gcacccagg acgcaggatt cacaaggaaa aatctctcat	1440
cgaagtgtac atgcggcctc tgtccaacaa ggctagcgc ttagtcttct tcagctgcag	1500
gaccgatatg cttatcgct accactcctc ccttgccag ctgaacttca ccgggtctgt	1560
gatatatgag gcccaggacg tctactcagg tgacatcatc agtggcctcc gagatgaaac	1620
caacttcaca gtgatcatca acccttcagg ggtagtgatg tggtagctgt atcccatcaa	1680
gaacctggag atgtcccagc agtgaggagc tgggacatgt gacaggctgt ggtggcacca	1740
ctgagcctag accatggagc cttggcatgc ccagggcaag tggggagggt ctctgctccc	1800
caggcctgct cggtgactga ccccatcata cccaaagtgc aatctcacgg ccaggttcta	1860
tgccctgtcc aagcgtaaac cctcttgga acttcttttg gggcaatttt cctgtggcct	1920
tcctggcctc tacttccatg tgcgcagccc cacagacgtt gctgagcaac tcgccagcct	1980
cctgagctcc atgcccatca ggactctagc ctctgacctt gctgttgact ctgaaatcag	2040
gatttggaag ttttcgaatt aggagtagag agatctgacc tcttgccagg aatgcccatg	2100
gatcatgtga ttggcttttc taccataga gggccttgca gcctgatacc actgggagtg	2160
agggtcacia aggagacctt ggctccctca ggtcaccaat aaacctgttc tttaatcaag	2220
tagttgtaat atggacctgg ggtaccttta gttagggact ctggtggcac tacacggggt	2280
gctggattca aatctcacct ctatggatga tgtctggcat cgtctggccc ctcttttcc	2340
aaagtgacca gaagattgta cttcctagag atgccagact tgccctcacac ccaggagctg	2400
cccctgctgt gcctgggatg ctggcagtgg tgatggtgac aacacaatga ggccaagtag	2460
caatgctccc aggtcctgca gcttgctgc tgcccagcag tcccctggcc agcacctcag	2520
cctgctcttc tctctgggtg ctccacccca accctactt cttttccttt atttctctcc	2580

EX05-002patentin.txt

caacctggct gcaaaggagg ttcatatccc	cagatgtgtc cacaaacctg tccaggagtt	2640
gtgtcttaaa attgatttcc tgtccctctt	cctaaggaca ggggtaacag tcaaagtga	2700
ggaatgatgg gttcttgcct gtcttgcttt	gggtccgtatt tcccaagccc tcctctttta	2760
gccaaggcta cagggcactt gtcttccctg	gtggctctcc cctttggaga gagctagtgg	2820
cagagaacct agctagggtc ccttgggctt	tgaatgcagg agcaccaggt gccccaggcc	2880
ttgcaactgt ctgccaagg agtatcttct	gggtggatct ccatactcc tcagggttct	2940
gaggtccttg tatttagggg atggtgtaaa	aacttacata tgcacatttt gttacatcat	3000
ttaagatgat tgaagcttta ctgggtaagt	acagggtcac cagagaaagt tcctttcccc	3060
agttgatgtc ttgaggctgt tgagaaactt	aggacagaag cctacctcat ccaggcctg	3120
cccctccgtg catagctctg cctttgggtc	ttgttcatag tgctgttcag gcaaaatgga	3180
atagtctcag gagggaacac cttctcttgc	tagctccagg aaggctttgt gggaaatgag	3240
ttgagaccat ggacttggga gttgggggcc	agagttgagc ctggacttga ccaattaatt	3300
cccttacctt tcagcccaag atagctacat	gtctttactt gctgtataag ttttcctttt	3360
gtcctggggg tgcttgattg atcctatctc	ttcacccttc attctttcaa caaacatgcc	3420
atctatctcc caggacattt attcccttct	attcaaggcc agttaggaat gcaattattt	3480
tttttttcag ttaaatacag acttgtttgg	acgcaaggta ccctttctct ttttaaaaac	3540
tttttatcat gaaaactttc aaatacaaaa	ataaaatggt agagagtga cctccatg	3598

<210> 39
 <211> 4576
 <212> DNA
 <213> Homo sapiens

<400> 39		
gaattccggg cggcggcggc caaactccgc	ggcgtcccca gggcgccacg ttcgcctcg	60
ccgccgcggc cgcgctgctc ttcggctccg	acatggaaga tggaccttct aataatgcga	120
gctgcttccg aaggctgacc gagtgttcc	tgagccccaag agctaattgt atagatatag	180
aagtcatcca cagagatgtt acagttgaag	agatgggggt agagaagact ttgaaggaaa	240
agaatgtaga atgaggatag aagagaggaa	atcccaacat ttaacagggt tgacagatga	300
aaaagtgaag gcatatcttt ctcttcccc	ccagggtatta gatgaatttg tatctgaaag	360
tgtagtgca gagacagtag agaaatggct	gaagagggaag aacaacaaat cagaagatga	420
atcagctcct aaggaagtca gcaggtagc	agatacgaat atgcaggag ttgtatatga	480
actaaacagc tatatagaac aacggttgg	cacaggagga gacaaccagc tactcctcta	540
tgaactgagc agcatcatta aaatagccac	aaaagccgat ggatttgcac tgtatttctt	600
tggagagtgc aataatagcc tgtgtatatt	cacgccacct gggataaagg aaggaaaacc	660
ccgcctcatc cctgctgggc ccatcactca	gggcaccacc gtctctgctt atgtggccaa	720
gtccaggaaa aactgctag tagaagacat	ccttggagat gaacgatttc caagaggtac	780
tggactggaa tcagggactc gtatccagtc	tggtctttgc ttaccaattg tcaactgcaat	840

EX05-002patentin.txt

tggtgacttg attggtattc tcgagctgta tcggcactgg ggcaaagaag ctttctgtct 900
tagtcaccag gaggttgcaa cagcaaattc tgcctgggct tcagtagcaa tacatcaggt 960
gcaggtatgc agaggccttg ccaaacagac agaattgaat gacttcctac tcgacgtatc 1020
aaaaacatat ttgataaca tagttgcaat agattctcta cttgaacaca taatgatata 1080
tgcaaaaaac ctggtgaatg ccgatcgttg tgcgcttttc caggtggacc ataagaacaa 1140
ggagttatat tcagaccttt ttgatattgg agaggaaaag gaaggaaaac ctgtcttcaa 1200
gaagaccaa gagataagat tttcaattga gaaaggaatt gctggccaag tagcaagaac 1260
aggggaagtc ctgaacattc cagatgccta tgcagacca cgctttaaca gagaagtaga 1320
cttgtagaca ggctacacca cgcggaacat cctgtgcatg cccatcgtca gccgaggcag 1380
cgtgataggt gtggtgcaga tggtaacaa aatcagtggc agtgccttct ctaaacaga 1440
tgaaaacaac ttcaaatgt ttgccgtctt ttgtgcttta gccttacact gtgctaatat 1500
gtatcataga attcgccact cagagtgcatt ttaccgggta acgatggaaa agctgtccta 1560
ccatagcatt tgtacttcag aagagtggca aggtctcatg caattcacc ttcccgtgcg 1620
tctctgcaa gaaattgaat tattccactt tgacattggt ccttttgaaa acatgtggcc 1680
tggaatTTTT gtctacatgg ttcatcggtc ctgtgggaca tcctgctttg agcttgaaaa 1740
gttgtgtcgt ttattatgt ctgtgaagaa gaactatcgg cgggttcctt atcacactg 1800
gaagcatgcg gtcactgtag cacactgcat gtatgccata cttcagaaca atcacacgt 1860
tttcacagac cttgagcgca aaggactgct gattgcgtgt ctgtgtcatg acctggacca 1920
caggggcttc agtaacagct acctgcagaa gttcgaccac cctctggccg ctctctactc 1980
cacttcacc atggagcagc accacttctc ccagactgtg tccatccttc agttggaagg 2040
gcacaatatc ttctccactc tgagctccag tgaatatgag caggtgcttg agatcatccg 2100
caaagccatc attgccacag accttgcttt atactttgga aacaggaagc agttggaaga 2160
gatgtaccag accggatcac taaaccttaa taatcaatca catagagacc gtgtaattgg 2220
tttgatgatg actgcctgtg acctttgttc tgtgacaaaa ctgtggcccg ttacaaaatt 2280
gacggcaaat gatatatatg cagaattctg ggctgagggt gatgaaatga agaaattggg 2340
aatacagcct attcctatga tggacagaga caagaaggat gaagtcccc aaggccagct 2400
tggtttctac aatgccgtgg ccattccctg ctatacaacc cttaccaga tcctccctcc 2460
cacggagcct cttctgaaag catgcaggga taatctcagt cagtgggaga aggtgattcg 2520
aggggaggag actgcaacct ggatttcac cccatccgtg gctcagaagg cagctgcac 2580
tgaagattga gactggtca ccctgacacg ctgtcccacc tacagatcct catcttgctt 2640
ctttgacatt cttttccttt ttttgggggg ggtgggggga acctgcacct ggtaactggg 2700
gtgcaaacct cttcaagaag gtaacatcaa ataaataagt caagcagagg acttcctgcc 2760
aatctcttct gtgaggcatc atagacactg agcaaccagg accaccccca cgttcagaaa 2820
tcagctggcc aagtgactcc atttgacttg caaaccagcc ttttctaata ggctaattatt 2880

EX05-002patentin.txt

gctgaggcct taaaggaaat ggacaaaaat tatccagaag gggacttttt ccattgtatc 2940
 tttctaataa gggtttaaaa tgggtactatt atgggtattgt acttgggctt taacatcaat 3000
 gttgctttga tgttggttga tataaatagg aattttacac attactattg tgaatggtga 3060
 atgttcatgt atgacctact tgtaattaac ttgagttgta gtccacagcc tcaggacaaa 3120
 tgtcgttgag gttacagagt aagaaatgat ggcaaacgt caaactctta tttcagagct 3180
 tcatgaatth agttagacta aacataattc ttttaagttca acctaaaggg ctgagatcaa 3240
 taaatttaac actagacgaa gtagacttcc tgtctttttg agaagagatg aggtatatgt 3300
 tacaataaat ctccagaactt caagtagcag ttcaaaagat gtcagttttt aaaattgttt 3360
 ttgttggtgt cttggcagtt ttactgaacc ctttgcataa agaacaaaat aaaagctcgg 3420
 cattgtaatt tttttaatgg acaagtctta tggatacgag gggtagattt ttcataatga 3480
 ttcctttata ttttcacttt gtgtcatatg cagaatttta gactctcatt cacaatgaaa 3540
 agtttattht aaacattggt taattaaaat accatacagt tctcttttaa acatcaaacc 3600
 ataaaaagtg tattttgtaa ttttactctg acctgccgca gtcacctctc acttatctct 3660
 tccacgtact gcacggctgt atttcatgag ctttctgtcc atagcacaga aacagagcag 3720
 aaagtagtac aatcatgttg gaccttcttt ctgttctctt tactcttctc acagatcaga 3780
 tctactcata gaagcctgtg ggtttcgatg gtttcttcta tacacctttt tggttgacca 3840
 gtattactat acaatgtaag tgttttaaaa aatacgaaag taatactctg cacccttcc 3900
 tacaagatg ataaagcagt cacttctggc gcattttaat aatttaaaga ttttagtg 3960
 aatggcacgg taacctcaa acctgaatta gacagagact cactcaggaa gtgacaggcc 4020
 catcatatca aataacttat tctcttttca tgtggcagga aactggaata tcgcttttaa 4080
 taaaatggaa aaatatgctt ctacatattt accaccatag gcgttttggt catatgagcc 4140
 tggtttggtg aaaattaaat cagaggcttc tacaacatgg tttatttatg ttgtagcaaa 4200
 gttggctcta cataaacatt gttcttattt taaaattaac actatgtgtt cagttttctt 4260
 gtgggcttct gaaagttgcc atcttccctc cgtggagctc catttgctat tttcattata 4320
 cactatgagg taaaatgtaa taacaaaaga gagagaagta ccactgtggc tagatatata 4380
 cacacacata tatatatgga tggatgtaat atatgtagca cacacacata gatgtatata 4440
 ggatacacac tcatgtatgt aaacgtatac atatgtgtat atatgataca tacacataca 4500
 cacacacgag agacagaagg aaagagagga agagagaagc aaacatgtag gaaaaaatat 4560
 aatcagccg gaattc 4576

<210> 40
 <211> 4240
 <212> DNA
 <213> Homo sapiens

<400> 40
 cagcagagct ggattggggg gttgagtcca ggctgagtag ggggcagccc actgctcttg 60

EX05-002patentin.txt

gtccctgtgc	ctgctggggg	tgccctgccc	tgaactccag	gcagcgggga	cagggcgagg	120
tgccacctta	gtctggctgg	ggaggcggac	gatgaggagt	gatggggcag	gcatgcggcc	180
actccatcct	ctgcaggagc	cagcagtacc	cggcagcgcg	accggctgag	ccgcggggcc	240
agcaggctct	cctcaagccg	gacgagccgc	cgccgccgcc	gcagccatgc	gccgacagcc	300
tgcaggacgc	cttgctgagt	ctgggctctg	tcctcgacat	ttcaggcctg	caacgtgctg	360
tcaaggaggc	cctgtcagct	gtgctcccc	gagtggaaac	tgtctacacc	tacctactgg	420
atggtgagtc	ccagctggtg	tgtgaggacc	ccccacatga	gctgccccag	gaggggaaag	480
tccgggaggc	tatcatctcc	cagaagcggc	tgggctgcaa	tgggctgggc	ttctcagacc	540
tgccagggaa	gcccttggcc	aggctggtgg	ctccactggc	tcctgatacc	caagtgtctg	600
tcctgcccgt	agcggacaag	gaggctgggg	ccgtggcagc	tgtcatcttg	gtgactgtg	660
gccagctgag	tgataatgag	gaatggagcc	tgcaggcggg	ggagaagcat	accctggtcg	720
ccctgcggag	ggtgcaggtc	ctgcagcagc	gcggggccag	ggaggctccc	cgagccgtcc	780
agaaccccc	ggaggggacg	gcggaagacc	agaagggcgg	ggcggcgtag	accgaccgcg	840
accgcaagat	cctccaactg	tgcggggaac	tctacgacct	ggatgcctct	tccctgcagc	900
tcaaagtgtc	ccaatacctg	cagcaggaga	cccgggcata	ccgctgtctg	ctcctgtctg	960
tgtcggagga	caatctccag	ctttcttgca	aggtcatcgg	agacaaagtg	ctcggggaag	1020
aggtcagctt	tcccttgaca	ggatgcctgg	gccagggtgg	ggaagacaag	aagtccatcc	1080
agctgaagga	cctcacctcc	gaggatgtac	aacagctgca	gagcatgttg	ggctgtgagc	1140
tgcaggccat	gctctgtgtc	cctgtcatca	gccggggcac	tgaccagggt	gtggccttgg	1200
cctgcgcctt	caacaagcta	gaaggagact	tgttcaccga	cgaggacgag	catgtgatcc	1260
agcactgctt	ccactacacc	agcaccgtgc	tcaccagcac	cctggccttc	cagaaggaac	1320
agaaactcaa	gtgtgagtgc	caggctcttc	tccaagtggc	aaagaacctc	ttcaccacc	1380
tggatgacgt	ctctgtcctg	ctccaggaga	tcatacggga	ggccagaaac	ctcagcaacg	1440
cagagatctg	ctctgtgttc	ctgctggatc	agaatgagct	ggtggccaag	gtgttcgacg	1500
ggggcgtggt	ggatgatgag	agctatgaga	tccgcatccc	ggccgatcag	ggcatcgagg	1560
gacacgtggc	gaccacgggc	cagatcctga	acatccctga	cgcataatgcc	catccgcttt	1620
tctaccgcgg	cgtggacgac	agcaccggct	tccgcacgcg	caacatcctc	tgcttcccca	1680
tcaagaacga	gaaccaggag	gtcatcggtg	tggccgagct	ggtgaacaag	atcaatgggc	1740
catggttcag	caagtgcgac	gaggacctgg	cgacggcctt	ctccatctac	tgcggcataca	1800
gcatcgccca	ttctctccta	tacaaaaaag	tgaatgaggc	tcagtatcgc	agccacctgg	1860
ccaatgagat	gatgatgtac	cacatgaagg	tctccgacga	tgagtatacc	aaacttctcc	1920
atgatgggat	ccagcctgtg	gctgccattg	actccaattt	tgcaagtttc	acctataccc	1980
ctcgttcctt	gcccagggat	gacacgtcca	tggccatcct	gagcatgctg	caggacatga	2040
atttcatcaa	caactacaaa	attgactgcc	cgaccctggc	ccggttctgt	ttgatggtga	2100

EX05-002patentin.txt

agaagggcta	ccgggatccc	ccctaccaca	actggatgca	cgccttttct	gtctcccact	2160
tctgctacct	gctctacaag	aacctggagc	tcaccaacta	cctcgaggac	atcgagatct	2220
ttgccttggt	tatttcctgc	atgtgtcatg	acctggacca	cagaggcaca	aacaactctt	2280
tccaggtggc	ctcgaaatct	gtgctggctg	cgctctacag	ctctgagggc	tccgtcatgg	2340
agaggcacca	ctttgctcag	gccatcgcca	tcctcaacac	ccacggctgc	aacatctttg	2400
atcattttct	ccggaaggac	tatcagcgca	tgctggatct	gatgcggggc	atcatcttgg	2460
ccacagacct	ggcccaccat	ctccgcatct	tcaaggacct	ccagaagatg	gctgaggtgg	2520
gctacgaccg	aaacaacaag	cagcaccaca	gactttctct	ctgcctctc	atgacctcct	2580
gtgacctctc	tgaccagacc	aagggtctga	agactacgag	aaagatcgcg	gagctgatct	2640
acaaagaatt	cttctcccag	ggagacctgg	agaaggccat	gggcaacagg	ccgatggaga	2700
tgatggaccg	ggagaaggcc	tatatccctg	agctgcaaat	cagcttcatg	gagcacattg	2760
caatgccccat	ctacaagctg	ttgcaggacc	tgttcccca	agcggcagag	ctgtacgagc	2820
gcgtggcctc	caaccgtgag	cactggacca	aggtgtccca	caagttcacc	atccgcggcc	2880
tcccaagtaa	caactcgctg	gacttcctgg	atgaggagta	cgaggtgcct	gatctggatg	2940
gcactagggc	ccccatcaat	ggctgctgca	gccttgatgc	tgagtgatcc	cctccaggac	3000
acttccctgc	ccaggccacc	tcccacagcc	ctccactggt	ctggccagat	gcactgggaa	3060
cagagccacg	ggctctgggt	cctagaccag	gacttcctgt	gtgaccctgg	acaagtacta	3120
ccttcctggg	cctcagcttt	ctcgtctgta	taatggaagc	aagacttcca	acctcacgga	3180
gactttgtaa	tttgcttctc	tgagagcaca	ggggtgacca	atgagcagtg	ggccctactc	3240
tgcacctctg	accacacctt	ggcaagtctt	tccaagcca	ttctttgtct	gagcagcttg	3300
atggttttct	cttgccccat	ttctgcccc	ccagatcttt	gctcctttcc	ctttgaggac	3360
tcccaccctt	tgggtctcca	ggatcctcat	ggaaggggaa	ggtgagacat	ctgagtgagc	3420
agagtgtggc	atcttgga	cagtccttag	ttctgtggga	ggactagaaa	cagccgcggc	3480
gaaggccccc	tgaggaccac	tactatactg	atggtgggat	tgggacctgg	gggatacagg	3540
ggccccagga	agaagctggc	cagaggggca	gctcagtgtc	ctgcagagag	gggccctggg	3600
gagaagcagg	atgggattga	tgggcaggag	ggatccccgc	actgggagac	aggcccaggt	3660
atgaatgagc	cagccatgct	tcctcctgcc	tgtgtgacgc	tgggcgagtc	tcttcccctg	3720
tctggggcaa	acagggagcg	ggtaagacaa	tccatgctct	aagatccatt	ttagatcaat	3780
gtctaaaata	gctctatggc	tctgcggagt	cccagcagag	gctatggaat	gtttctgcaa	3840
ccctaaggca	cagagagcca	accctgagtg	tctcagaggc	cccctgagtg	ttccccttgg	3900
cctgagcccc	ttaccatttc	ctgcagccag	tgagagacct	ggcctcagcc	tggcagcgct	3960
ctcttcaagg	ccatatccac	ctgtgccctg	gggcttggga	gaccccatag	gccgggactc	4020
ttgggtcagc	ccgccactgg	cttctctctt	tttctccgtt	tcattctgtg	tgcgttgtgg	4080
ggtgggggag	gggggtccacc	tgccttacct	ttctgagttg	ccttttagaga	gatgcgtttt	4140

EX05-002patentin.txt

tctaggactc tgtgcaactg tcgtatatgg tcccgtgggc tgaccgcttt gtacatgaga 4200
 ataaatctat ttctttctac caaaaaaaaa aaaaaaaaaa 4240

<210> 41
 <211> 3106
 <212> DNA
 <213> Homo sapiens

<400> 41
 gcggccgcgc tccggccgct ttgtcgaaag ccggcccgac tggagcagga cgaaggggga 60
 gggctctcgag gccgagtcct gttcttctga gggacggacc ccagctgggg tggaaaagca 120
 gtaccagaga gcctccgagg cgcgcggtgc caaccatgga gcgggcccgc cccagcttcg 180
 ggcagcagcg acagcagcag cagccccagc agcagaagca gcagcagagg gatcaggact 240
 cggtcgaagc atggctggac gatcactggg actttacctt ctcatacttt gttagaaaag 300
 ccaccagaga aatggtcaat gcatggtttg ctgagagagt tcacaccatc cctgtgtgca 360
 aggaaggatc cagaggccac accgaatctt gctcttgtcc cttgcagcag agtcctcgtg 420
 cagataacag tgtccctgga acaccaacca ggaaaatctc tgcctctgaa tttgaccggc 480
 ctcttagacc cattgttggtc aaggattctg agggaaactgt gagcttcctc tctgactcag 540
 aaaagaagga acagatgcct ctaaccctc caaggtttga tcatgatgaa ggggaccagt 600
 gctcaagact cttggaatta gtgaaggata tttctagtca tttggatgtc acagccttat 660
 gtcacaaaat tttcttgcat atccatggac tgatatctgc tgaccgctat tccctgttcc 720
 ttgtctgtga agacagctcc aatgacaagt ttcttatcag ccgcctcttt gatgttgctg 780
 aaggttcaac actggaagaa gtttcaaata actgtatccg cttagaatgg aacaaaggca 840
 ttgtgggaca tgtggcagcg cttggtgagc cttgaaatc caaagatgca tatgaggatc 900
 ctcggttcaa tgcagaagtt gaccaaatta caggctacaa gacacaaagc attctttgta 960
 tgccaattaa gaatcatagg gaagagggtt ttggtgtagc ccaggccatc aacaagaaat 1020
 caggaaacgg tgggacattt actgaaaaag atgaaaagga ctttgctgct tatttggtat 1080
 tttgtggtat tgttcttcat aatgctcagc tctatgagac ttcactgctg gagaacaaga 1140
 gaaatcaggt gctgcttgac cttgctagtt taatttttga agaacaaca tcattagaag 1200
 taattttgaa gaaaatagct gccactatta tctctttcat gcaagtgcag aaatgcacca 1260
 tttcatagt ggatgaagat tgctccgatt ctttttctag tgtgtttcac atggagtgtg 1320
 aggaattaga aaaatcatct gatacattaa caagggaaca tgatgcaaac aaaatcaatt 1380
 acatgtatgc tcagtatgtc aaaaatacta tggaaccact taatatcca gatgtcagta 1440
 aggataaaag atttccctgg acaactgaaa atacaggaaa tgtaaaccag cagtgcatta 1500
 gaagtttgct ttgtacacct ataaaaatg gaaagaagaa taaagttata ggggtttgcc 1560
 aacttgtaa taagatggag gagaatactg gcaagggtta gcctttcaac cgaaatgacg 1620
 aacagtttct ggaagctttt gtcattttt gtggcttggg gatccagaac acgcagatgt 1680
 atgaagcagt ggagagagcc atggccaagc aaatgggtcac attggagggt ctgtcgtatc 1740

EX05-002patentin.txt

atgcttcagc agcagaggaa gaaacaagag agctacagtc gttagcggct gctgtggtgc	1800
catctgcca gacctttaa attactgact ttagcttcag tgactttgag ctgtctgac	1860
tggaacagc actgtgtaca attcggatgt ttactgacct caaccttggt cagaacttcc	1920
agatgaaaca tgaggttctt tgcagatgga ttttaagtgt taagaagaat tatcggaaga	1980
atgttgcccta tcataattgg agacatgcct ttaatacagc tcagtgcagtg tttgctgctc	2040
taaaagcagg caaaattcag aacaagctga ctgacctgga gatacttgca ttgctgattg	2100
ctgcactaag ccacgatttg gatcaccgtg gtgtgaataa ctcttacata cagcgaagtg	2160
aacatccact tgcccagctt tactgccatt caatcatgga acaccatcat tttgaccagt	2220
gcctgatgat tcttaatagt ccaggcaatc agattctcag tggcctctcc attgaagaat	2280
ataagaccac gttgaaaata atcaagcaag ctatcttagc tacagaccta gactgtaca	2340
ttaagaggcg aggagaattt tttgaactta taagaaaaaa tcaattcaat ttggaagatc	2400
ctcatcaaaa ggagttgttt ttggcaatgc tgatgacagc ttgtgatctt tctgcaatta	2460
caaaaccctg gcctattcaa caacggatag cagaacttgt agcaactgaa ttttttgatc	2520
aaggagacag agagagaaaa gaactcaaca tagaaccac tgatctaata aacagggaga	2580
agaaaaacaa aatcccaagt atgcaagttg ggttcataga tgccatctgc ttgcaactgt	2640
atgaggccct gaccacgtg tcagaggact gtttcccttt gctagatggc tgcagaaaga	2700
acaggcagaa atggcaggcc cttgcagaac agcaggagaa gatgctgatt aatggggaaa	2760
gcgccaggc caagcggaac tgagtggcct atttcatgca gagttgaagt ttacagagat	2820
ggtgtgttct gcaatatgcc tagtttctta cacactgtct gtatagtgtc tgtatttggt	2880
atatactttg cactgctgt atttttattt ttgcacaact tttgagagta tagcatgaat	2940
gttttagag gactattaca tattttttgt atatttggtt tatgctactg aactgaaagg	3000
atcaacaaca tccactgtta gcacattgat aaaagcattg tttgtgatat ttcgtgtact	3060
gcaaagtgtg tgacgtattc ttgcactgag gtttttttgc ttgggg	3106

<210> 42
 <211> 2944
 <212> DNA
 <213> Homo sapiens

<400> 42	
agtatgtttt gcagacaaga cccagagaag tccagactgg acttggtgca gactgcaaaa	60
ctgccattgg aaggcctccg tcccagtcct tctacagagt agccagtggg actcccagcc	120
atgggcgagg tgacagcaga ggagggtggag aagttcctgg actcgaatat tggctttgcc	180
aaacagtact acaacctcca ctaccggggc aagctcatct ccgacctcct tggggccaag	240
gaggctgccg tggacttcag caactaccac tccccagca gcatggagga gagcgaaatc	300
atctttgatc tcctgcggga ctttcaggag aatttacaga cagagaaatg catcttcaat	360
gtcatgaaga agctgtgctt cctcctgcag gcagaccgca tgagcctgtt catgtaccgg	420

EX05-002patentin.txt

acccgcaatg gcatcgcaga gctggccacc aggccttttca atgtccacaa ggatgctgtc	480
ctcgaggact gcctggtgat gcccagacaa gagatcgtct tccctttgga catgggcatc	540
gtgggccatg tcgcacactc taagaagatt gctaacgtcc ccaacacaga ggaggatgag	600
catttctgtg actttgtgga catcctcaca gagtacaaga ccaagaacat cttggcttcc	660
cccataatga atgggaagga tgtggtggcc ataatcatgg ctgtgaataa agtggatgga	720
tcccacttca ccaagagaga tgaagagatt cttctcaagt acctcaattt tgcaaactta	780
atcatgaagt ggtaccacct gagttacctg cacaactgtg aaactcgacg tggccagata	840
ctgctgtggt ctgggagcaa agtctttgaa gaacttacgg acatcgaacg acagttccac	900
aaagccctgt acacagtccg tgctttcctc aactgtgaca gatactctgt gggctcttta	960
gacatgacca agcagaagga attttttgat gtgtggccgg ttctgatggg tgaagttcca	1020
ccttactctg gtcccaggac tccggatgga agagaaatta acttttaca ggtcattgac	1080
tacatcctgc atggcaaaga ggacatcaaa gtcatccga atccacctcc tgaccattgg	1140
gctttagtaa gcggtctccc cgcttatgtt gcccagaatg gcctgatttg caacatcatg	1200
aacgcgcctg cggaggactt ttttgcattt cagaaagaac ctctggatga gtctggatgg	1260
atgattaaaa atgtgctttc aatgccgatt gtgaacaaga aggaagaaat tgttggagt	1320
gccacatttt acaatcgtaa agatgggaag ccttttgatg aaatggatga gacgctcatg	1380
gagtctttga ctcaatttct gggctggtct gtcttaaata ctgacaccta tgagtcaatg	1440
aataaacttg aaaataggaa ggatattttc caggacatag taaaatatca tgtgaagtgt	1500
gacaatgaag aaattcagaa aatcttgaaa accagagagg tgtatgggaa ggagccatgg	1560
gagtgtgagg aagaggagct ggctgagatc ctgcaagcgg agctgccaga tgcagataaa	1620
tacgaaatta ataaatttca cttcagtgc ttaccctaa cagaactgga gctggtaaaa	1680
tgtggaatac agatgtatta tgagctcaaa gtggtggata aatttcacat tccacaagag	1740
gccctggtgc ggttcatgta ctccctgagt aagggctacc gcaagatcac ctaccacaac	1800
tggcggcacg gcttcaacgt ggggcagacc atgttctccc tgctggtgac gggaaagctg	1860
aagcgctact tcacggacct agaggccttg gccatggtca ctgctgcttt ctgccatgac	1920
attgaccaca gaggaccaa taacctctac cagatgaaat cccagaaccc actggccaag	1980
ctccatgggt cctctatctt ggaaagacac cacttggagt ttggcaaac actgctcaga	2040
gacgagagcc tgaatatctt tcaaaacctc aatcgtcgac agcatgagca tgccatccac	2100
atgatggaca ttgcaatcat tgccacagac ctcgccctgt atttcaagaa gaggacgatg	2160
ttccaaaaga tcgtggatca gtctaagaca tatgagagtg aacaggagtg gacacagtac	2220
atgatgctgg agcagacacg gaaggaaatc gttatggcca tgatgatgac cgcctgtgat	2280
ctctcagcca tcaccaaacc ctgggaggtg cagagccagg tagctctgct ggtggctgct	2340
gaattctggg aacaaggatga cctggagcgc acggtgctgc aacagaatcc cattcccatg	2400
atggacagaa acaaagcaga tgaactccct aagcttcaag tcggcttcat tgactttgtt	2460

EX05-002patentin.txt

tgcaccttcg	tctacaagga	attctcccgt	ttccacgagg	agatcacccc	aatgttggac	2520
gggatcacca	acaatcgcaa	ggagtggaag	gcgcttgctg	atgagtacga	tgccaagatg	2580
aaggtgcagg	aggagaagaa	gcagaaacag	cagtcggcca	agtcagcagc	cgcaggaaat	2640
cagccggggg	gaaacccag	cccagggggg	gcaactacat	ccaagtcctg	ctgcatccag	2700
taacaccact	ggggatgtgc	tggctggacg	gcaccaccct	ttcctgggaa	gagatgactc	2760
aagccagtgg	aagaccacac	accttgagaa	gtagaagagt	cataggattt	gaaagctgtt	2820
agagaattta	gcttccagga	ctgttcaatc	ttttggcttc	cctggggcac	attggaagaa	2880
ttgtcttggg	tcacacataa	aatacagtaa	cactaatgat	agctgttgaa	cttaaaaaaa	2940
aaaa						2944

<210> 43
 <211> 3231
 <212> DNA
 <213> Homo sapiens

<400> 43						
ctccagggac	aggcagccac	catgagcctc	agtgaggagc	aggcccggag	ctttctggac	60
cagaacccccg	attttgccccg	ccagtacttt	gggaagaaac	tgagccctga	gaatgttggc	120
cgcggtgcg	aggacgggtg	cccgccggac	tgcgacagcc	tccgggacct	ctgccagggtg	180
gaggagagca	cggcgctgct	ggagctggtg	caggatatgc	aggagagcat	caacatggag	240
cgcgtggtct	tcaaggtcct	gcggcgccctc	tgaccctcc	tgaggccga	ccgctgcagc	300
ctcttcatgt	accgccagcg	caacggcgctg	gccgagctgg	ccaccaggct	tttcagcgtg	360
cagccggaca	gcgtcctgga	ggactgcctg	gtgccccccg	actccgagat	cgtcttccca	420
ctggacatcg	gggtcgtggg	ccacgtggct	cagacaaaa	agatggtgaa	cgtcgaggac	480
gtggccgagt	gccctcactt	cagctcattt	gctgacgagc	tcactgacta	caagacaaag	540
aatatgctgg	ccacacccat	catgaatggc	aaagacgtcg	tggcggtgat	catggcagtg	600
aacaagctca	acggccccatt	cttcaccagc	gaagacgaag	atgtgttctt	gaagtacctg	660
aattttgcca	cgttgtagct	gaagatctat	cacctgagct	acctccacaa	ctgcgagacg	720
cgccgcggcc	aggtgctgct	gtggtcggcc	aacaaggtgt	ttgaggagct	gacggacatc	780
gagaggcagt	tccacaaggc	cttctacacg	gtgcgggcct	acctcaactg	cgagcggtag	840
tccgtgggcc	tcctggacat	gaccaaggag	aaggaatttt	ttgacgtgtg	gtctgtgctg	900
atgggagagt	cccagccgta	ctcggggcca	cgcacgcctg	atggccggga	aattgtcttc	960
tacaaagtga	tcgactacat	cctccacggc	aaggaggaga	tcaaggatcat	tcccacaccc	1020
tcagccgatc	actgggccct	ggccagcggc	cttccaagct	acgtggcaga	aagcggcttt	1080
atttgtaaca	tcataaatgc	ttccgctgac	gaaatgttca	aatttcagga	aggggacctg	1140
gacgactccg	ggtggctcat	caagaatgtg	ctgtccatgc	ccatcgtcaa	caagaaggag	1200
gagattgtgg	gagtcgccac	attttacaac	aggaaagacg	ggaagccctt	tgacgaacag	1260
gacgaggttc	tcatggagtc	cctgacacag	ttcctgggct	ggtcagtgat	gaacaccgac	1320

EX05-002patentin.txt

```

acctacgaca agatgaacaa gctggagaac cgcaaggaca tcgcacagga catggtcctt 1380
taccacgtga agtgcgacag ggacgagatc cagctcatcc tgccaaccag agcgcgctg 1440
gggaaggagc ctgctgactg cgatgaggac gagctgggagc aaatcctgaa ggaggagctg 1500
ccagggccca ccacatttga catctacgaa ttccacttct ctgacctgga gtgcaccgaa 1560
ctggacctgg tcaaattgtg catccagatg tactacgagc tgggctggtt ccgaaagtct 1620
cagatccccc aggaggtcct ggtgctggtt ctgttctcca tcagcaaagg gtaccggaga 1680
atcacctacc acaactggcg ccacggcttc aacgtggccc agacgatgtt cacgctgctc 1740
atgaccggca aactgaagag ctactacacg gacctggagg ctttcgccat ggtgacagcc 1800
ggcctgtgcc atgacatcga ccaccgaggc accaacaacc tgtaccagat gaagtccag 1860
aacccttgg ctaagctcca cggtcctcg attttgagc ggcaccacct ggagtttggg 1920
aagttcctgc tctcgaggga gacctgaac atctaccaga acctgaaccg gcggcagcac 1980
gagcacgtga tccacctgat ggacatcgcc atcatcgcca cggacctggc cctgtacttc 2040
aagaagagag cgatgtttca gaagatcgtg gatgagtcca agaactacca ggacaagaag 2100
agctgggtgg agtacctgtc cctggagacg acccggaagg agatcgctcat ggccatgatg 2160
atgacagcct gcgacctgtc tgccatcacc aagccctggg aagtccagag caaggtcgca 2220
cttctcgtgg ctgctgagtt ctgggagcaa ggtgacttgg aaaggacagt cttggatcag 2280
cagcccatc ctatgatgga ccggaacaag gcggccgagc tcccaagct gcaagtgggc 2340
ttcatcgact tcgtgtgcac attcgtgtac aaggagtctt ctcgtttcca cgaagagatc 2400
ctgccccatgt tcgaccgact gcagaacaat aggaaagagt ggaaggcgct ggctgatgag 2460
tatgaggcca aagtgaaggc tctggaggag aaggaggagg aggagagggg ggcagccaag 2520
aaagtaggca cagaaatttg caatggcggc ccagcaccga agtcttcaac ctgctgtatc 2580
ctgtgagcac tgggtcccgtg gggaccctat ggctccctca atcttcaccc actaggattt 2640
gggttctgcc tgtggctatt tgctacaaga ggtaggaag cccaagaaaa tgactgaaga 2700
tcattctgga tattttaatt tttttttttt tttttttttt gagatggagt cttgctctgt 2760
caccaggct ggagtgccgt ggcacgatct cagctcactg caacctccac ctcccaggtt 2820
caagcgattc tcgtgcctca gcctcctgag tagctgggac tacaggcgcc caccaccaca 2880
catgctaatt tttgtatttt cagtacagat ggggtttcac catattgggc aggctggtct 2940
cgaactcctg acctcaggtg atcaccgcct cagcttcctg aagtgtctggg attacaggca 3000
tgagccacca cggccagcct gtttttataa actgaagcca actgtgaata aactgtagcc 3060
tacattactc atccattttt ggatagttac cactgggaga cttttgaaaa ggggtccatga 3120
actctgaaat cactgagaac atttgcagcc acacatgtac atatgtgtac acaggtagac 3180
agatggacac aggccgtttc tcatccagtt taggaaaaca cacatgctca g 3231

```

<210> 44
<211> 2969

EX05-002patentin.txt

<212> DNA

<213> Homo sapiens

<400> 44

```

ctttggaagt cctatgaggg accattttacg gtttcctcag taattttccac caggatgaat      60
ttcctttctca tcaactctgcc tcaggtagtg ctctgaaggt cgtcctttct gaacaaacgc      120
agcaaagcaa gccacaccat ggggtgagatc aaccaagttg ccgtggagaa atacctggag      180
gagaaccctc agtttgccaa ggagtacttt gacaggaagt tgcgggtgga ggtgctggga      240
gaaatcttca agaacagcca ggtgccagtc cagtccagca tgtcctttct tgagctgacc      300
cagggtggagg agtcagccct gtgcttggag ctgctgtgga ccgtgcagga ggaggggggc      360
accccagagc aggggggttca cagggcccta cagaggctgg cccacctgct ccaggctgac      420
cgctgcagca tgttcctgtg ccggtcccgg aacggcatac ctgagggtggc ctctagggttg      480
ctggtagtca cccccacctc caagtttgag gacaacctgg tgggccctga caaagaagtt      540
gtgtttccat tggacattgg gatagtgggt tgggctgctc acacgaagaa aactcataat      600
gtcccagatg tgaaaaagaa cagccatttt tctgacttca tggacaagca aactgggtat      660
gtcactaaga acctgctggc aaccccgatc gtggtgggca aggaggttct tgctgtgac      720
atggcagtta acaaagtaaa tgcacttgaa ttttccaaac aggatgaaga ggtcttttcc      780
aaatacctca actttgtgtc tatcatccta aggccttcac acaccagcta catgtacaat      840
attgaatccc gaagaagcca gatccttatg tggtcagcca ataaagtatt tgaagaactc      900
acagatgttg agcgacagtt tcacaaagcg ctctacacgg ttagatcata tctgaactgt      960
gaacgatact ccattggact gctggacatg accaaggaga aggaattcta cgatgaatgg     1020
ccaatcaagc ttggagaagt agagccttat aaagggtccaa agacacctga tggcagggaa     1080
gtcaactttt ataaaatcat tgattacatt ttacatggaa aagaagagat caaagtgatt     1140
ccgacgcctc ctgcagacca ctggacactc attagtgggt tgccaacata tgttgctgaa     1200
aatggattta tctgtaacat gatgaatgcc cctgcggatg aatacttcac atttccgaaa     1260
ggacctgtag acgaaactgg ttgggtcatt aagaatgttt tgtccctgcc tattgtcaac     1320
aagaaagaag atattgtggg agtggctaca ttttacaaca ggaaggatgg aaaacctttc     1380
gatgagcatg atgaatacat taccgagact ctacacaaat ttcttgatg gtctctttta     1440
aatactgaca cctacgataa gatgaataag ctagaaaaca gaaaggacat tgctcaggaa     1500
atgctcatga accaaaccaa agccactctt gaagaaatta agtccatttt gaaatttcaa     1560
gagaagttaa atgttgatgt aattgacgac tgtgaagaaa aacaacttgt tgcaattttg     1620
aaagaggact tgccagacct acgctcagca gaactgtacg aattccgctt cagtgacttc     1680
ccccttacag agcacggatt gattaaatgt ggaatacgac tgttttttga aataaatgtg     1740
gtggagaaat tcaaagtacc tgtagagggt cttaccagat ggatgtacac tgtgaggaaa     1800
gggtaccgag ctgtcactta ccacaattgg cagcatgggt tcaacgtggg gcagaccatg     1860
tttactttgc tgatgacagg aagattaaag aagtactaca cagatctcga agcctttgcc     1920

```

EX05-002patentin.txt

atgcttgctg ctgctttctg ccatgatatt gaccacagag gcaccaataa tttgtaccag 1980
 atgaaatcca cgtctccatt agcaagactt catggttctt ctatcttga gaggcaccac 2040
 ctggagtaca gtaagactct gttgcaggat gagagtttaa acatcttcca gaacctaaat 2100
 aagcggcagt ttgaaacagt tttcatttg ttcgaggtcg caataatagc aactgacctg 2160
 gctttatatt tcaagaagag gaccatgttt caaaaaattg ttgatgcctg tgaacaaatg 2220
 caaacggaag aagaagccat caaatatgta actgttgatc caaccaagaa agagattatc 2280
 atggcaatga tgatgacggc atgtgacttg tctgctatta ccaagccctg ggaggtgcaa 2340
 agtcaggtag cacttatggt tgcaaatgaa ttttgggaac aaggagatct ggagagaaca 2400
 gtgttgacgc aacaacccat tcctatgatg gacagaaaca aaagagatga attacctaaa 2460
 cttcaagttg gatttattga ttttgtttgt acttttgtat ataaggagtt ctcacggttt 2520
 cacaaagaaa tcacacctat gctgagtggc cttcagaata acagagtaga atggaaatca 2580
 ctagctgatg agtatgatgc aaagatgaag gtcattgaag aggaggcaaa aaagcaagaa 2640
 ggaggagccg aaaaagctgc tgaagattca ggaggtggtg atgacaaaaa gtccaaaaca 2700
 tgtttaatgt tgtaatatta tctaactggc ctaaacttca aatatcattt tacctttgaa 2760
 gaaaaccaga aaacattcaa aagaacttca acaaatcatc acgtaacagg atcttcagaa 2820
 aaactaccct gtgactatga agaaaatata tattgctagc ccaaaaatcc caggggcaaa 2880
 ataaagtcca acaaaagtgc aaaatatgac aaaaataggt acatttttgg tgccaattta 2940
 ttttaatta aaaaatcatg caatcctga 2969

<210> 45
 <211> 5695
 <212> DNA
 <213> Homo sapiens

<400> 45
 tgctatccac cccagctgga atttagacca gacttacagg ctttctgctc cttccttcag 60
 tgaagaagag tctccagggt ccctctagtg cagggtcaaag aagtcagtc cagctgagtt 120
 cagctcccta gggcctcccc agccagtctc ctgggccaag agctggcttt gcaagaaaac 180
 atcctactaa agccctggga aaagagacaa atgggtgaaga ggagaatgaa aggttgacgg 240
 agggagctcc tgtttttagc ctgccaccta cctgggggcc ctctggctac cagtgtcctt 300
 ggaggggctt ccttgctgct tctccacta aggagctctg gagccttagg accatggacg 360
 ctctcaatag gaaccaaata ggccctggat gccagaccca gaccatggtg cagaaaggac 420
 ccttggaact gatcgagaca ggcaaagggc tgaaagtgca aacggacaaa cccacctgg 480
 tgagcctggg cagtgggcga ctgagcacag ccatcaccct cctgccgctg gaggaagggg 540
 ggacggtgat tggctctgca gccagagaca tctcactaca gggcccaggc ctggctccag 600
 agcactgcta catcgagaac ctgcggggca ccctcaccct ctaccctgt ggcaatgcct 660
 gcaactattga tgggctccct gtccggcagc ctaccggct cactcagggc tgcattgtgt 720
 gcctgggtca gtccaccttc cttcgcttta accacccggc tgaagccaag tggatgaaaa 780

EX05-002patentin.txt

gcatgattcc agcagggggc cgagcccctg gggcccccta cagccctgtt cctgcagaat	840
cagaaagtct ggtaaatggg aaccacaccc cacagactgc aacacgggga ccctctgcct	900
gtgccagcca cagttccctg gtgagctcta ttgagaagga cctgcaagag atcatggact	960
cactggtgct agaggagcct ggagctgctg gcaagaagcc tgccgcaacc tctccactgt	1020
caccgatggc taatggtggg cgctacctgc tgtctcccc aaccagcccc ggcgcatgt	1080
ctgtgggctc cagctatgag aacacctctc cagccttctc tccactctct tcaccagcca	1140
gcagtggaaag ctgtgccagt cactcaccca gtgggcaaga gccaggacct tctgtgcccc	1200
cgctggtacc tgcccgttcc tccagctacc atctggccct acagccccca cagtcccgcc	1260
caagtggcgc tcgctccgag agtcctcggc tgagcaggaa agggggccat gagaggcctc	1320
ccagccctgg cctccggggg ctgctgacag acagccctgc agctactgtc ttggcgagg	1380
cccggagagc cactgagagc ccccggtggt gtgggcagct gcctgtggtg gccatcagcc	1440
tgagtgaata cccagcttct ggtgctctca gtcaaccac cagcattcct ggcagcccca	1500
agtttcagcc tccagtcctt gctccccgaa acaagattgg cacactccag gaccgccctc	1560
ccagcccttt ccgtgagcct ccaggcagtg agcgggtgct aacaaccagc ccctcacgcc	1620
aactggtggg ccgaacattt tcagatgggt tagccacccg taccctgcag cctcctgaga	1680
gtccccgcct gggccggcgg ggcctggaca gtatgcgaga actaccccc ttaagtccat	1740
ctctgtcccg gcgagctctc tccccgctgc ccacccgag caccacagat cccaagctaa	1800
acaggggaagt ggcagagagt cctcggcccc ggcgctgggc agcccatggg gcttcaccag	1860
aggacttctc cctgacgctg ggggcacggg gccgtaggac acggagcccc tcaccacac	1920
tgggtgagtc tctggcacc cacaagggca gcttcagtgg caggctgagc ccagcctaca	1980
gtctgggctc tcttactggg gcttcaccct gccagagtcc ctgtgtccag aggaagctct	2040
ccagcgggga cttgcgggtg cctgtcaca gggagcggaa aaatagcatc acagagatca	2100
gtgacaatga ggacgacctc ctggagtacc accggcgaca gcgccaagag cggctccggg	2160
agcaggagat ggagaggctg gaacgccagc gcctggagac catcctgaac ctgtgtgccg	2220
aatacagccg ggctgatggg ggacctgagg ctggggagct tcccagcatt ggggaggcca	2280
ccgcagcatt ggcaactggc ggcggaggc cctcacgagg ccttgaggg gcctctgggc	2340
ggagcagcga ggagcctggc gttgccaccc aacgcctatg ggagagtatg gagcgctcag	2400
atgaggaaaa tctcaaggag gagtgcagca gcaactgagag caccagcag gagcacgaag	2460
atgcacctag caccaagctc caggagagag tgctagccct ggaagaagag cgggctcagg	2520
tgctggggca cgtggagcag ctcaaggctc gtgtgaagga gctagagcag cagctgcagg	2580
agtcagcccc agaggccgaa atggagcggg cactgctgca gggagagagg gaggcagagc	2640
gggcaactgt gcagaaggag cagaaggcag tggatcagct gcaggagaag ctggtggcct	2700
tggagacagg catccagaag gagagggaca aggaggcaga ggcctggag actgagacaa	2760
agctctttga ggacttggag ttccagcagt tggagcggga gagccgcgtg gaggaggagc	2820

EX05-002patentin.txt

gcgagctggc	cggccagggg	ctgctccgga	gcaaggctga	gctgctccgc	agcatcgcca	2880
agaggaagga	gcgcttgcc	atcctggaca	gtcaggctgg	gcagatccgg	gctcaggccg	2940
tgcaggagtc	agaacgcctg	gcccgggaca	agaatgcctc	cttacagctg	ctgcaaaagg	3000
agaaggagaa	gctgactgtg	ctggaaaagga	gataccactc	actcacaggg	ggcaggcctt	3060
tcccgaagac	cacatcgacc	ctcaaagaga	tggagaagct	gctgctccct	gctgtagact	3120
tagagcagtg	gtaccaggag	ctgatggccg	ggctggggac	tggccccgct	gcagcctccc	3180
ctcactcttc	tccccgcct	ctgcccgcc	aagcttccc	tcagctgcag	gtttaccgct	3240
ccaagatgga	tggcgaggcc	accagcccc	ttccccggac	ccgcagcggc	cccctcccct	3300
cctcctctgg	ctcttcctcc	tcctcctccc	agctcagcgt	ggctaccctg	gggcgtagcc	3360
cctcccaaaa	gagcgtcta	ctcaccaga	atggcacggg	cagccttcct	cgcaacctgg	3420
cagccacact	gcaggacatc	gagaccaagc	gccaaactagc	tctgcagcag	aagggacaac	3480
aagtgattga	agagcagcgg	cggcgactgg	ctgagctgaa	gcagaaagcg	gcagctgagg	3540
cacagtgcc	gtgggatgcc	cttcacgggg	cagcaccctt	cccagcgggc	ccctcgggct	3600
tccccctct	catgcaccac	tctatcctac	accacctgcc	tgcggggcgg	gagcgtgggg	3660
aggaggggtga	gcacgcctat	gatacgctga	gtctggagag	ctctgacagc	atggagacca	3720
gcatctccac	cgggggcaac	tcggcctgct	cccctgacaa	catgtccagc	gcgagtggtc	3780
tggacatggg	gaagatcgag	gagatggaga	agatgctgaa	agaggctcat	gcagagaaga	3840
accggctcat	ggagtgcagg	gagcgggaga	tggagctgcg	gcggcaggcc	ctggaggagg	3900
agcggcggag	gcgtgagcag	gtagaacgga	ggctgcagag	tgagagtgcc	cggaggcagc	3960
agctggctga	gaaggaggct	aagatgcggg	agaaacaatt	ttcccaggca	cgaccctga	4020
cccgtacct	gccaatccgg	aaggaggact	ttgacctgaa	gacacatatt	gagtcacg	4080
gccatggtgt	tgatacctgc	ctgcacgtgg	tgctcagcag	caaggctctgc	cgtggctact	4140
tggatcaagat	gggcggcaag	attaaatcat	ggaagaagcg	ctggtttgtc	ttcgaccggc	4200
tcaagcgac	cctttcctat	tatgtggaca	agcatgagac	gaagctgaag	ggagtcatct	4260
atttcaggc	cattgaggaa	gtgtactacg	accacctgcg	cagtgcagcc	aagaagaggt	4320
ttttccgctt	cactatggtg	actgagagcc	cgaaccagc	cctcaccttc	tgcgtaaaga	4380
cccatgaccg	gctgtactac	atggtggccc	catctgcaga	ggccatgcgt	atctggatgg	4440
atgtcattgt	cacaggggct	gagggctaca	ctcagttcat	gaactaactg	tcgtgggcct	4500
cctggcagag	cacaactggg	gcttttgtat	aagaagactt	taatattctg	taaggagctt	4560
ggctcctgtga	gtttctgggc	tctggcctcc	tgaagaacca	gccagaagaa	gaaaagtaga	4620
ggtggctttg	ctgcctcctg	ggagcccaga	acttgcaagta	accctttagg	gtcctgcccc	4680
aggcccagcc	agggtgagg	agctgtcaca	gagagggcct	cagctctgac	ctgacacctg	4740
ctctccccag	cctgttttct	cttttctaaa	agacaaatta	tggtagcata	agctgcaaaa	4800
gatccccctc	tgcctcagac	ccctttgcc	ggggctttgg	gggctgagca	gagccacatc	4860

EX05-002patentin.txt

cagagtgggg taatagctca ggcggccccgc ttcccatctc tcaaaccgctg ctctgccccca 4920
 ttgttctcct ttcccttata ctttttatta ccttgctcaa gggccagaga tctcaagtgt 4980
 caaccttgag gtcccagctc catcccctag ttgcagactc atcaccatgg ttaccatagt 5040
 gactgcttca ttgccatggg tacatactaa ttgctgcagc tctgtggccc agcccactgc 5100
 ttcagctgtg ggccatctga ggggtacgtgc catcatctct ccagcccagg cccctgggca 5160
 tctcatgctg gggggaaggg actgaatacc tttttccttc cccctgcctg tgtcttcagc 5220
 cctgatgcac aggctgccag cccccagtc cagccctctc ccttccactg gtgccttgct 5280
 tagagccaga agggatgaag ccgggggagc tatggaacag aggaggagcg atgcagttgg 5340
 gagaggaagc tagaagggtt atggttgag ttctgtacag tgttgagttt ccgacaggga 5400
 aagaggattc ctccaatgcg cctagagaga aagcctgagc aggagatgat gcagcagagg 5460
 ggaaggggcc tgtggtgccg ccgccccttc ttcagcctcc gaagggtgat ggaaatggag 5520
 agtggaggac caggcctcca gctgtctggc ctgcgcccct acgccttaac actaagccca 5580
 cctcccctgc tctccttccc agcattgagc ccttggttgc ctggggccag gctgggggtt 5640
 ttcagtattt gtaagcattt cagcagaaca ataaagcctt tggactacgg aagtg 5695

<210> 46
 <211> 2920
 <212> DNA
 <213> Homo sapiens

<400> 46
 cgccaggaga cccaagctg catcgccgag tggaagcaac tagaactcca gggctgtgaa 60
 agccacagggt gggggctgag cgaggcgtgg cctcaggagc ggaggacccc cccccactct 120
 ccctcgagcg ccgcagtcca ccgtagcggg tggagcccg cttggtgctg agttggaaaa 180
 cctcggagcc ccgctggatc tcctggctgc caccgcacc ccccgccagc ctacgccccca 240
 ccgtagagat gccttcttcg gtgacggcgc tgggtcaggc caggctctct ggccccggga 300
 tggccccgag cgctgctgc tgctcccctg cggccctgca gaggaggctg cccatcctgg 360
 cgtggctgcc cagctactcc ctgcagtggc tgaagatgga tttcgtcgcc ggcctctcag 420
 ttggcctcac tgccattccc caggcgtgg cctatgctga agtggctgga ctcccgcctc 480
 agtatggcct ctactctgcc ttcattgggt gcttcgtgta tttcttctg ggcacctccc 540
 gggatgtgac tctgggcccc accgccatta tgtccctcct ggtctccttc tacaccttcc 600
 atgagcccg ctagctgtg ctgctggcct tcctgtccgg ctgcatccag ctggccatgg 660
 gggctcctgc tttgggggtc ctgctggact tcatttccta ccccgctatt aaaggcttca 720
 cctctgctgc tgccgtcacc atcggcttgg gacagatcaa gaacctgctg ggactacaga 780
 acatccccag gccgttcttc ctgcagggtg accacacctt cctcaggatt gcagagacca 840
 gggtaggtga cgccgtcctg gggctgggtc gcatgctgct gctgctgggt ctgaagctga 900
 tgcgggacca cgtgcctccc gtccaccccg agatgcccc tgggtgtgcgg ctgagccgtg 960

EX05-002patentin.txt

```

ggctggtctg ggctgccacg acagctcgca acgccctggt ggtctccttc gcagccctgg 1020
ttgcgtactc cttcgagggtg actggatacc agcctttcat cctaacaggg gagacagctg 1080
aggggctccc tccagtccgg atcccgccct tctcagtgac cacagccaac gggacgatct 1140
ccttcaccga gatggtgcag gacatgggag ccgggctggc cgtggtgccc ctgatgggcc 1200
tcctggagag cattgcggtg gccaaagcct tcgcatctca gaataattac cgcacgatg 1260
ccaaccagga gctgctggcc atcgggtctca ccaacatggt gggctccctc gtctcctcct 1320
acccggtcac aggcagcttt ggacggacag ccgtgaacgc tcagtcgggg gtgtgcaccc 1380
cggcgggggg cctggtgacg ggagtgctgg tgctgctgtc tctggactac ctgacctcac 1440
tgttctacta catccccaag tctgccctgg ctgccgtcat catcatggcc gtggccccgc 1500
tgttcgacac caagatcttc aggacgctct ggcgtgttaa gaggctggac ctgctgcccc 1560
tgtgcgtgac cttcctgctg tgcttctggg aggtgcagta cggcatcctg gccggggccc 1620
tggtgtctct gctcatgctc ctgcactctg cagccaggcc tgagaccaag gtgtcagagg 1680
ggccggttct ggtcctgcag ccggccagcg gcctgtcctt ccctgccatg gaggctctgc 1740
gggaggagat cctaagccgg gccctggaag tgtccccgcc acgctgcctg gtcctggagt 1800
gcacccatgt ctgcagcatc gactacactg tggtgctggg actcggcgag ctctccagg 1860
acttccagaa gcagggcgct gccctggcct ttgtgggcct gcaggtcccc gttctccgtg 1920
tcctgctgtc cgctgacctg aaggggttcc agtacttctc taccctggaa gaagcagaga 1980
agcacctgag gcagaagcca gggaccagc cctacaacat cagagaagac tccattctgg 2040
acaaaaaggt tgcctgctc aaggcataat ggggccaccc gtgggcatcc acagtttgca 2100
gggtgttccg gaaggttctt gtcactgtga ttggatgctg gatgccgcct gatagacatg 2160
ctggcctggc tgagaaaccc ctgagcaggt aacccagggg agagaaggaa gccaggcctg 2220
gaggtccacg gcagtgggag tggggctcac tggcttcctg tgggatgact ggaaaatgac 2280
ctcgtgctg ttcctggca tgacctctt tggaaagtg gtttgagag agccttctag 2340
aatgacagac tgtgcgagga agcaggggca ggggtttcca gcccgggctg tgcgaggcat 2400
cctggggctg gcagcacctt cccggctcac cagtgccacc tgcgggggag ggacggggca 2460
ggcaggagtc tgggaggcgg gtccgctcct cttgtctgct gcacgtgtgc tctccgagag 2520
aaaaccaagg tgtgtcaaat gacgtcaagt ctctatttaa aaataatttt gtgttttcta 2580
aatggaaaaa gtgatagctt tggtgatttt gtaaaagtca taaatgctta ttgtaaaaaa 2640
tacaggaaac caccctcac cctgtccact tgggtgatca ttccagaccc ctccccaaac 2700
atgcatatgt acctgtccgt cagtgtgtgg atgtatgttt acagttctac ataaatggga 2760
tcattttata catggtgctc tggaaccac atttttcatg cagtcatttg cagtgaatta 2820
tttattgtga taataaatag cattagaata caaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2880
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2920

```

EX05-002patentin.txt

<211> 3250

<212> DNA

<213> Homo sapiens

<400> 47

```

ccggaggatt ttgaggacac ttgtggagag ctcgaattcc agaatgatga aattgttagg      60
ttgtgacagt tggaagtgtc atgtacaaca tgcggcgatt aagtctttca cccacctttt      120
caatgggatt tcatctgtta gttactgtga gtctcttatt ttcccatgtg gaccatgtaa      180
ttgctgagac agaaatggaa ggagaaggaa atgaaactgg tgaatgtact ggatcatatt      240
actgtaagaa aggggtgatt ttgcccattt gggaacccca agacccttct tttggggaca      300
aaattgctag agctactgtg tattttgtgg ccatgggtcta catgtttctt ggagtctcta      360
tcatagctga tcggttcatt tcctctatag aagtcacac atctcaagaa aaagaaataa      420
ccataaagaa acccaatgga gagaccacca agacaactgt gaggatctgg aatgaaacag      480
tttctaacct gaccttgatg gccctgggat cttctgtccc tgagattctc ctttcagtaa      540
ttgaagtgtg tggccataac ttcactgcag gagacctcgg tcctagcacc atcgtgggaa      600
gtgctgcatt caatatgttc atcattattg cactctgtgt ttatgtggtg cctgacggag      660
agacaaggaa gattaagcat ttgcgtgtct tctttgtgac agcagcctgg agcatctttg      720
cctacacctg gctttacatt attttgtctg tcatatctcc tgggtgtgtg gaggtctggg      780
aaggtttgct tactttcttc ttctttccca tctgtgttgt gttcgcttgg gtagcggata      840
gggagacttct gttttacaag tatgtctaca agaggtatcg agctggcaag cagaggggga      900
tgattattga acatgaagga gacaggccat cttctaagac tgaaattgaa atggacggga      960
aagtgggcaa ttctcatgtt gaaaatttct tagatggtgc tctggttctg gaggtggatg     1020
agaggggacca agatgatgaa gaagctaggc gagaaatggc taggattctg aaggaactta     1080
agcagaagca tccagataaa gaaatagagc aattaataga attagctaac taccaagtcc     1140
taagtcagca gcaaaaaagt agagcatttt atcgcattca agctactcgc ctcatgactg     1200
gagctggcaa cattttaaag aggcattgcag ctgaccaagc aaggaaggct gtcagcatgc     1260
acgagggtcaa cactgaagtg actgaaaatg accctgttag taagatcttc tttgaacaag     1320
ggacatatca gtgtctggag aactgtggta ctgtggccct taccattatc cgcagagggtg     1380
gtgatttgac taactactgtg tttgttgact tcagaacaga ggatggcaca gcaaatgctg     1440
ggctctgatta tgaatttact gaaggaactg tggtgtttta gcctggtgat acccagaagg     1500
aaatcagagt ggggtatcata gatgatgata tctttgagga ggatgaaaat ttccttgtgc     1560
atctcagcaa tgtcaaagta tcttctgaag cttcagaaga tggcatactg gaagccaatc     1620
atgtttctac acttgcttgc ctcggatctc cctccactgc cactgtaact atttttgatg     1680
atgaccacgc aggcattttt acttttgagg aacctgtgac tcatgtgagt gagagcattg     1740
gcatcatgga ggtgaaagta ttgagaacat ctggagctcg aggaaatgtt atcgttccat     1800
ataaaacat cgaagggact gccagagggtg gaggggagga ttttgaggac acttgtggag     1860
agctcgaatt ccagaatgat gaaattgtca aaacaatatc agtcaaggta attgatgatg     1920

```

EX05-002patentin.txt

```

aggagtatga gaaaaacaag accttcttcc ttgagattgg agagccccgc ctggtggaga 1980
tgagtgagaa gaaagccctg ttattgaatg agcttggtgg cttcacaata acaggaaaat 2040
acctgtttgg ccaacctgtc ttcaggaagg ttcagtctag agaacatccg attctctcta 2100
ctgtaatcac cattgcagac gaatatgatg acaagcagcc actgaccagc aaagaggaag 2160
aggagaggcg cattgcagaa atggggcgcc ccatcctggg agagcacacc aagttggaag 2220
tgatcattga agaatcctat gaattcaaga gtactgtgga caaactcatt aagaagacaa 2280
acctggccct tgtggttggg actaacagct ggagagaaca gttcattgaa gctatcactg 2340
tcagtgctgg ggaagatgat gacgacgatg aatgtgggga agagaagctg ccctcctggt 2400
tcgattacgt gatgcacttt ctgactgtgt tctggaaggt cctgtttgcc ttcgtcccc 2460
ctactgaata ctggaatggc tgggcgtgtt tcattgtctc catcctcatg attggcctac 2520
tgacagcttt cattggagac ctggcttccc actttggctg caccattggc ctgaaagatt 2580
ctgtgactgc agtcgtgttc gtcgcacttg gaacatcagt gccagacaca ttgcccagca 2640
aagtggcagc caccaggac cagtatgcag acgcctccat aggtaacgtc acgggcagca 2700
acgcggtgaa tgtcttcctg ggaatcgggtg tggcctgggtc catcgctgcc atctaccacg 2760
cagccaatgg ggaacagttc aaagtgtccc ctggcacact agctttctct gtcactctct 2820
tcaccatttt tgctttcatc aatgtggggg tgctgctgta tcggcggagg ccagaaatcg 2880
gaggtgagct ggggtgggcc cggactgcca agctcctcac atcctgcctc tttgtgctcc 2940
tatggctctt gtacattttc ttctcctccc tggaggccta ctgccacata aaaggcttct 3000
aaaggaacta tcagatatag taaatttata tatatacata tatatacata aaaattatgt 3060
ataatggaca gaggaaactg acatttgtca tgttacttta cctgctgatg gaatccagct 3120
tcaagagcat actctgtact agggccgaag taaaaaacca tcacctcca ttcccagggg 3180
catcatcatg ttcaacaagg catggaggca gggccatctt tgcagctcag tctagaaggg 3240
ctgcactctc 3250

```

```

<210> 48
<211> 4282
<212> DNA
<213> Homo sapiens

```

```

<400> 48
ctctctctct ttcgggcgga gtcgcccacc actgccagcc cagcgctggg gggacctgct 60
ccaggctgta gccgcaggac cccaccaccc cccatggctc ccctggcctt ggtgggggtc 120
acactcctcc tggcggctcc cccatgctcc ggggcagcca cccaacccc ctccctgccg 180
cctcccccg ccaatgacag cgacaccagc acaggggggt gccaggggtc ctaccgctgc 240
cagccggggg tgctgctgcc cgtgtgggag cccgacgacc cgtcgctggg tgacaaggcg 300
gcacgggcag tgggtgtact tgtggccatg gtctacatgt ttctgggagt gtccatcatc 360
gccgaccgtt tcatggcggc catcgagggt atcacgtcaa aagagaagga gatcaccatc 420

```

EX05-002patentin.txt

accaaggcca	acggtgagac	cagcgtgggc	accgttcgca	tctggaatga	gacggtgtcc	480
aacctcacgc	tcatggccct	gggctcctcc	gcacctgaga	tcctgctgtc	agtcatcgaa	540
gtctgcggcc	acaacttcca	ggcgggtgag	ctgggcccag	gcaccatcgt	gggcagcgct	600
gccttcaaca	tgtttgtggt	catcgccgtg	tgcactctacg	tcatcccagc	cggcgagagc	660
cgcaagatca	agcacctgag	agtcttcttt	gtcactgcct	cttgagcat	cttcgcctat	720
gtctggcttt	atctcatcct	tgtgtttttt	tccccgggtg	tgggtccaggt	gtgggaggcg	780
ctgctgaccc	tgggtcttctt	cccgggtgtgc	gtgggtattcg	cctggatggc	cgacaagcgg	840
ctgctcttct	acaagtacgt	gtacaagcgc	taccgcaccg	accacgcag	cggcatcatc	900
ataggcgccg	agggcgaccc	cccgaagagc	atcgagctgg	acggcacgtt	cgtgggcgcc	960
gaggccccag	gtgagctggg	cggcctgggc	ccgggccccg	ccgaggcgcg	cgagctggac	1020
gccagccgcc	gcgaggtcat	ccagatcctc	aaggacctca	agcagaagca	cccggacaag	1080
gatctggagc	agctgggtggg	catcgccaac	tactacgcgc	tgctgcacca	gcagaagagc	1140
cgcgcttct	accgcatcca	ggccacgcgg	ctgatgaccg	gcgccgggaa	cgtgctgcgc	1200
agacacgcgg	cggacgcctc	gcgcagggcg	gcgccggccg	agggcgcggg	cgaggacgaa	1260
gacgacggcg	ccagccgcat	cttcttcgag	cctagcctct	accactgcct	ggagaactgc	1320
ggctccgtgc	tgctgtccgt	cacgtgccag	ggcggcgagg	gcaacagcac	cttctacgtg	1380
gactaccgca	ctgaggacgg	ctctgccaa	gcgggctccg	actacgagta	cagcgagggc	1440
acgctgggtg	tcaaaccagg	cgagacgcag	aaggagctgc	gcatcggcat	catcgacgac	1500
gacatcttcg	aggaggacga	gcatttcttc	gtgcggctgc	tgaacctgcg	cgtgggcgac	1560
gcgcagggca	tgctcgagcc	ggacggcggc	gggcggccca	aggggcggct	ggtggcgccg	1620
ctgctggcca	ccgtcaccat	cctggacgac	gaccacgcag	gcatcttctc	cttccaggac	1680
cgcctgctgc	acgtgagcga	gtgcatgggc	accgtggacg	tgcgcgctcg	gcgcagctcg	1740
ggcgcgcgcg	gcaccgtgcg	ccttccctac	cgcacggtgg	acggcacggc	gcgcggcggc	1800
ggcgtgcact	acgaggacgc	gtgcggagag	ctggagtttg	gcgacgacga	gaccatgaaa	1860
actcttcagg	tgaagatagt	tgatgacgag	gaatatgaga	aaaaggataa	tttcttcatt	1920
gagctggggc	agccccagtg	gcttaagcga	gggatttcag	ctctgctact	caatcaaggg	1980
gatggggaca	ggaagctaac	agccgaggag	gaggaggctc	ggaggatagc	agagatgggc	2040
aagccagttc	ttggggagaa	ctgccggctg	gagggtcatca	tcgaggagtc	atatgatttt	2100
aagaacacgg	tggataaact	catcaagaaa	acgaacttgg	ccttggtaat	tgggacccat	2160
tcatggaggg	agcagttttt	agaggcaatt	acggtgagcg	caggggacga	ggaggaggag	2220
gaggacgggt	cccgggagga	gcggctgccg	tcgtgctttg	actacgtgat	gcacttcctg	2280
acggtgttct	ggaaggtgct	cttcgcctgt	gtgcccccca	ccgagtactg	ccacggctgg	2340
gcctgctttg	gtgtctccat	cctgggtcatc	ggcctgctca	ccgccctcat	tggggacctc	2400
gcctcccact	tcggctgcac	cgttggcctc	aaggactctg	tcaatgctgt	tgtcttcggt	2460

EX05-002patentin.txt

gccctgggca cctccatccc tgacacgttc gccagcaagg tggcggcgct gcaggaccag 2520
 tgcgccgacg cgtccatcgg caacgtgacc ggctccaacg cggatgaacgt gttccttggc 2580
 ctgggcgctg cctggtctgt ggccgccgtg tactgggcgg tgcaggggccg ccccttcgag 2640
 gtgcgcactg gcacgctggc cttctccgtc acgctcttca ccgtcttcgc cttcgtgggc 2700
 attgccgtgc tgctgtaccg gcgcccggccg cacatcggcg gcgagctggg cggcccgcgc 2760
 ggaccaaacg tcgccaccac cgcgctcttc ctgggcctct ggctcctgta catcctcttc 2820
 gccagcctgg aggcgtactg ccacatccgg ggcttctagg gcctcgcgca gagactcgtc 2880
 cccaccgccc gcccggggct agggactcgg ctgcacctgc tcttggaacc tggctctcctt 2940
 ttccccccag actcggcctc ctctcctggg actcggcctc cttctctcgc cccctcccct 3000
 ggctttgatt gccctgttgc tgtgtcccca gtagctcagc cttccctctt cctctcggga 3060
 gcctccccgg ttcctcccct gcggtgacct caactccagc ccatcctgtt ggtgaccgtc 3120
 tatatccctg gggaaatttc caccacagtc cctccccag ggaaccaccc ccagtaacca 3180
 tcctggggag tttaaggtct ctctccttgg tcaccagcc tggctttgcc cccaaagtct 3240
 cccttcccct agtgaccccc cccacttca ccccatgtcc cagagcctca gaaccaccc 3300
 tcctgggggg accctcgaag gaggtgtgca gaggcgctc cagctcccag cccttcccc 3360
 cagccctcag ggagctccgc tcagccccgg cggggaggag cgggtgggtg tgcgcgcaag 3420
 gagggcgac acctttcctt ccaatccctc cactcgggtt cttgggagga cactcattct 3480
 ccaggctcgg agacgagggg agaagtttgg gggttcagtc ccagggtta gccggaggaa 3540
 gcacattttg aacctgcaac ttcagacatt ccagctcccc cactcgcctt cactacctc 3600
 tgagagccca gccacgcctt ggagggaggg gcttgtgtgt gtatatagtg tgtttggggg 3660
 aggggggacg cgggagggtg catgtcttgg gaaaaggggg tgacagacaa cttttgagag 3720
 ggcagcagac tccctcagcc atgagaacca gctttgggga ggaggccggg aatcaaagcg 3780
 agtccagttg atctcccctg acaatctgga aggttcattt tgccctcagt gccagccaat 3840
 ccgggcagga ccctcgaaga ggagaccgag ggtcccagag gaccaatgct acaagccagc 3900
 aaatgctgcc acatctctgc ctgatggggg gtgggggatg gtggggggat gggactgggc 3960
 caagggatct ggggtggcat ttttaacttt ggaggccttc catctgtcgg taggccatct 4020
 gcattttctt actgttgatg tttcctgccc aaaggacaca tttgggcagt gccaccact 4080
 ccttgggccc ctaggatgac ccaactaccc ccataacttt ctgcttccca caggttttca 4140
 gcattctatc gtcctgttgt gctcagcccc aacatcccag acccgttacc cgctaccctt 4200
 ctctcccca gctcatcatc agtcgctgtc tcttttctgt gatttctgta aaagttgcca 4260
 taaaactttg aaattctgcc tg 4282

<210> 49
 <211> 5262
 <212> DNA
 <213> Homo sapiens

EX05-002patentin.txt

<400> 49
 cggcgctgtc tcccagctga taggggtgacg ttccgtttgg aggcttggag attggcctttt 60
 tgattttggct tcttccggca gcttaatggg caaagctctc cgctcgccca gaaaccagcc 120
 tctccgcgcg tccccctctgc gcgcggcgag gccgagacgt ctcccgcggt gacagcgtgc 180
 aaggcggaga cccggcgcg ccccagccca gggaaagccc aggcgacgcg accgcaagcc 240
 cgagcccagg tccctcgag cgcgcagggc gcgcggggct gcttgccttc ctgccccttc 300
 ctgcaggaat ccccgccgc ccgcggccgg gactccgggc ctctcccggg cgtagattcc 360
 agtcaccgct ctgggtcggg gtttccctct ttctgaaatc cgtgcggaag gacccctccc 420
 ggggccccctc gccctggccc cagacaccct ccctcccaga ccccgcgctc cagatgcgct 480
 gccccgcagc tccctgacag ctgcgagccc acgaaccccg gcgggagggc ggcggcggcg 540
 gactgacatg ccccgacgc ggctgcggcc ggcgggcagc ccgcgggggc gatgagccgc 600
 tgcgaccggt gaggcgccgg gcggcggggg catcgcgtag cttcctcacc cccctccctt 660
 gcccactccg ctcgggaggc cgagaggaaa cgggtctctgg cctatcagga ggacaactgg 720
 tgctgcaata gaagccagt gctaagtctc gtgtatggcg tggttaaggt tgcagcctct 780
 cacctctgcc ttcctccatt ttgggtcggg tacctttgtg ctcttcctga atggctcttcg 840
 agcagaggct ggtggctcag gggacgtgcc aagcacaggc cagaacaatg agtcctgttc 900
 agggcatcg gactgcaagg aggggtgcat cctgccaatc tggtaaccgg agaacccttc 960
 ccttggggac aagattgcca ggggtcattgt ctattttgtg gccctgatat acatgttctt 1020
 tggggtgtcc atcattgctg accgcttcat ggcattctatt gaagtcatca cctctcaaga 1080
 gagggagggtg acaattaaga aacccaatgg agaaaccagc acaaccacta ttcgggtctg 1140
 gaatgaaact gtctccaacc tgacccttat ggccctgggt tcctctgctc ctgagatact 1200
 cctctcttta attgagggtg gtgggtcatg gttcattgct ggtgatctgg gaccttctac 1260
 cattgtaggg agtgcagcct tcaacatggt catcatcatt ggcattctgtg tctacgtgat 1320
 cccagacgga gagactcgca agatcaagca tctacgagtc ttcttcatca ccgctgcttg 1380
 gagtatcttt gcctacatct ggctctatat gattctggca gtcttctccc ctgggtgtgg 1440
 ccagggtttgg gaaggcctcc tactctctt cttctttcca gtgtgtgtcc ttctggcctg 1500
 ggtggcagat aaacgactgc tcttctacaa atacatgcac aaaaagtacc gcacagacaa 1560
 acaccgagga attatcatag agacagaggg tgaccaccct aagggcattg agatggatgg 1620
 gaaaatgatg aattcccatt ttctagatgg gaacctggtg cccctggaag ggaaggaagt 1680
 ggatgagtcc cgagagaga tgatccggat tctcaaggat ctgaagcaaa aacaccagaa 1740
 gaaggactta gatcagctgg tggagatggc caattactat gctctttccc accaacagaa 1800
 gagccgtgcc ttctaccgta tccaagccac tcgtatgatg actggtgcag gcaatatcct 1860
 gaagaaacat gcagcagaac aagccaagaa ggcctccagc atgagcgagg tgcacaccga 1920
 tgagcctgag gactttatctt ccaaggctctt ctttgaccca tgttcttacc agtgcttgga 1980
 gaactgtggg gctgtactcc tgacagtggg gagggaaagg ggagacatgt caaagaccat 2040

EX05-002patentin.txt

gtatgtggac	tacaaaacag	aggatggttc	tgccaatgca	ggggctgact	atgagttcac	2100
agagggcacg	gtggttctga	agccaggaga	gacccagaag	gagttctccg	tgggcataat	2160
tgatgacgac	atTTTTgagg	aggatgaaca	cttctttgta	aggttgagca	atgtccgcat	2220
agaggaggag	cagccagagg	aggggatgcc	tccagcaata	ttcaacagtc	ttcccttgcc	2280
tcgggctgtc	ctagcctccc	cttgtgtggc	cacagttacc	atcttgatg	atgaccatgc	2340
aggcatcttc	acttttgaat	gtgatactat	tcatgtcagt	gagagtattg	gtgttatgga	2400
ggtcaagggtt	ctgcgacat	caggtgccc	gggtacagtc	atcgtcccct	ttaggacagt	2460
agaagggaca	gccaagggtg	gcggtgagga	ctttgaagac	acatatggg	agttggaatt	2520
caagaatgat	gaaactgtca	aaacaattca	catcaaggta	attgatgatg	aggcatatga	2580
gaaaaacaag	aattacttca	ttgagatgat	gggccccgc	atggtggata	tgagttttca	2640
gaaagcgctc	ctgttatctc	cagacaggaa	gctgactatg	gaagaagagg	aggccaagag	2700
gatagcagag	atgggaaagc	cagtattggg	tgaacacccc	aaactagaag	tcatcattga	2760
agagtcctat	gagttcaaga	ctacggtgga	caaactgatc	aagaagacaa	acctggcctt	2820
ggttgtgggg	acccattcct	ggagggacca	gttcatggag	gccatcaccg	tcagtgcagc	2880
aggggatgag	gatgaggatg	aatccgggga	ggagaggctg	ccctcctgct	ttgactacgt	2940
catgcacttc	ctgactgtct	tctggaaggt	gctgtttgcc	tgtgtgcccc	ccacagagta	3000
ctgccacggc	tgggcctgct	tcgccgtctc	catcctcatc	attggcatgc	tcaccgccat	3060
cattggggac	ctggcctcgc	acttcggctg	caccattggt	ctcaaagatt	cagtcacagc	3120
tgttgttttc	gtggcatttg	gcacctctgt	cccagatacg	tttgccagca	aagctgctgc	3180
cctccaggat	gtatatgcag	acgcctccat	tggcaacgtg	acgggcagca	acgccgtcaa	3240
tgtcttcctg	ggcatcggcc	tggcctggtc	cgtggccgcc	atctactggg	ctctgcaggg	3300
acaggagttc	cacgtgtcgg	ccggcacact	ggccttctcc	gtcacctctt	tcaccatctt	3360
tgcatttgtc	tgcattcagc	tgctcttgta	ccgaaggcgg	ccgcacctgg	gaggggagct	3420
tggtgggccc	cgtggctgca	agctcgccac	aacatggctc	tttgtgagcc	tgtggctcct	3480
ctacatactc	tttgccacac	tagaggccta	ttgctacatc	aaggggttct	aagccacaca	3540
acagagcctc	cagcagggca	ggcctaggac	ttctcctaag	agaagggcac	ttccccacca	3600
gtgatctctc	ccgactgcac	tgccctggag	aggcagcatc	aggacctaa	ccccaggaac	3660
ttcacccaac	ttaggccctg	gcaattaact	gaaagggcaa	agtcttaatc	aatcaaacaa	3720
tggaggaatc	accgacttta	cacagtatTT	aattgaatac	aaacaagcaa	cagcaacaaa	3780
tccacctcca	ccccatctcc	ccctcatatc	cctgacccaa	agcaaaggtc	agagcctttc	3840
gcctccttct	attccatctt	ttgattattc	ctttgcctct	catttctttg	gaagcagggg	3900
ttctcctctc	tgcccaattc	catatgtccc	tattatctca	ctcagctgac	aagacgtgaa	3960
aatgagtcac	attcatgtgg	ctgggggtgg	gttctttttt	cattgtaatc	attattgtgg	4020
ttgctttcgt	tttgccatta	ggttttgctt	attatTTTgt	tttgtctttt	ttttctgaag	4080

EX05-002patentin.txt

tgagtgaaaa	aggtgccaca	aaggaattcc	aggtccgagc	caacagagag	aaacatgaat	4140
ttttagacac	atgctctcct	gccacctctt	ggctccatca	agatccagtt	ccccatctca	4200
ctgtttttctc	tgagtctcttg	ggaggagtga	tggtgttggg	gtagaaataa	gctcactcac	4260
ccacgcaggg	tactaaagat	cttacaggag	cttcaactgg	agcaggagga	gctttttatg	4320
cttatgttga	atcaagtcag	atacaaaaag	caattgtccc	tctttgcca	agcctttcca	4380
attctgtgtg	tcttggtgtg	tcagtgtcca	cttgtgtatc	cttctgcagg	aagacccgcc	4440
aaatagaaga	gatgggacaa	aaataggaat	gggtgtgtgac	gacaaagggc	tactggaaga	4500
acaaaagga	tacaggcctt	cttgattatc	tttggctttg	tacctgaggc	aggagagaag	4560
agatgtccaa	ccagtgaagat	ctttaagaga	aaagtttgta	ttttaaatgt	caatgtgcct	4620
gagaaatgtc	agcttcacca	cgctcttgct	tcctaattgct	ctatacaaag	agggctgact	4680
atatttcttg	aagtgggtga	aaaacttaga	gattttataa	gagaaccagg	ggctcccttc	4740
acctctcctg	gtccctcagg	tcacatatga	aagcattttt	acaagatagg	aactggaatt	4800
cctcatttct	cccatgttcc	tgcttgcttct	taaacttcat	gaagctatct	ttccagccta	4860
tggggtagtt	cttgctccag	taagaggaat	cttagttgtc	ataatccctt	ggagcctggg	4920
tttttgga	aagagatctc	cgtgccctac	agaccttttc	tcaacgaatg	tgggaaggac	4980
ctggctttaa	aacacgcaca	caaacacaca	aataaacaga	cataagatgt	catcacgaaa	5040
ctgcccacgg	atcttttaggc	tttctgcatt	gacataaata	catttttctaa	gggggggggg	5100
gaagaaatta	aaaaacacct	gttaatttta	aacacatttt	ttaagaaaaa	aataattaaa	5160
aaagaaacag	tgctcatgtc	ataagctatg	ttgacagttg	ccagtggaaa	tggtgggttg	5220
gttcaaaaaa	aaaataaaaag	ctatactata	tctctctaca	ta		5262

<210> 50
 <211> 1335
 <212> DNA
 <213> Homo sapiens

<400> 50	
atgattgaag	acaataagga gaacaaagac cattccttag aaaggggaag agcaagtctc 60
attttttctt	taaagaatga agttggagga cttataaaag ccctgaaaat ctttcaggag 120
aagcatgtga	atctgttaca tatcgagtcc cgaaaatcaa aaagaagaaa ctcagaattt 180
gagatttttg	ttgactgtga catcaacaga gaacaattga atgatatttt tcatctgctg 240
aagtctcata	ccaatgttct ctctgtgaat ctaccagata attttacttt gaaggaagat 300
ggatatgaaa	ctgttccttg gtttccaaag aagatttctg acctggacca ttgtgccaac 360
agagttctga	tgtatggatc tgaactagat gcagaccatc ctggcttcaa agacaatgtc 420
taccgtaaac	gtcgaaagta ttttgcggac ttggctatga actataaaca tggagacccc 480
attccaaagg	ttgaattcac tgaagaggag attaaagacct ggggaaccgt attccaagag 540
ctcaacaaac	tctacccaac ccattgctgc agagagtatc tcaaaaactt acctttgctt 600

EX05-002patentin.txt

tctaaatatt gtggatatcg ggaggataat atccccacaat tggaagatgt ctccaacttt 660
 ttaaaagagc gtacagggtt ttccatccgt cctgtggctg gttacttata accaagagat 720
 ttcttatcag gtttagcctt tcgagttttt cactgcactc aatatgtgag acacagttca 780
 gatcccttct ataccccaga gccagatacc tgccatgaac tcttaggtca tgtcccgctt 840
 ttggctgaac ctagttttgc ccaattctcc caagaaattg gcttggcttc tcttggcgct 900
 tcagaggagg ctgttcaaaa actggcaacg tgctactttt tctactgtga gtttgggtcta 960
 tgtaaacaag atggacagct aagagtcttt ggtgctggct tactttcttc tatcagtga 1020
 ctcaaactat cactttctgg acatgccaaa gtaaagccct ttgatcccaa gattacctgc 1080
 aaacaggaat gtcttatcac aacttttcaa gatgtctact ttgtatctga aagttttgaa 1140
 gatgcaaagg agaagatgag agaatttacc aaaacaatta agcgtccatt tggagtgaag 1200
 tataatccat atacacggag tattcagatc ctgaaagaca ccaagagcat aaccagtgcc 1260
 atgaatgagc tgcagcatga tctcgatgtt gtcagtgatg cccttgctaa ggtcagcagg 1320
 aagccgagta tctaa 1335

<210> 51
 <211> 2350
 <212> DNA
 <213> Homo sapiens

<400> 51
 cattgctctt cagcaccagg gttctggaca gcgccccaa caggcagctg atcgcacgcc 60
 ccttcctctc aatctccgcc agcgtgcta ctgcccctct agtaccacct gctgcagaga 120
 aagaatatta caccgggatc catgcagcca gcaatgatga tgttttccag taaatactgg 180
 gcacggagag ggttttccct ggattcagca gtgcccgaag agcatcagct acttggcagc 240
 tcaacactaa ataaaccta ctctggcaaa aatgacgaca aaggcaaca ggaagcagc 300
 aaacgtgaag ctgctaccga aagtggcaag acagcagttg ttttctcctt gaagaatgaa 360
 gttggtggat tggtaaaagc actgaggctc ttccaggaaa aacgtgtcaa catggttcat 420
 attgaatcca ggaaatctcg gcgaagaagt tctgaggttg aaatctttgt ggactgtgag 480
 tgtgggaaaa cagaattcaa tgagctcatt cagttgctga aatttcaaac cactattgtg 540
 acgctgaatc ctccagagaa catttggaag gaggaagaag agctagagga tgtgccctgg 600
 ttccctcgga agatctctga gttagacaaa tgctctcaca gagttctcat gtatgggtct 660
 gagcttgatg ctgaccaccc aggatttaag gacaatgtct atcgacagag aagaaagtat 720
 tttgtggatg tggccatggg ttataaatat ggtcagccca ttcccagggt ggagtatact 780
 gaagaagaaa ctaaaacttg ggggtgttga ttccgggagc tctccaaact ctatcccact 840
 catgcttgcc gagagtattt gaaaaacttc cctctgctga ctaaatactg tggctacaga 900
 gaggacaatg tgcctcaact cgaagatgtc tccatgtttc tgaaagaaag gtctggcttc 960
 acggtgaggg cgggtggctgg atacctgagc ccacgagact ttctggcagg actggcctac 1020
 agagtgttcc actgtacca gtacatccgg catggctcag atccccctta cccccagaa 1080

EX05-002patentin.txt

```

ccagacacat gccatgaact cttgggacat gttccactac ttgcggatcc taagtttgct 1140
cagttttcac aagaaatagg tctggcgtct ctgggagcat cagatgaaga tgttcagaaa 1200
ctagccacgt gctatttctt cacaatcgag tttggccttt gcaagcaaga agggcaactg 1260
cgggcatatg gagcaggact cctttcctcc attggagaat taaagcacgc cctttctgac 1320
aaggcatgtg tgaaagcctt tgacccaaag acaacttgct tacaggaatg ccttatcacc 1380
accttccagg aagcctactt tgtttcagaa agttttgaag aagccaaaga aaagatgagg 1440
gactttgcaa agtcaattac ccgtcccttc tcagtatact tcaatcccta cacacagagt 1500
attgaaattc tgaaagacac cagaagtatt gaaaatgtgg tgcaggacct tcgcagcgac 1560
ttgaatacag tgtgtgatgc tttaaacaaa atgaaccaat atctggggat ttgatgcctg 1620
gaactatggt gttgccagca tgatcttttt ggggcttagc agcagttcag tcaatgtcat 1680
ataacgcaaa taaccttctg tgtcatggct tggctaataa gcatgcaatt ccatatatct 1740
ataccatctt gtaactcact gtgttagtat ataaagcacc ataagaaatc caatggcaga 1800
taacctgaaa taacgtatta tgtttaaaca tcttaaaaag atttgacatt cctgcttagt 1860
gtccttaacc aaactgcac tagttaaaat ttgtaacaaa tagccctctt atgagtctca 1920
tttatgccct tttctttttc agatctaagc ctttcctctg tgttcattag ataaaatgaa 1980
aaaaagcagt gaagctgttt ccattttcaa tagtatcagt gttttcacgc attatttgag 2040
ataaaccag aattgtagga aacttcccat cacaataaca aaggttcaat attctatttc 2100
aaaaattggt gaggtaacac agcagttgga atgattttta gggtgagtat ttacacaatg 2160
caagaaaaca cctttttaca aatggaatta tgtaggttgc gttgaccttg tagaacctga 2220
gttatgacaa gcttcctgaa gtattttgga agatagtact tccggaaagg acattaggaa 2280
agactaaaca gtggacaatc aatcttgga ctatgaattt tatgctggaa taaagtaa 2340
tatcatgttc 2350

```

```

<210> 52
<211> 2011
<212> DNA
<213> Homo sapiens

```

```

<400> 52
cccatgcctc aattggtttc ttttagggag ctacaaattt acgtgttcac tggtgattga 60
tcttttcac cagcacaatg gacagaagtc taaggaacgt ccttggtggt tcctttgggt 120
tcctgcttct ctttacagcc tatggaggtc tgacagacct gcagagcagc ctgtacagcg 180
aggagggcct ggggtgcaca gcgctcagca ccctctatgg aggcattgct ctgtcctcca 240
tgttcctccc accgctcctc atcgagaggc tgggctgcaa ggggaccatc atcctctcca 300
tgtgtggcta cgtggccttc tccgtgggca acttcttcgc cagctggtac actttgatcc 360
ccacctcat actgctggga ctcggggccg ccccgctgtg gtctgcacag tgcacatacc 420
tcacgatcac gggaaacaca catgcagaga aggcgggaaa gcgtggcaaa gacatggtga 480

```

EX05-002patentin.txt

accagtattt tggcatcttc ttcctcatat tccagtcata cgggtgtgtg ggcaacttga 540
 tctcatcgct ggtatttggc cagactccca gccaaagagac ccttccagaa gagcagctca 600
 cgtcctgtgg ggccagtgcac tgcctgatgg ccaccacaac caccaacagc acccagaggc 660
 cctcccagca gctgggtctac accctcctgg gcatctacac tgggagtggt gtcctggctg 720
 tcctgatgat agctgcgttc ctccaaccca tacgagatgt tcagcgggaa agtgaaggag 780
 agaagaaatc agtacctttc tgggtccactt tactgtcgac tttcaagcta tatagagata 840
 aacgtctgtg cctcttaatt ctgctgccgc tgtacagtgg attgcagcaa ggattcctct 900
 ccagcgaata cacaagggtcc tatgtcacct gcaccctggg catccagttc gtcggctacg 960
 tgatgatctg cttctcggcc actgacgcgc tgtgtctcgt gttgtatgga aagggtctcg 1020
 agtacacggg cagggctgtg ctgtacgtgc tgggcgcggt gaccacgtg tcctgcatga 1080
 ttgccctact gctgtggaga cctcgtgctg accatctggc agtggtcttc gtattctctg 1140
 gcctgtgggg cgtggcagat gccgtctggc agacacaaaa caatgctctc tacggcgttc 1200
 tgtttgagaa gagcaaggaa gctgccttcg ccaattaccg cctgtgggag gccctgggct 1260
 tcgtcattgc cttcgggtac agcatgtttt tgtgcgtgca cgtcaagctc tacattctgc 1320
 tgggggtcct gagctgacc atggtggcgt atgggcttgt ggagtgcgtg gagtccaaga 1380
 acccgatcag accccacgct ccaggacagg tcaaccaggc agaggatgaa gaaatacaaa 1440
 caaaaatgtg agagcagtga ggtccgagga ggatgaactc agaaagcacc agccagagaa 1500
 ttttcttaga agatgcctca ggacatagag cggctcctca tcaccatctc agcacaattt 1560
 ggccattctg aagagatcat gttatttcac tcttcatgta ttttttcta ttctaacaaa 1620
 ttttctgccc accatcttaa cagagatcaa gtgtatacat gaaggatatca gttcatttaa 1680
 ttttagatgc aaaagaaaaa ggtctaactg acaatcagcc aattagaatt tgcctgaaat 1740
 catagactca ccctagtttt attgctgtag ttgtttttaa gaattggaag cctgcttaaa 1800
 aaatgtagtt gagccccata attttacaaa tgggcgaact tttaaacttc taactctact 1860
 tggatcaaaa cctcatacat tttaaaaagg ggtcctgaca agtcagctga ctcaacctca 1920
 cagagtcagg gggtgacaaa gccagactgg ggctcaggat tcctgaaacg tgtggggctc 1980
 gcgtttctaa ataaagacgg ttatttaatg g 2011

<210> 53
 <211> 2282
 <212> DNA
 <213> Homo sapiens

<400> 53
 gactccgggg cgaccgccgc gagtccgcag tagttcgggc catggaggcg gagccgccgc 60
 tctaccgat ggcgggggct gcggggccgc agggcgacga ggacctgctc ggggtcccgg 120
 acggggccga ggccccgctg gacgagctgg tgggcgcgta ccccaactac aacgaggagg 180
 aggaggagcg ccgctactac cgccgcaagc gcctgggctg gctcaagaac gtgctggctg 240
 ccagcgccgg gggcatgctc acctacggcg tctacctggg cctcctgcag atgcagctga 300

EX05-002patentin.txt

tcctgcacta	cgacgagacc	taccgcgagg	tgaagtatgg	caacatgggg	ctgcccagaca	360
tcgacagcaa	aatgctgatg	ggcatcaacg	tgactcccat	cgccgccctg	ctctacacac	420
ctgtgctcat	caggtttttt	ggaacgaagt	ggatgatggt	cctcgctgtg	ggcatctacg	480
ccctctttgt	ctccaccaac	tactgggagc	gctactacac	gcttgtgccc	tcggctgtgg	540
ccctgggcat	ggccatcgtg	cctctttggg	cttccatggg	caactacatc	accaggatgg	600
cgcagaagta	ccatgagtac	tcccactaca	aggagcagga	tgggcagggg	atgaagcagc	660
ggcctccgcg	gggctcccac	gcgccctatc	tcctgggtctt	ccaagccatc	ttctacagct	720
tcttccatct	gagcttcgcc	tgcgcccagc	tgcccatgat	ttatttcctg	aaccactacc	780
tgtatgacct	gaaccacacg	ctgtacaatg	tgcagagctg	cggcaccaac	agccacggga	840
tcctcagcgg	cttcaacaag	acggttctgc	ggacgctccc	gcggagcggg	aacctcattg	900
tgggtggagag	cgtgctcatg	gcagtggcct	tcctggccat	gctgctgggtg	ctgggtttgt	960
gcggagccgc	ttaccggccc	acggaggaga	tcgatctgcg	cagcgtgggc	tggggcaaca	1020
tcttccagct	gcccttcaag	cacgtgcgtg	actaccgcct	gcgccacctc	gtgcctttct	1080
ttatctacag	cggcttcgag	gtgctctttg	cctgcactgg	tatgccttg	ggctatggcg	1140
tgtgctcggg	ggggctggag	cggctggcct	acctcctcgt	ggcttacagc	ctgggcgcct	1200
cagccgcctc	actcctgggc	ctgctgggcc	tgtggctgcc	acgcccgggtg	cccctggtgg	1260
ccggagcagg	ggtgcacctg	ctgctcacct	tcatcctctt	tttctggggc	cctgtgcctc	1320
gggtcctgca	acacagctgg	atcctctatg	tggcagctgc	cctttggggg	gtgggcagtg	1380
ccctgaacaa	gactggactc	agcacactcc	tgggaatctt	gtacgaagac	aaggagagac	1440
aggacttcat	cttcaccatc	taccactggg	ggcaggctgt	ggccatcttc	accgtgtacc	1500
tgggctcgag	cctgcacatg	aaggctaagc	tggcgggtgct	gctgggtgacg	ctgggtggcg	1560
ccgcggtctc	ctacctgcgg	attgagcaga	agctgcggcg	gggcgtggcc	ccgcgccagc	1620
cccgcattcc	gcggccccag	cacaagggtgc	gcggttaccg	ctacttggag	gaggacaact	1680
cggacgagag	cgacgcggag	ggcgagcatg	gggacggcgc	ggaggaggag	gcgccgccc	1740
cagggcccg	gcctggcccc	gagcccgtg	gactcgggcg	ccggccctgc	ccgtacgaac	1800
aggcgcaggg	gggagacggg	ccggaggagc	agtgaggggc	cgcttgggtc	ccggactcag	1860
cctccctcct	cgccggcctc	agtttaccac	gtctgaggtc	ggggggaccc	cctccgagtc	1920
ccgcgctgtc	ttcaaaggcc	cctgtctccc	ctccccgacg	ttggggacgc	ccctcccaga	1980
gcccagggtca	cctccgggct	tccgcagccc	cctccaaggc	ggagtggagc	cttgggaacc	2040
cctcggccaa	gcacaggggt	tcgaaaatac	agctgaaacc	ccgcggggcc	ttagcacgcg	2100
ccccagcgcc	ggagcacggg	cagggctctt	ttgcgacccg	gcccgtcca	gatccccaca	2160
gctttcggcc	gcggacccgg	gccgcgtgtg	agcgcacttt	gcacctccta	tccccagggg	2220
ccgccgagag	ccacgatttt	ttacagaaaa	tgagcaataa	agagattttg	tactgtcaaa	2280
aa						2282

EX05-002patentin.txt

<210> 54
 <211> 2339
 <212> DNA
 <213> Homo sapiens

<400> 54
 cctgtggtcc cgggtttctg cagagtctac ttcagaagcg gaggcactgg gagtccggtt 60
 tgggattgcc aggctgtggt tgtgagtctg agcttgtgag cggctgtggc gcccgaactc 120
 ttcgccagca tatcatcccg gcaggcgata aactacattc agttgagtct gcaagactgg 180
 gaggaactgg ggtgataaga aatctattca ctgtcaaggt ttattgaagt caaaatgtcc 240
 aaaaaaatca gtggcgggtc tgtggtagag atgcaaggag atgaaatgac acgaatcatt 300
 tgggaattga ttaaagagaa actcattttt ccctacgtgg aattggatct acatagctat 360
 gatttaggca tagagaatcg tgatgccacc aacgaccaag tcaccaagga tgctgcagaa 420
 gctataaaga agcataatgt tggcgtcaaa tgtgccacta tcactcctga tgagaagagg 480
 gttgaggagt tcaagttgaa acaaatgtgg aaatcaccaa atggcaccat acgaaatatt 540
 ctgggtggca cggctctcag agaagccatt atctgcaaaa atatcccccg gcttgtgagt 600
 ggatgggtaa aacctatcat cataggtcgt catgcttatg gggatcaata cagagcaact 660
 gatthttgtt ttcctgggcc tggaaaagta gagataacct acacaccaag tgacggaacc 720
 caaaagggtga catacctggt acataacttt gaagaagggt gtggtgttgc catggggatg 780
 tataatcaag ataagtcaat tgaagatttt gcacacagtt ccttccaaat ggctctgtct 840
 aagggttggc ctttgtatct gagcaccaa aacactattc tgaagaaata tgatgggcgt 900
 tttaaagaca tctttcagga gatatatgac aagcagtaca agtcccagtt tgaagctcaa 960
 aagatctggt atgagcatag gctcatcgac gacatggtgg cccaagctat gaaatcagag 1020
 ggaggcttca tctgggcctg taaaaactat gatggtgacg tgcagtcgga ctctgtggcc 1080
 caagggtatg gctctctcgg catgatgacc agcgtgctgg tttgtccaga tggcaagaca 1140
 gtagaagcag aggctgcccc cgggactgta acccgctact accgcatgta ccagaaagga 1200
 caggagacgt ccaccaatcc cattgcttcc atttttgcct ggaccagagg gtttagccac 1260
 agagcaaagc ttgataacaa taaagagctt gccttctttg caaatgcttt ggaagaagtc 1320
 tctattgaga caattgaggc tggcttcatg accaaggact tggctgcttg cattaaaggt 1380
 ttacccaatg tgcaacgttc tgactacttg aatacatttg agttcatgga taaacttgga 1440
 gaaaacttga agatcaaact agctcaggcc aaactttaag ttcataacctg agctaagaag 1500
 gataattgtc ttttggtaac taggtctaca ggtttacatt tttctgtgtt aactcaagg 1560
 ataaaggcaa aatcaatttt gtaatttgtt tagaagccag agtttatctt ttctataagt 1620
 ttacagcctt tttcttatat atacagttat tgccacctt gtgaacatgg caagggactt 1680
 ttttacaatt tttattttat tttctagtac cagcctagga attcgggttag tactcatttg 1740
 tattcactgt cactttttct catgttctaa ttataaatga ccaaaatcaa gattgctcaa 1800

EX05-002patentin.txt

aagggtaaat gatagccaca gtattgctcc ctaaaatatg cataaagtag aaattcactg	1860
ccttccccctc ctgtccatga ccttgggcac agggaagttc tgggtgcata gatatcccgt	1920
tttgtgaggt agagctgtgc attaaacttg cacatgactg gaacgaagta tgagtgaac	1980
tcaaatgtgt tgaagatact gcagtcattt ttgtaaagac cttgctgaat gtttccaata	2040
gactaaatac tgtttaggcc gcaggagagt ttggaatccg gaataaatac tacctggagg	2100
tttgtcctct ccatttttct ctttctcctc ctggcctggc ctgaatatta tactactcta	2160
aatagcatat ttcattccaag tgcaataatg taagctgaat ctttttttga cttctgctgg	2220
cctgttttat ttcttttata taaatgtgat ttctcagaaa ttgatattaa acactatctt	2280
atcttctcct gaactgttga ttttaattaa aattaagtgc taattaccaa aaaaaaaaa	2339

<210> 55
 <211> 1740
 <212> DNA
 <213> Homo sapiens

<400> 55	
ccagcgtag cccgcggcca ggcagccggg aggagcggcg cgcgctcggc cctctcccgc	60
cctgctcgtt cgctctccag cttgggatgg ccggctacct gcgggtcgtg cgctcgtctt	120
gcagagcctc aggctcgcgg ccggcctggg cgccggcggc cctgacagcc cccacctcgc	180
aagagcagcc gcggcgccac tatgccgaca aaaggatcaa ggtggcgaag cccgtggtgg	240
agatggatgg tgatgagatg acccgattta tctggcagtt catcaaggag aagctcatcc	300
tgccccacgt ggacatccag ctaaagtatt ttgacctcgg gctcccaaac cgtgaccaga	360
ctgatgacca ggtcaccatt gactctgcac tggccaccca gaagtacagt gtggctgtca	420
agtgtgccac catcacccct gatgaggccc gtgtggaaga gttcaagctg aagaagatgt	480
ggaaaagtcc caatggaact atccggaaca tcctgggggg gactgtcttc cgggagccca	540
tcatctgcaa aaacatccca cgcctagtcc ctggctggac caagcccatc accattggca	600
ggcacgcccc tggcgaccag tacaaggcca cagactttgt ggcagaccgg gccggcactt	660
tcaaatggt cttacccca aaagatggca gtggtgtcaa ggagtgggaa gtgtacaact	720
tccccgcagg cggcgtgggc atgggcatgt acaacaccga cgagtccatc tcaggttttg	780
cgcacagctg cttccagtat gccatccaga agaaatggcc gctgtacatg agcaccaaga	840
acaccatact gaaagcctac gatgggcggt tcaaggacat cttccaggag atctttgaca	900
agcactataa gaccgacttc gacaagaata agatctggta tgagcaccgg ctcatgtatg	960
acatggtggc tcaggtcctc aagtcttcgg gtggctttgt gtgggcctgc aagaactatg	1020
acggagatgt gcagtcagac atcctggccc agggcttttg ctcccttggc ctgatgacgt	1080
ccgtcctggt ctgccctgat gggaagacga ttgaggctga ggccgctcat gggaccgtca	1140
cccgcacta tcgggagcac cagaagggcc ggcccaccag caccaacccc atcgccagca	1200
tctttgcctg gacacgtggc ctggagcacc gggggaagct ggatgggaac caagacctca	1260
tcaggtttgc ccagatgctg gagaagggtg gcgtggagac ggtggagagt ggagccatga	1320

EX05-002patentin.txt

ccaaggacct	ggcgggctgc	attcacggcc	tcagcaatgt	gaagctgaac	gagcacttcc	1380
tgaacaccac	ggacttcctc	gacaccatca	agagcaacct	ggacagagcc	ctgggcaggc	1440
agtaggggga	ggcgccaccc	atggctgcag	tggagggggc	agggctgagc	cggcgggtcc	1500
tcctgagcgc	ggcagagggg	gagcctcaca	gccccctctt	ggaggccttt	ctaggggatg	1560
tttttttata	agccagatgt	ttttaaaagc	atatgtgtgt	ttccccctcat	ggtgacgtga	1620
ggcaggagca	gtgcgtttta	cctcagccag	tcagtatgtt	ttgcatactg	taattttatat	1680
tgcccttgga	acacatggtg	ccatatttag	ctactaaaaa	gctcttcaca	aaaaaaaaaa	1740

<210> 56
 <211> 4540
 <212> DNA
 <213> Homo sapiens

<400> 56	
cgctgctggg	ctgcggcggc ggcggcggcg gcggtggtta ctatggcgga gtcggccgga 60
gcctcctcct	tcttccccct tgttgcctc ctgctcgccg gcagcggcgg gtccggggccc 120
cgggggggtcc	aggctctgct gtgtgcgtgc accagctgcc tccaggccaa ctacacgtgt 180
gagacagatg	gggcctgcat ggtttccatt ttcaatctgg atgggatgga gcaccatgtg 240
cgcacctgca	tccccaaagt ggagctggtc cctgccggga agcccttcta ctgcctgagc 300
tcggaggacc	tgcgcaacac cactgctgc taaactgact actgcaacag gatcgacttg 360
agggtgcccc	gtggtcacct caaggagcct gagcaccctg ccatgtgggg cccgggtggag 420
ctggtaggca	tcatcgccgg cccgggtgtt ctcctgttcc tcatcatcat cattgttttc 480
cttgtcatta	actatcatca gcgtgtctat cacaaccgcc agagactgga catggaagat 540
ccctcatgtg	agatgtgtct ctccaaagac aagacgctcc aggatcttgt ctacgatctc 600
tccacctcag	ggtctggctc agggttaccc ctctttgtcc agcgcacagt ggcccgaacc 660
atcgttttac	aagagattat tggcaagggt cggtttgggg aagtatggcg gggccgctgg 720
aggggtggtg	atgtggctgt gaaaatattc tcttctcgtg aagaacggtc ttggttcagg 780
gaagcagaga	tataccagac ggtcatgctg cgccatgaaa acatccttgg atttattgct 840
gctgacaata	aagataatgg cacctggaca cagctgtggc ttgtttctga ctatcatgag 900
cacgggtccc	tgtttgatta tctgaaccgg tacacagtga caattgaggg gatgattaag 960
ctggccttgt	ctgctgctag tgggctggca cacctgcaca tggagatcgt gggcacccaa 1020
gggaagcctg	gaattgctca tcgagactta aagtcaaaga acattctggt gaagaaaaat 1080
ggcatgtgtg	ccatagcaga cctgggcctg gctgtccgtc atgatgcagt cactgacacc 1140
attgacattg	ccccgaatca gaggggtggg accaaacgat acatggcccc tgaagtactt 1200
gatgaaacca	ttaatatgaa acactttgac tcctttaaat gtgctgatat ttatgccctc 1260
gggcttgtat	attgggagat tgctcgaaga tgcaattctg gaggagtcca tgaagaatat 1320
cagctgccat	attacgactt agtgccctct gacccttcca ttgaggaaat gcgaaagggt 1380

EX05-002patentin.txt

gtatgtgatc	agaagctgcg	tcccaacatc	cccaactggt	ggcagagtta	tgaggcactg	1440
cggtgatgg	ggaagatgat	gcgagagtgt	tggtatgcca	acggcgagc	ccgcctgacg	1500
gccctgcgca	tcaagaagac	cctctcccag	ctcagcgtgc	aggaagacgt	gaagatctaa	1560
ctgctccctc	tctccacacg	gagctcctgg	cagcgagaac	tacgcacagc	tgccgcgttg	1620
agcgtacgat	ggaggcctac	ctctcgtttc	tgcccagccc	tctgtggcca	ggagccctgg	1680
cccgcaagag	ggacagagcc	cgggagagac	tcgctcactc	ccatgttggg	tttgagacag	1740
acaccttttc	tatttacctc	ctaattggcat	ggagactctg	agagcgaatt	gtgtggagaa	1800
ctcagtgcc	cacctgaac	tggttgtagt	gggaagtccc	gcgaaacccg	gtgcatctgg	1860
cacgtggcca	ggagccatga	caggggcgct	tgggaggggc	cggaggaacc	gaggtgttgc	1920
cagtgctaag	ctgccctgag	ggtttccttc	ggggaccagc	ccacagcaca	ccaaggtggc	1980
ccggaagaac	cagaagtgca	gccccctctca	caggcagctc	tgagccgcgc	tttccctcc	2040
tccctgggat	ggacgctgcc	gggagactgc	cagtggagac	ggaatctgcc	gctttgtctg	2100
tccagccgtg	tgtgcatgtg	ccgaggtgcg	tccccggtg	tgcttggttc	gtgccatgcc	2160
cttacacgtg	cgtgtgagtg	tgtgtgtgtg	tctgtaggtg	cgcacttacc	tgcttgagct	2220
ttctgtgcat	gtgcaggtcg	ggggtgtggt	cgatcatgctg	tccgtgcttg	ctggtgcctc	2280
ttttcagtag	tgagcagcat	ctagtttccc	tggtgccctt	ccctggaggt	ctctccctcc	2340
cccagagccc	ctcatgccac	agtggctactc	tgtgtctggc	aggctactct	gcccacccca	2400
gcatcagcac	agctctcctc	ctccatctca	gactgtggaa	ccaaagctgg	cccagttgtc	2460
catgacaaaa	gaggcttttg	ggccaaaatg	tgagggtggt	gggtgggatg	ggcagggaa	2520
gaatcctggt	ggaagtcttg	ggtgttagtg	tcagccgtgg	gaaatgagcc	agcccaagg	2580
catcatcctc	agcagcatcg	aggaagggcc	gaggaatgtg	aagccagatc	tcgggactca	2640
gattggaatg	ttacatctgt	ctttcatctc	ccagatcctg	gaaacagcag	tgtatatattt	2700
tggtggtggt	gggtttgggg	tggggaagg	aaggcgggc	aaggagtggg	gaggaggtct	2760
ggggtgggag	ggaggcatct	gcatgggtct	tcttttactg	gactgtctga	tcagggtgga	2820
gggaagggtga	gaggtttgca	tccacttcag	gagccctact	gaagggaaca	gcctgagccg	2880
aacatgttat	ttaacctgag	tatagtattt	aacgaagcct	agaagcacgg	ctgtgggtgg	2940
tgatttggtc	agcatatctt	aggtatataa	taactttgaa	gccataactt	ttaactggag	3000
tggtttgatt	tcttttttta	attttattgg	gagggtttgg	attttaactt	tttttaattg	3060
tgttaaatat	taagtttttg	taaaaggaaa	accatctctg	tgattacctc	tcaatctatt	3120
tgtttttaaa	gaaatcccta	aaaaaaaaaa	ttatccaatt	gaacgcacat	agctcaatca	3180
cactggaaat	gtttgtcggt	gcacctgagc	ctgttccac	tcagcagtga	gagttcctct	3240
ttgccctgag	gctcagtctc	tctcgtattt	tgtccccacc	ccaattcct	tgagtggttt	3300
ttgctctagg	gccctttctt	gcactgtcca	gctgggtgta	ccctctccag	gcattttattc	3360
aacaaatgtg	ggtgaagtgc	ctgctgggtg	ccaggtgctg	ggaatacatc	tgtggacaag	3420

EX05-002patentin.txt

acatgcttgg gtcctactcc tggagcactg taaaaagagc tgattcaagt aagtagatgc	3480
ctgttttgag accagaaggt ttcataattg gttctacgac ccttttgagc ctagaattat	3540
tgttcttata taagatcact gaagaaagag gaacccccac aaccccctcc acaaagagac	3600
caggggcggg tgatgagacc tgggggttag aaccccaggt gagacctcaa atcactgcat	3660
tcattctgag ccccttccct gtccccaggg gaggtgtatt gtgtatgtag ccttagagca	3720
tctctgcctc caaccagca gttctctgcc aaagcttgtg gaggagggag agccctgtcc	3780
ctgccctcag gtcccccagt gtccttgccc cttctattta ttgactgat tattgcttct	3840
ttccttgcat taaaggagat cttcccctaa cctttgggcc aatttactgg ccactaattt	3900
cgtttaaata ccattgtgtc attgggggga ccgtctttac ccctgctgac ctcccaccta	3960
tccgccctgc agcagaacct tggcggttta taggtaatga tggaaactag actcctcttc	4020
ccagagtcac aagtagcctc tgggatctgc caacacacgt ccactcccaa gccactagcc	4080
cactccccag ttggcccttc tgcccttacc ccacacacag tccaactctt ccacctctgg	4140
ggaagatgga gcaggctctt gggaagctcc cacaccacc tctgccactc ttaacactaa	4200
gtgagagttg gggagaaact gaagccgtgt ttttggcccc ccgaggctaa ccctgatcca	4260
tagtgctacc tgcacctctg gattctggat tcacagacca agtccaagcc cgttcttacg	4320
tcgccataaa ggccccgaa cggcattctc ggtacttctg tttgttttg tacattttat	4380
tagaaaggac tgtaaaatag ccacttagac actttacctc ttcagtatgc aaatgtaaat	4440
aaattgtaat ataggaaatc ttttgtttta atataagaat gagcctgtcc aatttctgct	4500
gtacattatt aaaagtttta ttcacaaaaa aaaaaaaaaa	4540

<210> 57
 <211> 3267
 <212> DNA
 <213> Homo sapiens

<400> 57	
ggtcaccgcc cggctgcggg gccagtggca ggagcgccac gcaccgccag ccgcaggggg	60
cgtgggatgg gggcgccgg ggaggggggc gccacactg actagagcca accgcgcact	120
tcaaaagggt gtcggtgccg cgctccctc ccgcggccc ggaacttcaa agcgggcccgt	180
gctgccccgg ctgcctcgt ctgctctggg gcctcgagc cccggcgcg ccgcctggtg	240
gcgatgaccc gggcgctctg ctgagcgctc cgccaggctc tcctgctgct cgagcggcc	300
gccgagctct cgccaggact gaagtgtgta tgtcttttgt gtgattcttc aaactttacc	360
tgccaaacag aaggagcatg ttgggcatca gtcatgctaa ccaatggaaa agagcagggtg	420
atcaaatcct gtgtctccct tccagaactg aatgctcaag tcttctgtca tagttccaac	480
aatgttacca aaaccgaatg ctgcttcaca gatTTTTgca acaacataac actgcacctt	540
ccaacagcat caccaaatgc cccaaaactt ggacccatgg agctggccat cattattact	600
gtgcctgttt gcctcctgtc catagctgcg atgctgacag tatgggcatg ccagggtcga	660
cagtgtcct acaggaagaa aaagagacca aatgtggagg aaccactctc tgagtgcaat	720

EX05-002patentin.txt

ctggtaaatg	ctggaaaaac	tctgaaagat	ctgatttatg	atgtgaccgc	ctctggatct	780
ggctctggtc	tacctctggt	ggttcaaagg	acaattgcaa	ggacgattgt	gcttcaggaa	840
atagtaggaa	aaggtagatt	tggtagggtg	tggcatggaa	gatgggtgtg	ggaagatgtg	900
gctgtgaaaa	tattctcctc	cagagatgaa	agatattggt	ttcgtgaggc	agaaatttac	960
cagacggtca	tgctgcgaca	tgaaaacatc	cttggtttca	ttgctgctga	caacaaagat	1020
aatggaactt	ggactcaact	ttggctggta	tctgaatatc	atgaacaggg	ctccttatat	1080
gactatttga	atagaaatat	agtgaccatg	gctggaatga	tcaagctggc	gctctcaatt	1140
gctagtggtc	tggcacacct	tcatatggag	attgttggta	cacaaggtaa	acctgctatt	1200
gctcatcgag	acataaaatc	aaagaatatc	ttagtaaaaa	agtgtgaaac	ttgtgccata	1260
gcggacttag	ggttggctgt	gaagcatgat	tcaatactga	acactatcga	catacctcag	1320
aatcctaaag	tggaaccaa	gaggtatatg	gctcctgaaa	tgcttgatga	tacaatgaat	1380
gtgaatatct	ttgagtcctt	caaacgagct	gacatctatt	ctgttggtct	ggtttactgg	1440
gaaatagccc	ggagggtgtc	agtcggagga	attgttgagg	agtaccaatt	gccttattat	1500
gacatgggtc	cttcagatcc	ctcgatagag	gaaatgagaa	aggttgtttg	tgaccagaag	1560
tttcgaccaa	gtatcccaaa	ccagtggcaa	agttgtgaag	cactccgagt	catggggaga	1620
ataatgcgtg	agtgttggtg	tgccaacgga	gcggcccgcc	taactgctct	tcgtattaag	1680
aagactatat	ctcaactttg	tgtcaaagaa	gactgcaaag	cctaattgat	ataattatgt	1740
taaaaagaaa	tctctcatag	ctttcttttc	cattttcccc	tttatgtgaa	tgtttttgcc	1800
atTTTTTTTT	tgttctacct	caaagataag	acagtacagt	atttaagtgc	ccataaggca	1860
gcatgaaaag	ataactctaa	agttaagcat	gggcaggagt	tgacttcatc	caatctctat	1920
gttatgttta	atTTTTTTTT	gaaagcaaca	cctcaactca	tctttttatt	taataaggaa	1980
gaaatatatt	acaaaagtat	aaaataagct	ctataaaaa	gttatagtca	ttaagttttt	2040
atTTTacttg	aaccaagagc	acatgaatga	acaggaaaag	atgtaaaaac	atTTTTTTct	2100
gagatgaaaa	catattaatt	aaacatgcaa	attagagcat	gctatcttta	ggtgatgcaa	2160
tctatgtttc	ccccttttta	agttagcagg	actttttaaa	aataaatatt	gctctaaact	2220
ttaatatatc	gaacgtgaga	gtggagctgc	ttagtggaag	atgtaagtga	ggtgggtgtc	2280
ccatgtgctt	ggtctcccc	tctgctgttc	tcctgttctt	cataatccac	tactgcagca	2340
gtccctgaac	cactaaactt	gttcctttca	tttacaaaag	agatacctga	catcctgaga	2400
cactgagaaa	tgctctgaag	tcacacagct	aatggcagaa	ctggcactag	gtccaaatct	2460
tgtgataatg	aacaccgtaa	ggttagctag	cttcctactt	tcccttgaat	agtgtttttc	2520
tccctatgta	atatctttta	ttatgatatt	tgtggtttag	aaggcatatt	gagttatTTT	2580
gcagaatcat	aatggacccg	cacaaaatct	cagaaccata	tctgttgaca	ttttttctca	2640
tagaaatatc	atgggttacc	catttggttaa	tgagcattaa	tgTTTTctga	acacttccaa	2700
agattaatca	aacataaata	ttcattgtct	gaaaatgtct	ttaagataca	attcagaggt	2760

EX05-002patentin.txt

```

ccctattttcc tttgtacata cacacttaga aagaaaagac agaaaaggaa gaggaaggaa 2820
ggaaatattt tgagaatata ttgagaagaa ttaagaaaac tcttcaatga agtgtaaca 2880
accaaaccct` acagacggta tcagaaacag caaatagata ttcctctacc ctttcacagt 2940
gagtgagtga gtacagaaga atgctcatga tagttttgcc ttcattctac tttctgtgga 3000
cacagagtaa tgaatattta atgggacatt aaatatgcc ttcaaacta taattttact 3060
ttggtaaacy agatttaaca tgatgtcttt tatgctccta aaacatcttt tttcaaactc 3120
cattccttag aacattcttc tactgagatg atccaagacc aaaagtgttc tttggtactt 3180
gcttataaag tgatagtaca tgttagcata taatgtattt tgaagagtga agtaaatgct 3240
attgataaca gaaaaaaaaa aaaaaaa 3267

```

```

<210> 58
<211> 2308
<212> DNA
<213> Homo sapiens

```

```

<400> 58
ggcgaggcga ggtttgctgg ggtgaggcag cggcgcggcc gggccgggcc gggccacagg 60
cgggtggcggc gggacatgg aggcggcggc cgctgctccg cgtccccggc tgctcctcct 120
cgtgctggcg gcggcggcgg cggcggcggc ggcgctgctc ccgggggcca cggcggtaca 180
gtgtttctgc cacctctgta caaaagacaa ttttacttgt gtgacagatg ggctctgctt 240
tgtctctgtc acagagacca cagacaaagt tatacacaac agcatgtgta tagctgaaat 300
tgacttaatt cctcgagata ggccgtttgt atgtgcaccc tcttcaaaaa ctgggtctgt 360
gactacaaca tattgctgca atcaggacca ttgcaataaa atagaacttc caactactgt 420
aaagtcacat cctggccttg gtcctgtgga actggcagct gtcattgctg gaccagtgtg 480
cttcgtctgc atctcactca tgttgatggt ctatatctgc cacaaccgca ctgtcattca 540
ccatcgagtg ccaaatgaag aggacccttc attagatcgc ctttttattt cagagggtac 600
tacgttgaaa gacttaattt atgatatgac aacgtcaggt tctggctcag gtttaccatt 660
gcttggtcag agaacaattg cgagaactat tgtgttaca gaaagcattg gcaaaggctc 720
atgtggagaa gtttgagag gaaagtggcg gggagaagaa gttgctgtta agatattctc 780
ctctagagaa gaacgttcgt ggttccgtga ggcagagatt tatcaaactg taatgttacg 840
tcatgaaaac atcctgggat ttatagcagc agacaataaa gacaatggta cttggactca 900
gctctgggtg gtgtcagatt atcatgagca tggatccctt tttgattact taaacagata 960
cacagttact gtggaaggaa tgataaaact tgctctgtcc acggcgagcg gtcttgccca 1020
tcttcacatg gagattgttg gtacccaagg aaagccagcc attgctcata gagatttgaa 1080
atcaaagaat atcttggtta agaagaatgg aacttgctgt attgcagact taggactggc 1140
agtaagacat gattcagcca cagataccat tgatattgct ccaaaccaca gagtgggaac 1200
aaaaaggtag atggcccctg aagttctcga tgattccata aatatgaaac attttgaatc 1260

```

EX05-002patentin.txt

```

cttcaaacgt gctgacatct atgcaatggg cttagtattc tgggaaattg ctcgacgatg 1320
ttccattggg ggaattcatg aagattacca actgccttat tatgatcttg taccttctga 1380
cccatcagtt gaagaaatga gaaaagtgtg ttgtgaacag aagttaaggc caaatatccc 1440
aaacagatgg cagagctgtg aagccttgag agtaatggct aaaattatga gagaatgttg 1500
gtatgccaat ggagcagcta ggcttacagc attgcggtt aagaaaacat tatcgcaact 1560
cagtcaacag gaaggcatca aaatgtaatt ctacagcttt gcctgaactc tccttttttc 1620
ttcagatctg ctcttggtt ttaatttggg aggtcagttg ttctacctca ctgagagggg 1680
acagaaggat attgcttcct tttgcagcag tgtaataaag tcaattaaaa acttcccagg 1740
atttctttgg acccaggaaa cagccatgtg ggtcctttct gtgcactatg aacgcttctt 1800
tcccaggaca gaaaatgtgt agtctacctt ttttttttat taacaaaact tgttttttaa 1860
aaagatgatt gctggtctta actttaggta actctgctgt gctggagatc atctttaagg 1920
gcaaaggagt tggattgctg aattacaatg aaacatgtct tattactaaa gaaagtgatt 1980
tactcctggg tagtacattc tcagaggatt ctgaaccact agagtttcct tgattcagac 2040
tttgaatgta ctgttctata gtttttcagg atcttaaaac taacacttat aaaactctta 2100
tcttgagtct aaaaatgacc tcatatagta gtgaggaaca taattcatgc aattgtatct 2160
tgtatactat tattgttctt tcacttattc agaacattac atgccttcaa aatgggattg 2220
tactatacca gtaagtgcc cttctgtgtc tttctaattg aaatgagtag aattgctgaa 2280
agtctctatg ttaaaaccta tagtgttt 2308

```

<210> 59
<211> 5131
<212> DNA
<213> Homo sapiens

```

<400> 59
gaagtgggccc tggcaccttc ccggcctgcc gcagggatgg ggcagctgtg ctggctgccg 60
ctgctggcac cgctcctgtt gctgcgaccg ccaggggtcc agtccgccgg ccccatccgg 120
gccttcgtgg tgccccacag ccacatggac gtgggctggg tctacactgt gcaggaaagc 180
atgcgggcgt acgccgcaa tgtctacacc tcagtgtggg aagagctggc ccgcggccag 240
cagcggcggg tcatcgctgt ggagcaggag tttttccggc tgtggtggga tggcgtcgcc 300
tcggaccagc agaaatacca ggtccgccag ctctggagg aaggacgcct ggaatttgtc 360
atcgagggcc aggtcatgca tgacgaggct gtgacgcacc ttgatgacca gatcctgcag 420
ctcacagaag gacacgggtt tctctatgaa acatttggga tccggccaca gttctcctgg 480
cacgttgacc cgtttgccgc ctctgccacg acgcccaccc tatttgcgct ggcgggcttc 540
aatgccacc tcggctcccc gatcgactac gacctgaagg cagccatgca ggaggcccgg 600
gggctgcagt tcgtgtggcg agggccccca tccctctcag agcggcagga aatcttcacg 660
cacatcatgg accagtacag ctactgcacc ccgtcccaca tccctttctc caacaggtca 720
ggattttact ggaatggcgt ggctgtcttc cccaagcctc cccaagatgg ggtgtacccc 780

```

EX05-002patentin.txt

aacatgagtg	agcctgtcac	cccagccaac	atcaacctct	atgccgaggc	cctggtggcc	840
aacgtgaagc	agagggccgc	ctggttccgc	acaccgcacg	tcctctggcc	ctggggatgt	900
gacaagcagt	tcttcaatgc	ctcgggtgcag	tttgccaaca	tggacccgct	gctggaccac	960
atcaacagcc	atgctgccga	gctcgggtgc	tcgggtgcagt	atgccacgct	gggcgactac	1020
ttccgtgccc	tgcacgctct	caatgtcacc	tggcgtgtcc	gcgaccacca	cgacttcctg	1080
ccctattcca	cagaaccatt	ccaggcctgg	acgggcttct	acacgtcccg	cagctcactg	1140
aaggggctgg	cccggcgagc	cagcgccttg	ttgtatgccg	gggagtccat	gttcacacgc	1200
tacctgtggc	cggccccccg	tgggcatctg	gaccccacct	gggccctgca	gcagctccag	1260
cagcttcgct	gggccgtctc	cgagggtccag	caccatgatg	ccatcactgg	gactgagtcc	1320
cccaagggtga	gagacatgta	cgcaacgcac	ctggcctcgg	ggatgctggg	catgcgcaag	1380
ctgatggcct	ccatcgctct	agatgagctc	cagccccagg	cacccatggc	ggccagctcc	1440
gatgcaggac	ctgcaggaca	ttttgcctcg	gtctacaacc	cgctggcctg	gacggtcacc	1500
accatcgta	ccctgactgt	tggtttccct	ggagtccgcg	tcacagatga	ggcggggcac	1560
ccagtgccct	cgcagatcca	gaactcaaca	gagaccccat	ctgcgtatga	cctgcttatt	1620
ctgaccacaa	tcccaggcct	cagttaccgg	cactacaaca	tcagaccac	tgcagggggc	1680
caagagggca	cccaggagcc	ggctgccact	gtggcgagca	cccttcaatt	tggccgcagg	1740
ctgaggagac	gcaccagcca	tgcgggcagg	tacttggtgc	ctgtggcaaa	cgactgctac	1800
attgtgctgc	tcgaccagga	taccaacctg	atgcacagca	tctgggagag	acagagtaac	1860
cgaacgggtgc	gcgtgaccca	ggaattcctg	gagtaccacg	tcaacgggga	tgtgaaacag	1920
ggccccatth	ccgataacta	cctgttcaca	ccgggcaagg	ccgcggtgcc	tgcgtgggaa	1980
gctgtggaaa	tggagattgt	ggcgggacag	cttgtgactg	agatccggca	gtactttctac	2040
aggaacatga	cagcacagaa	ttacacgtat	gcaatccgct	cccggctcac	ccatgtgccg	2100
cagggccatg	acggggagct	gctctgccac	cggatagagc	aggagtacca	agccggcccc	2160
ctggagctga	accgtgaggc	tgtcctgagg	accagcacca	acctaaccag	ccagcaggctc	2220
atctactcag	acaacaacgg	ctaccagatg	cagcggaggc	cctacgtttc	ctatgtgaac	2280
aacagcatcg	cccgaatta	ctaccccatg	gttcagtcgg	ccttcatgga	ggatggcaaa	2340
agcaggcttg	tgttgctgtc	ggagcgggca	catggcatct	ccagccaagg	gaatgggcag	2400
gtggaggctca	tgtccaccgc	gcggctgtgg	aacaacttcg	actgggacct	gggctacaac	2460
ctcacgctga	acgacacctc	agtcgtccac	ccagtgtctt	ggcttctgct	gggatcctgg	2520
tccctcacca	ctgccctgcg	ccagaggagc	gactggcgcc	tgcagcacag	gcccgtgggtg	2580
ctgttcggag	acctcgctgg	gactgcggcg	aagctcccag	gaccccagca	gcaagaggcc	2640
gtgacgctgc	ccccgaatct	tcacctgcag	atcctgagca	tccctggctg	gcgctacagc	2700
tccaaccaca	cggagcactc	tcagaatctc	cggaaaggcc	atcgagggga	agcccaggct	2760
gacctccgcc	gtgtcctgct	gcggctctac	cacctatatg	aagtgggcga	ggacccagtc	2820

EX05-002patentin.txt

ctgtctcagc	cagtgcagct	gaatctggag	gctgtgctgc	aggcgctggg	gtccgtggtg	2880
gcagtggagg	agcgctcgct	cacagggacc	tgggatttga	gcatgctgca	ccgctggagc	2940
tggaggacgg	ggcctggccg	ccacagaggt	gacaccacct	ctccctcgag	gccaccagga	3000
ggcccatca	tcaccgtcca	cccaaaggaa	atccggacgt	tctttattca	ctttcaacag	3060
cagtgcagccc	tgggcagatg	ccccggcccc	agggttccc	ccaggaactc	catgtaacag	3120
aacagaccca	ggacagggaa	aagcagtgcg	gagggatggg	actggggagt	cagctgctca	3180
tctgcaggct	aatggcagga	aatggtcata	tttggggttt	ttccctaatt	tttttaaaca	3240
aaaattacat	tacaagatcc	aggttcttcc	ccccacact	caatcaagcc	agccctctcc	3300
tcttctgtca	cgtaaaggat	atttggcaca	ctcatgcgtc	attcattcac	aaaacacaaa	3360
cccaggactt	tctgcctaag	gcagagcaca	agactcacag	cagcaccgaa	gcgcatctgc	3420
cgccccggcc	ctgccaggct	tgccaggctg	ccagtggtaa	ctgtggacct	actgcgtgcc	3480
acgtgttttc	atagactcat	cccatgctgg	caacagccct	gcaaggggct	tggctctgcc	3540
acagggcagg	agaggaagtt	gtagcgccca	gcgagagtcc	cagccccaga	cgccacctg	3600
tgccctcagg	caccgcctgc	cgagcagaga	aggcacagca	gccgtcagag	tccatgagag	3660
gtgaaaccac	acagcagggg	tgtccaatat	cagaactatt	aatatcaata	aaagtataac	3720
cttcccagg	ctatgcccc	gagaattgaa	aacatccatc	cacacaatac	ctgtgctccc	3780
gcgttcatag	cagcattact	caaaagtcaa	acggtagcaa	caacccaaat	gtccatccac	3840
agatgaatta	agacatgaag	tgtgttctgt	ccatacaatg	gaatattatt	tggccataaa	3900
aaggaaggaa	attctgacgc	atgccacagc	ctgagtgaat	cctacaaata	ttacgctaag	3960
tgaagaagc	caatcacgag	tttatgtgaa	atgtccagaa	taggcaaatc	tgtgtatcag	4020
agacaaagca	cattggtggt	tgccagggtac	tggaggaaga	gagaagaggc	atgacagcta	4080
acagggacgg	gctttctttg	gaagatgatg	aaattgtgga	atgatggttg	cacaactttg	4140
tgaatatact	agaaaccaat	gaattaaaaa	ctttggaaga	tgaattttat	ggtctgtgaa	4200
ttatatctca	attttaaaac	tttttttttt	ttttcccag	acagagtctc	actctgtcgc	4260
ccaggctgga	gtgcagtgtc	aagatctcag	ctcactgcga	cctgcacctc	ctgggttcaa	4320
gcaattctcc	agcctctgcc	tcccagtag	ctgctactag	agatgcacca	ctgcgtcagc	4380
taatttttgt	atttttagta	gagacgggga	ttcaccatgt	tggccaggct	gatctggaac	4440
tcctgacctc	aggatgatctg	cctgccccgg	cctcccaaag	tgccaggatt	acaggcgtga	4500
gccaatgtgc	ccggcctaaa	ccgttttaaa	gagtaaaactg	taagatgtag	gaaattattt	4560
ggtactctag	ggctgaagga	aagtaccag	aaaggaccag	cttggaagga	gtcagacctc	4620
tggacaacgt	gcagtttggc	caccagacag	caaagacagt	ctctggtttg	gccaggcagg	4680
agctgggctg	gagttgctga	ccaagcaata	ggccaccctt	gtgaggtggg	gtcaggtgag	4740
cagccaccag	aggcatggat	gtgcagtggg	aggttgaggc	acaaggagtg	aggcaggagc	4800
cctttagagc	atgtgggctg	catgaggctt	ggtttctgtg	tcaagaagac	tatggaggct	4860

EX05-002patentin.txt

gggcagtggg	tcatgcctta	atcccagcac	tttgggaggg	caaagcaacc	ggatcactgg	4920
tggtcagtag	ttcaagacca	ggctggccaa	catggtgaaa	ccccatctct	actaaaaata	4980
caaagttaac	cgggtgtggg	ggtgtgcgcc	tgtagtccca	gctactcggg	aggctgaggg	5040
aggagaatca	atcacttgaa	cctgggaggg	ggaggagacc	tccgcctctg	cactccagcc	5100
tgggtgacaa	gagtgagact	ccgtctcaaa	a			5131

<210> 60
 <211> 2020
 <212> DNA
 <213> Homo sapiens

<400> 60						
gcgcagaggc	gtcacgcact	ccatggtaac	gacgctcggc	ccgaagatgg	cggccgaatg	60
gggcggagga	gtgggttact	cgggctcagg	cccgggcccg	agccggtggc	gctggagcgg	120
gtctgtgtgg	gtccgaagcg	ttttactcct	gttgggcccg	ctccgggcca	gcgccacatc	180
tactcccgtc	tccttgggca	gttccccctc	ctgccggcac	cacgtcccct	ctgacactga	240
ggtcataaat	aaagttcatc	ttaaggcaaa	tcatgtggtc	aagagagatg	ttgatgagca	300
tttaagaatc	aagactgtct	atgataaaaag	tgttgaagag	ttgctccctg	agaaaaagaa	360
tcttgtaaag	aacaagcttt	tcccacaagc	gatttcttat	ttagagaaga	cttttcaggt	420
ccgtcgacct	gcgggcacta	tcttacttag	cagacaatgt	gcaacaaacc	aatacctccg	480
gaaggaaaaac	gatcctcaca	ggtactgcac	cggggagtg	gccgcacaca	caaagtgcgg	540
ccccgttatt	gttcctgagg	aacatctcca	gcaatgccgg	gtctaccgtg	ggggtaagtg	600
gcctcatgga	gcagtgggtg	tgccagacca	agaaggcatc	tcagatgcag	actttgttct	660
ttacgttggg	gctctggcca	ccgagagatg	cagccatgaa	aacatcatct	cttatgcagc	720
ctattgtcag	caggaagcaa	acatggacag	gccaatagca	ggatatgcta	acctgtgtcc	780
aaatatgatc	tctaccacag	ctcaggagtt	tgttgggatg	ctgtccacag	tgaacatga	840
ggttattcat	gccctgggtt	tctctgctgg	gctgtttgca	ttctaccatg	ataaagatgg	900
aaatcctctc	acttcaagat	ttgcagatgg	cctccacctt	tttaattata	gtctgggatt	960
atatcaatgg	agtgataaag	tagttcgaaa	agtgagagaa	ttatgggatg	ttcgagataa	1020
taagatagtt	cgtcacactg	tgtatctcct	ggtaacgcct	cgtgttggtg	aggaagcacg	1080
aaaacatttt	gattgtccag	ttctagaggg	aatggaactt	gaaaatcaag	gtggtgtggg	1140
cactgagctc	aaccattggg	aaaaaagggt	attagagaat	gaagcgatga	ctggttctca	1200
cactcagaat	cgagtactct	ctcgaatcac	tctggcatta	atggaggaca	ctgggagaca	1260
gatgctgagc	ccttactgtg	acacgctcag	aagtaaccca	ctgcagctaa	cttgagaca	1320
ggaccagaga	gcagttgccg	tgtgtaattt	gcagaagttc	cctaagcctt	taccacagga	1380
atatcagtac	tttgatgaac	tcagtggaa	acctgcagaa	gatttgcctt	attatggtgg	1440
ctccgtggaa	attgctgact	actgcccttt	cagtcaggaa	ttcagttggc	atttaagtgg	1500

EX05-002patentin.txt

tgaatatcag cgcagctcag attgtagaat attggaaaat caaccagaaa tttttaagaa 1560
 ctatggcgct gaaaagtatg gacctcattc cgtttgtcta attcagaaat cagcattcgt 1620
 tatggagaag tgtgagaaga agctgagtta cccagactgg ggaagcggat gctatcaggt 1680
 ttcttgttct cctcaaggctc tgaaagtttg ggtccaagat acttcatatt tgtgtagtcg 1740
 ggctgggcag gtcctccctg tcagtatcca gatgaatggc tggattcacg atggaaacct 1800
 gctctgcccc tcatgttggg acttctgtga gctctgtcct ccagaaacag atcctccagc 1860
 cactaacctg acccgagctc tgccacttga tctttgttcc tgttcctcga gcctggtggt 1920
 caccctctgg cttctgctag gcaatctggt tcctctgctg gctggatttc ttctgtgtat 1980
 atggcactag gaatggaaaa gtggatcttc aagatattct 2020

<210> 61
 <211> 1203
 <212> PRT
 <213> Homo sapiens

<400> 61

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

Leu Gly Leu Gly Leu Gly Leu Gly Leu Cys Gly Lys Gln Gly Pro Ala
 20 25 30

Thr Pro Ala Pro Glu Pro Ser Arg Ala Pro Ala Ser Leu Leu Pro Pro
 35 40 45

Ala Pro Glu His Ser Pro Pro Ser Ser Pro Leu Thr Gln Pro Pro Glu
 50 55 60

Gly Pro Lys Phe Pro Arg Val Lys Asn Trp Glu Val Gly Ser Ile Thr
 65 70 75 80

Tyr Asp Thr Leu Ser Ala Gln Ala Gln Gln Asp Gly Pro Cys Thr Pro
 85 90 95

Arg Arg Cys Leu Gly Ser Leu Val Phe Pro Arg Lys Leu Gln Gly Arg
 100 105 110

Pro Ser Pro Gly Pro Pro Ala Pro Glu Gln Leu Leu Ser Gln Ala Arg
 115 120 125

Asp Phe Ile Asn Gln Tyr Tyr Ser Ser Ile Lys Arg Ser Gly Ser Gln
 130 135 140

Ala His Glu Gln Arg Leu Gln Glu Val Glu Ala Glu Val Ala Ala Thr
 145 150 155 160

Gly Thr Tyr Gln Leu Arg Glu Ser Glu Leu Val Phe Gly Ala Lys Gln
 165 170 175

EX05-002patentin.txt

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

EX05-002patentin.txt

Val Pro Pro Ile Ser Gly Ser Leu Thr Pro Val Phe His Gln Glu Met
 450 455 460
 Val Asn Tyr Phe Leu Ser Pro Ala Phe Arg Tyr Gln Pro Asp Pro Trp
 465 470 475 480
 Lys Gly Ser Ala Ala Lys Gly Thr Gly Ile Thr Arg Lys Lys Thr Phe
 485 490 495
 Lys Glu Val Ala Asn Ala Val Lys Ile Ser Ala Ser Leu Met Gly Thr
 500 505 510
 Val Met Ala Lys Arg Val Lys Ala Thr Ile Leu Tyr Gly Ser Glu Thr
 515 520 525
 Gly Arg Ala Gln Ser Tyr Ala Gln Gln Leu Gly Arg Leu Phe Arg Lys
 530 535 540
 Ala Phe Asp Pro Arg Val Leu Cys Met Asp Glu Tyr Asp Val Val Ser
 545 550 555 560
 Leu Glu His Glu Thr Leu Val Leu Val Val Thr Ser Thr Phe Gly Asn
 565 570 575
 Gly Asp Pro Pro Glu Asn Gly Glu Ser Phe Ala Ala Ala Leu Met Glu
 580 585 590
 Met Ser Gly Pro Tyr Asn Ser Ser Pro Arg Pro Glu Gln His Lys Ser
 595 600 605
 Tyr Lys Ile Arg Phe Asn Ser Ile Ser Cys Ser Asp Pro Leu Val Ser
 610 615 620
 Ser Trp Arg Arg Lys Arg Lys Glu Ser Ser Asn Thr Asp Ser Ala Gly
 625 630 635 640
 Ala Leu Gly Thr Leu Arg Phe Cys Val Phe Gly Leu Gly Ser Arg Ala
 645 650 655
 Tyr Pro His Phe Cys Ala Phe Ala Arg Ala Val Asp Thr Arg Leu Glu
 660 665 670
 Glu Leu Gly Gly Glu Arg Leu Leu Gln Leu Gly Gln Gly Asp Glu Leu
 675 680 685
 Cys Gly Gln Glu Glu Ala Phe Arg Gly Trp Ala Gln Ala Ala Phe Gln
 690 695 700
 Ala Ala Cys Glu Thr Phe Cys Val Gly Glu Asp Ala Lys Ala Ala Ala
 705 710 715 720

EX05-002patentin.txt

Arg Asp Ile Phe Ser Pro Lys Arg Ser Trp Lys Arg Gln Arg Tyr Arg
 725 730 735
 Leu Ser Ala Gln Ala Glu Gly Leu Gln Leu Leu Pro Gly Leu Ile His
 740 745 750
 Val His Arg Arg Lys Met Phe Gln Ala Thr Ile Arg Ser Val Glu Asn
 755 760 765
 Leu Gln Ser Ser Lys Ser Thr Arg Ala Thr Ile Leu Val Arg Leu Asp
 770 775 780
 Thr Gly Gly Gln Glu Gly Leu Gln Tyr Gln Pro Gly Asp His Ile Gly
 785 790 795 800
 Val Cys Pro Pro Asn Arg Pro Gly Leu Val Glu Ala Leu Leu Ser Arg
 805 810 815
 Val Glu Asp Pro Pro Ala Pro Thr Glu Pro Val Ala Val Glu Gln Leu
 820 825 830
 Glu Lys Gly Ser Pro Gly Gly Pro Pro Gly Trp Val Arg Asp Pro
 835 840 845
 Arg Leu Pro Pro Cys Thr Leu Arg Gln Ala Leu Thr Phe Phe Leu Asp
 850 855 860
 Ile Thr Ser Pro Pro Ser Pro Gln Leu Leu Arg Leu Leu Ser Thr Leu
 865 870 875 880
 Ala Glu Glu Pro Arg Glu Gln Gln Glu Leu Glu Ala Leu Ser Gln Asp
 885 890 895
 Pro Arg Arg Tyr Glu Glu Trp Lys Trp Phe Arg Cys Pro Thr Leu Leu
 900 905 910
 Glu Val Leu Glu Gln Phe Pro Ser Val Ala Leu Pro Ala Pro Leu Leu
 915 920 925
 Leu Thr Gln Leu Pro Leu Leu Gln Pro Arg Tyr Tyr Ser Val Ser Ser
 930 935 940
 Ala Pro Ser Thr His Pro Gly Glu Ile His Leu Thr Val Ala Val Leu
 945 950 955 960
 Ala Tyr Arg Thr Gln Asp Gly Leu Gly Pro Leu His Tyr Gly Val Cys
 965 970 975
 Ser Thr Trp Leu Ser Gln Leu Lys Pro Gly Asp Pro Val Pro Cys Phe
 980 985 990

EX05-002patentin.txt

Ile Arg Gly Ala Pro Ser Phe Arg Leu Pro Pro Asp Pro Ser Leu Pro
 995 1000 1005

Cys Ile Leu Val Gly Pro Gly Thr Gly Ile Ala Pro Phe Arg Gly
 1010 1015 1020

Phe Trp Gln Glu Arg Leu His Asp Ile Glu Ser Lys Gly Leu Gln
 1025 1030 1035

Pro Thr Pro Met Thr Leu Val Phe Gly Cys Arg Cys Ser Gln Leu
 1040 1045 1050

Asp His Leu Tyr Arg Asp Glu Val Gln Asn Ala Gln Gln Arg Gly
 1055 1060 1065

Val Phe Gly Arg Val Leu Thr Ala Phe Ser Arg Glu Pro Asp Asn
 1070 1075 1080

Pro Lys Thr Tyr Val Gln Asp Ile Leu Arg Thr Glu Leu Ala Ala
 1085 1090 1095

Glu Val His Arg Val Leu Cys Leu Glu Arg Gly His Met Phe Val
 1100 1105 1110

Cys Gly Asp Val Thr Met Ala Thr Asn Val Leu Gln Thr Val Gln
 1115 1120 1125

Arg Ile Leu Ala Thr Glu Gly Asp Met Glu Leu Asp Glu Ala Gly
 1130 1135 1140

Asp Val Ile Gly Val Leu Arg Asp Gln Gln Arg Tyr His Glu Asp
 1145 1150 1155

Ile Phe Gly Leu Thr Leu Arg Thr Gln Glu Val Thr Ser Arg Ile
 1160 1165 1170

Arg Thr Gln Ser Phe Ser Leu Gln Glu Arg Gln Leu Arg Gly Ala
 1175 1180 1185

Val Pro Trp Ala Phe Asp Pro Pro Gly Ser Asp Thr Asn Ser Pro
 1190 1195 1200

<210> 62
 <211> 331
 <212> PRT
 <213> Homo sapiens

<400> 62

Met Glu Thr Val Ile Ser Ser Asp Ser Ser Pro Ala Val Glu Asn Glu
 1 5 10 15

EX05-002patentin.txt

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

EX05-002patentin.txt

Ile Asn Arg Leu Val Glu Ala Glu Val His Arg Leu Val Val Val Asp
 290 295 300

Glu Asn Asp Val Val Lys Gly Ile Val Ser Leu Ser Asp Ile Leu Gln
 305 310 315 320

Ala Leu Val Leu Thr Gly Gly Glu Lys Lys Pro
 325 330

<210> 63
 <211> 569
 <212> PRT
 <213> Homo sapiens
 <400> 63

Met Gly Ser Ala Val Met Asp Thr Lys Lys Lys Lys Asp Val Ser Ser
 1 5 10 15

Pro Gly Gly Ser Gly Gly Lys Lys Asn Ala Ser Gln Lys Arg Arg Ser
 20 25 30

Leu Arg Val His Ile Pro Asp Leu Ser Ser Phe Ala Met Pro Leu Leu
 35 40 45

Asp Gly Asp Leu Glu Gly Ser Gly Lys His Ser Ser Arg Lys Val Asp
 50 55 60

Ser Pro Phe Gly Pro Gly Ser Pro Ser Lys Gly Phe Phe Ser Arg Gly
 65 70 75 80

Pro Gln Pro Arg Pro Ser Ser Pro Met Ser Ala Pro Val Arg Pro Lys
 85 90 95

Thr Ser Pro Gly Ser Pro Lys Thr Val Phe Pro Phe Ser Tyr Gln Glu
 100 105 110

Ser Pro Pro Arg Ser Pro Arg Arg Met Ser Phe Ser Gly Ile Phe Arg
 115 120 125

Ser Ser Ser Lys Glu Ser Ser Pro Asn Ser Asn Pro Ala Thr Ser Pro
 130 135 140

Gly Gly Ile Arg Phe Phe Ser Arg Ser Arg Lys Thr Ser Gly Leu Ser
 145 150 155 160

Ser Ser Pro Ser Thr Pro Thr Gln Val Thr Lys Gln His Thr Phe Pro
 165 170 175

Leu Glu Ser Tyr Lys His Glu Pro Glu Arg Leu Glu Asn Arg Ile Tyr
 180 185 190

EX05-002patentin.txt

Ala Ser Ser Ser Pro Pro Asp Thr Gly Gln Arg Phe Cys Pro Ser Ser
 195 200 205

Phe Gln Ser Pro Thr Arg Pro Pro Leu Ala Ser Pro Thr His Tyr Ala
 210 215 220

Pro Ser Lys Ala Ala Ala Leu Ala Ala Ala Leu Gly Pro Ala Glu Ala
 225 230 235 240

Gly Met Leu Glu Lys Leu Glu Phe Glu Asp Glu Ala Val Glu Asp Ser
 245 250 255

Glu Ser Gly Val Tyr Met Arg Phe Met Arg Ser His Lys Cys Tyr Asp
 260 265 270

Ile Val Pro Thr Ser Ser Lys Leu Val Val Phe Asp Thr Thr Leu Gln
 275 280 285

Val Lys Lys Ala Phe Phe Ala Leu Val Ala Asn Gly Val Arg Ala Ala
 290 295 300

Pro Leu Trp Glu Ser Lys Lys Gln Ser Phe Val Gly Met Leu Thr Ile
 305 310 315 320

Thr Asp Phe Ile Asn Ile Leu His Arg Tyr Tyr Lys Ser Pro Met Val
 325 330 335

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

Tyr Leu Gln Glu Thr Phe Lys Pro Leu Val Asn Ile Ser Pro Asp Ala
 355 360 365

Ser Leu Phe Asp Ala Val Tyr Ser Leu Ile Lys Asn Lys Ile His Arg
 370 375 380

Leu Pro Val Ile Asp Pro Ile Ser Gly Asn Ala Leu Tyr Ile Leu Thr
 385 390 395 400

His Lys Arg Ile Leu Lys Phe Leu Gln Leu Phe Met Ser Asp Met Pro
 405 410 415

Lys Pro Ala Phe Met Lys Gln Asn Leu Asp Glu Leu Gly Ile Gly Thr
 420 425 430

Tyr His Asn Ile Ala Phe Ile His Pro Asp Thr Pro Ile Ile Lys Ala
 435 440 445

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

EX05-002patentin.txt

Glu Ser Gly Lys Val Val Asp Ile Tyr Ser Lys Phe Asp Val Ile Asn
 465 470 475 480

Leu Ala Ala Glu Lys Thr Tyr Asn Asn Leu Asp Ile Thr Val Thr Gln
 485 490 495

Ala Leu Gln His Arg Ser Gln Tyr Phe Glu Gly Val Val Lys Cys Asn
 500 505 510

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

Val His Arg Leu Val Val Val Asn Glu Ala Asp Ser Ile Val Gly Ile
 530 535 540

Ile Ser Leu Ser Asp Ile Leu Gln Ala Leu Ile Leu Thr Pro Ala Gly
 545 550 555 560

Ala Lys Gln Lys Glu Thr Glu Thr Glu
 565

<210> 64
 <211> 492
 <212> PRT
 <213> Homo sapiens

<400> 64

Met Glu Pro Gly Leu Glu His Ala Leu Arg Arg Thr Pro Ser Trp Ser
 1 5 10 15

Ser Leu Gly Gly Ser Glu His Gln Glu Met Ser Phe Leu Glu Gln Glu
 20 25 30

Asn Ser Ser Ser Trp Pro Ser Pro Ala Val Thr Ser Ser Ser Glu Arg
 35 40 45

Ile Arg Gly Lys Arg Arg Ala Lys Ala Leu Arg Trp Thr Arg Gln Lys
 50 55 60

Ser Val Glu Glu Gly Glu Pro Pro Gly Gln Gly Glu Gly Pro Arg Ser
 65 70 75 80

Arg Pro Ala Ala Glu Ser Thr Gly Leu Glu Ala Thr Phe Pro Lys Thr
 85 90 95

Thr Pro Leu Ala Gln Ala Asp Pro Ala Gly Val Gly Thr Pro Pro Thr
 100 105 110

Gly Trp Asp Cys Leu Pro Ser Asp Cys Thr Ala Ser Ala Ala Gly Ser
 115 120 125

Ser Thr Asp Asp Val Glu Leu Ala Thr Glu Phe Pro Ala Thr Glu Ala
 Page 113

EX05-002patentin.txt

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

EX05-002patentin.txt

405

410

415

Val Gly Glu Ala Leu Arg Lys Arg Thr Leu Cys Leu Glu Gly Val Leu
 420 425 430

Ser Cys Gln Pro His Glu Ser Leu Gly Glu Val Ile Asp Arg Ile Ala
 435 440 445

Arg Glu Gln Val His Arg Leu Val Leu Val Asp Glu Thr Gln His Leu
 450 455 460

Leu Gly Val Val Ser Leu Ser Asp Ile Leu Gln Ala Leu Val Leu Ser
 465 470 475 480

Pro Ala Gly Ile Asp Pro Ser Gly Pro Glu Lys Ile
 485 490

<210> 65
 <211> 1153
 <212> PRT
 <213> Homo sapiens

<400> 65

Met Ala Cys Pro Trp Lys Phe Leu Phe Lys Thr Lys Phe His Gln Tyr
 1 5 10 15

Ala Met Asn Gly Glu Lys Asp Ile Asn Asn Asn Val Glu Lys Ala Pro
 20 25 30

Cys Ala Thr Ser Ser Pro Val Thr Gln Asp Asp Leu Gln Tyr His Asn
 35 40 45

Leu Ser Lys Gln Gln Asn Glu Ser Pro Gln Pro Leu Val Glu Thr Gly
 50 55 60

Lys Lys Ser Pro Glu Ser Leu Val Lys Leu Asp Ala Thr Pro Leu Ser
 65 70 75 80

Ser Pro Arg His Val Arg Ile Lys Asn Trp Gly Ser Gly Met Thr Phe
 85 90 95

Gln Asp Thr Leu His His Lys Ala Lys Gly Ile Leu Thr Cys Arg Ser
 100 105 110

Lys Ser Cys Leu Gly Ser Ile Met Thr Pro Lys Ser Leu Thr Arg Gly
 115 120 125

Pro Arg Asp Lys Pro Thr Pro Pro Asp Glu Leu Leu Pro Gln Ala Ile
 130 135 140

Glu Phe Val Asn Gln Tyr Tyr Gly Ser Phe Lys Glu Ala Lys Ile Glu
 145 150 155 160

EX05-002patentin.txt

Glu His Leu Ala Arg Val Glu Ala Val Thr Lys Glu Ile Glu Thr Thr
 165 170 175

Gly Thr Tyr Gln Leu Thr Gly Asp Glu Leu Ile Phe Ala Thr Lys Gln
 180 185 190

Ala Trp Arg Asn Ala Pro Arg Cys Ile Gly Arg Ile Gln Trp Ser Asn
 195 200 205

Leu Gln Val Phe Asp Ala Arg Ser Cys Ser Thr Ala Arg Glu Met Phe
 210 215 220

Glu His Ile Cys Arg His Val Arg Tyr Ser Thr Asn Asn Gly Asn Ile
 225 230 235 240

Arg Ser Ala Ile Thr Val Phe Pro Gln Arg Ser Asp Gly Lys His Asp
 245 250 255

Phe Arg Val Trp Asn Ala Gln Leu Ile Arg Tyr Ala Gly Tyr Gln Met
 260 265 270

Pro Asp Gly Ser Ile Arg Gly Asp Pro Ala Asn Val Glu Phe Thr Gln
 275 280 285

Leu Cys Ile Asp Leu Gly Trp Lys Pro Lys Tyr Gly Arg Phe Asp Val
 290 295 300

Val Pro Leu Val Leu Gln Ala Asn Gly Arg Asp Pro Glu Leu Phe Glu
 305 310 315 320

Ile Pro Pro Asp Leu Val Leu Glu Val Ala Met Glu His Pro Lys Tyr
 325 330 335

Glu Trp Phe Arg Glu Leu Glu Leu Lys Trp Tyr Ala Leu Pro Ala Val
 340 345 350

Ala Asn Met Leu Leu Glu Val Gly Gly Leu Glu Phe Pro Gly Cys Pro
 355 360 365

Phe Asn Gly Trp Tyr Met Gly Thr Glu Ile Gly Val Arg Asp Phe Cys
 370 375 380

Asp Val Gln Arg Tyr Asn Ile Leu Glu Glu Val Gly Arg Arg Met Gly
 385 390 395 400

Leu Glu Thr His Lys Leu Ala Ser Leu Trp Lys Asp Gln Ala Val Val
 405 410 415

Glu Ile Asn Ile Ala Val Leu His Ser Phe Gln Lys Gln Asn Val Thr
 420 425 430

EX05-002patentin.txt

Ile Met Asp His His Ser Ala Ala Glu Ser Phe Met Lys Tyr Met Gln
 435 440 445
 Asn Glu Tyr Arg Ser Arg Gly Gly Cys Pro Ala Asp Trp Ile Trp Leu
 450 455 460
 Val Pro Pro Met Ser Gly Ser Ile Thr Pro Val Phe His Gln Glu Met
 465 470 475 480
 Leu Asn Tyr Val Leu Ser Pro Phe Tyr Tyr Tyr Gln Val Glu Ala Trp
 485 490 495
 Lys Thr His Val Trp Gln Asp Glu Lys Arg Arg Pro Lys Arg Arg Glu
 500 505 510
 Ile Pro Leu Lys Val Leu Val Lys Ala Val Leu Phe Ala Cys Met Leu
 515 520 525
 Met Arg Lys Thr Met Ala Ser Arg Val Arg Val Thr Ile Leu Phe Ala
 530 535 540
 Thr Glu Thr Gly Lys Ser Glu Ala Leu Ala Trp Asp Leu Gly Ala Leu
 545 550 555 560
 Phe Ser Cys Ala Phe Asn Pro Lys Val Val Cys Met Asp Lys Tyr Arg
 565 570 575
 Leu Ser Cys Leu Glu Glu Glu Arg Leu Leu Leu Val Val Thr Ser Thr
 580 585 590
 Phe Gly Asn Gly Asp Cys Pro Gly Asn Gly Glu Lys Leu Lys Lys Ser
 595 600 605
 Leu Phe Met Leu Lys Glu Leu Asn Asn Lys Phe Arg Tyr Ala Val Phe
 610 615 620
 Gly Leu Gly Ser Ser Met Tyr Pro Arg Phe Cys Ala Phe Ala His Asp
 625 630 635 640
 Ile Asp Gln Lys Leu Ser His Leu Gly Ala Ser Gln Leu Thr Pro Met
 645 650 655
 Gly Glu Gly Asp Glu Leu Ser Gly Gln Glu Asp Ala Phe Arg Ser Trp
 660 665 670
 Ala Val Gln Thr Phe Lys Ala Ala Cys Glu Thr Phe Asp Val Arg Gly
 675 680 685
 Lys Gln His Ile Gln Ile Pro Lys Leu Tyr Thr Ser Asn Val Thr Trp
 690 695 700

EX05-002patentin.txt

Asp Pro His His Tyr Arg Leu Val Gln Asp Ser Gln Pro Leu Asp Leu
 705 710 715 720
 Ser Lys Ala Leu Ser Ser Met His Ala Lys Asn Val Phe Thr Met Arg
 725 730 735
 Leu Lys Ser Arg Gln Asn Leu Gln Ser Pro Thr Ser Ser Arg Ala Thr
 740 745 750
 Ile Leu Val Glu Leu Ser Cys Glu Asp Gly Gln Gly Leu Asn Tyr Leu
 755 760 765
 Pro Gly Glu His Leu Gly Val Cys Pro Gly Asn Gln Pro Ala Leu Val
 770 775 780
 Gln Gly Ile Leu Glu Arg Val Val Asp Gly Pro Thr Pro His Gln Thr
 785 790 795 800
 Val Arg Leu Glu Ala Leu Asp Glu Ser Gly Ser Tyr Trp Val Ser Asp
 805 810 815
 Lys Arg Leu Pro Pro Cys Ser Leu Ser Gln Ala Leu Thr Tyr Phe Leu
 820 825 830
 Asp Ile Thr Thr Pro Pro Thr Gln Leu Leu Leu Gln Lys Leu Ala Gln
 835 840 845
 Val Ala Thr Glu Glu Pro Glu Arg Gln Arg Leu Glu Ala Leu Cys Gln
 850 855 860
 Pro Ser Glu Tyr Ser Lys Trp Lys Phe Thr Asn Ser Pro Thr Phe Leu
 865 870 875 880
 Glu Val Leu Glu Glu Phe Pro Ser Leu Arg Val Ser Ala Gly Phe Leu
 885 890 895
 Leu Ser Gln Leu Pro Ile Leu Lys Pro Arg Phe Tyr Ser Ile Ser Ser
 900 905 910
 Ser Arg Asp His Thr Pro Thr Glu Ile His Leu Thr Val Ala Val Val
 915 920 925
 Thr Tyr His Thr Arg Asp Gly Gln Gly Pro Leu His His Gly Val Cys
 930 935 940
 Ser Thr Trp Leu Asn Ser Leu Lys Pro Gln Asp Pro Val Pro Cys Phe
 945 950 955 960
 Val Arg Asn Ala Ser Gly Phe His Leu Pro Glu Asp Pro Ser His Pro
 965 970 975

EX05-002patentin.txt

Cys Ile Leu Ile Gly Pro Gly Thr Gly Ile Ala Pro Phe Arg Ser Phe
 980 985 990

Trp Gln Gln Arg Leu His Asp Ser Gln His Lys Gly Val Arg Gly Gly
 995 1000 1005

Arg Met Thr Leu Val Phe Gly Cys Arg Arg Pro Asp Glu Asp His
 1010 1015 1020

Ile Tyr Gln Glu Glu Met Leu Glu Met Ala Gln Lys Gly Val Leu
 1025 1030 1035

His Ala Val His Thr Ala Tyr Ser Arg Leu Pro Gly Lys Pro Lys
 1040 1045 1050

Val Tyr Val Gln Asp Ile Leu Arg Gln Gln Leu Ala Ser Glu Val
 1055 1060 1065

Leu Arg Val Leu His Lys Glu Pro Gly His Leu Tyr Val Cys Gly
 1070 1075 1080

Asp Val Arg Met Ala Arg Asp Val Ala His Thr Leu Lys Gln Leu
 1085 1090 1095

Val Ala Ala Lys Leu Lys Leu Asn Glu Glu Gln Val Glu Asp Tyr
 1100 1105 1110

Phe Phe Gln Leu Lys Ser Gln Lys Arg Tyr His Glu Asp Ile Phe
 1115 1120 1125

Gly Ala Val Phe Pro Tyr Glu Ala Lys Lys Asp Arg Val Ala Val
 1130 1135 1140

Gln Pro Ser Ser Leu Glu Met Ser Ala Leu
 1145 1150

<210> 66
 <211> 1434
 <212> PRT
 <213> Homo sapiens

<400> 66

Met Glu Asp His Met Phe Gly Val Gln Gln Ile Gln Pro Asn Val Ile
 1 5 10 15

Ser Val Arg Leu Phe Lys Arg Lys Val Gly Gly Leu Gly Phe Leu Val
 20 25 30

Lys Glu Arg Val Ser Lys Pro Pro Val Ile Ile Ser Asp Leu Ile Arg
 35 40 45

EX05-002patentin.txt

Gly Gly Ala Ala Glu Gln Ser Gly Leu Ile Gln Ala Gly Asp Ile Ile
 50 55 60

Leu Ala Val Asn Gly Arg Pro Leu Val Asp Leu Ser Tyr Asp Ser Ala
 65 70 75 80

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

Leu Arg Gly Pro Glu Gly Phe Thr Thr His Leu Glu Thr Thr Phe Thr
 100 105 110

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

Pro Thr Lys Ala Val Asp Leu Ser His Gln Pro Pro Ala Gly Lys Glu
 130 135 140

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

His Ala Tyr Asp Asp Gly Gln Glu Ala Gly Ser Leu Pro His Ala Asn
 165 170 175

Gly Leu Ala Pro Arg Pro Pro Gly Gln Asp Pro Ala Lys Lys Ala Thr
 180 185 190

Arg Val Ser Leu Gln Gly Arg Gly Glu Asn Asn Glu Leu Leu Lys Glu
 195 200 205

Ile Glu Pro Val Leu Ser Leu Leu Thr Ser Gly Ser Arg Gly Val Lys
 210 215 220

Gly Gly Ala Pro Ala Lys Ala Glu Met Lys Asp Met Gly Ile Gln Val
 225 230 235 240

Asp Arg Asp Leu Asp Gly Lys Ser His Lys Pro Leu Pro Leu Gly Val
 245 250 255

Glu Asn Asp Arg Val Phe Asn Asp Leu Trp Gly Lys Gly Asn Val Pro
 260 265 270

Val Val Leu Asn Asn Pro Tyr Ser Glu Lys Glu Gln Pro Pro Thr Ser
 275 280 285

Gly Lys Gln Ser Pro Thr Lys Asn Gly Ser Pro Ser Lys Cys Pro Arg
 290 295 300

Phe Leu Lys Val Lys Asn Trp Glu Thr Glu Val Val Leu Thr Asp Thr
 305 310 315 320

EX05-002patentin.txt

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

EX05-002patentin.txt

Tyr Met Gly Thr Glu Ile Gly Val Arg Asp Tyr Cys Asp Asn Ser Arg
595 600 605

Tyr Asn Ile Leu Glu Glu Val Ala Lys Lys Met Asn Leu Asp Met Arg
610 615 620

Lys Thr Ser Ser Leu Trp Lys Asp Gln Ala Leu Val Glu Ile Asn Ile
625 630 635 640

Ala Val Leu Tyr Ser Phe Gln Ser Asp Lys Val Thr Ile Val Asp His
645 650 655

His Ser Ala Thr Glu Ser Phe Ile Lys His Met Glu Asn Glu Tyr Arg
660 665 670

Cys Arg Gly Gly Cys Pro Ala Asp Trp Val Trp Ile Val Pro Pro Met
675 680 685

Ser Gly Ser Ile Thr Pro Val Phe His Gln Glu Met Leu Asn Tyr Arg
690 695 700

Leu Thr Pro Ser Phe Glu Tyr Gln Pro Asp Pro Trp Asn Thr His Val
705 710 715 720

Trp Lys Gly Thr Asn Gly Thr Pro Thr Lys Arg Arg Ala Ile Gly Phe
725 730 735

Lys Lys Leu Ala Glu Ala Val Lys Phe Ser Ala Lys Leu Met Gly Gln
740 745 750

Ala Met Ala Lys Arg Val Lys Ala Thr Ile Leu Tyr Ala Thr Glu Thr
755 760 765

Gly Lys Ser Gln Ala Tyr Ala Lys Thr Leu Cys Glu Ile Phe Lys His
770 775 780

Ala Phe Asp Ala Lys Val Met Ser Met Glu Glu Tyr Asp Ile Val His
785 790 795 800

Leu Glu His Glu Thr Leu Val Leu Val Val Thr Ser Thr Phe Gly Asn
805 810 815

Gly Asp Pro Pro Glu Asn Gly Glu Lys Phe Gly Cys Ala Leu Met Glu
820 825 830

Met Arg His Pro Asn Ser Val Gln Glu Glu Arg Lys Ser Tyr Lys Val
835 840 845

Arg Phe Asn Ser Val Ser Ser Tyr Ser Asp Ser Gln Lys Ser Ser Gly
850 855 860

EX05-002patentin.txt

Asp Gly Pro Asp Leu Arg Asp Asn Phe Glu Ser Ala Gly Pro Leu Ala
 865 870 875 880
 Asn Val Arg Phe Ser Val Phe Gly Leu Gly Ser Arg Ala Tyr Pro His
 885 890 895
 Phe Cys Ala Phe Gly His Ala Val Asp Thr Leu Leu Glu Glu Leu Gly
 900 905 910
 Gly Glu Arg Ile Leu Lys Met Arg Glu Gly Asp Glu Leu Cys Gly Gln
 915 920 925
 Glu Glu Ala Phe Arg Thr Trp Ala Lys Lys Val Phe Lys Ala Ala Cys
 930 935 940
 Asp Val Phe Cys Val Gly Asp Asp Val Asn Ile Glu Lys Ala Asn Asn
 945 950 955 960
 Ser Leu Ile Ser Asn Asp Arg Ser Trp Lys Arg Asn Lys Phe Arg Leu
 965 970 975
 Thr Phe Val Ala Glu Ala Pro Glu Leu Thr Gln Gly Leu Ser Asn Val
 980 985 990
 His Lys Lys Arg Val Ser Ala Ala Arg Leu Leu Ser Arg Gln Asn Leu
 995 1000 1005
 Gln Ser Pro Lys Ser Ser Arg Ser Thr Ile Phe Val Arg Leu His
 1010 1015 1020
 Thr Asn Gly Ser Gln Glu Leu Gln Tyr Gln Pro Gly Asp His Leu
 1025 1030 1035
 Gly Val Phe Pro Gly Asn His Glu Asp Leu Val Asn Ala Leu Ile
 1040 1045 1050
 Glu Arg Leu Glu Asp Ala Pro Pro Val Asn Gln Met Val Lys Val
 1055 1060 1065
 Glu Leu Leu Glu Glu Arg Asn Thr Ala Leu Gly Val Ile Ser Asn
 1070 1075 1080
 Trp Thr Asp Glu Leu Arg Leu Pro Pro Cys Thr Ile Phe Gln Ala
 1085 1090 1095
 Phe Lys Tyr Tyr Leu Asp Ile Thr Thr Pro Pro Thr Pro Leu Gln
 1100 1105 1110
 Leu Gln Gln Phe Ala Ser Leu Ala Thr Ser Glu Lys Glu Lys Gln
 1115 1120 1125

EX05-002patentin.txt

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

EX05-002patentin.txt

Val Phe Ile Ser Arg Met Arg Asp Asp Asn Arg Tyr His Glu Asp
 1385 1390 1395

Ile Phe Gly Val Thr Leu Arg Thr Tyr Glu Val Thr Asn Arg Leu
 1400 1405 1410

Arg Ser Glu Ser Ile Ala Phe Ile Glu Glu Ser Lys Lys Asp Thr
 1415 1420 1425

Asp Glu Val Phe Ser Ser
 1430

<210> 67
 <211> 904
 <212> PRT
 <213> Homo sapiens

<400> 67

Met Glu Trp Gly Ser Glu Ser Ala Ala Val Arg Arg His Arg Val Gly
 1 5 10 15

Val Glu Arg Arg Glu Gly Ala Ala Ala Ala Pro Pro Pro Glu Arg Glu
 20 25 30

Ala Arg Ala Gln Glu Pro Leu Val Asp Gly Cys Ser Gly Gly Gly Arg
 35 40 45

Thr Arg Lys Arg Ser Pro Gly Gly Ser Gly Gly Ala Ser Arg Gly Ala
 50 55 60

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

Leu Ile Ala Leu Arg Thr Leu Val Gln Leu Ser Leu Gln Gln Leu Val
 85 90 95

Leu Arg Gly Ala Ala Gly His Arg Gly Glu Phe Asp Ala Leu Gln Ala
 100 105 110

Arg Asp Tyr Leu Glu His Ile Thr Ser Ile Gly Pro Arg Thr Thr Gly
 115 120 125

Ser Pro Glu Asn Glu Ile Leu Thr Val His Tyr Leu Leu Glu Gln Ile
 130 135 140

Lys Leu Ile Glu Val Gln Ser Asn Ser Leu His Lys Ile Ser Val Asp
 145 150 155 160

Val Gln Arg Pro Thr Gly Ser Phe Ser Ile Asp Phe Leu Gly Gly Phe
 165 170 175

EX05-002patentin.txt

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

EX05-002patentin.txt

Asp Phe Leu Cys Gly Leu Gly Ile Thr Leu Ile Ser Trp Phe Thr Ser
 450 455 460

Leu Val Thr Val Leu Ile Ile Ala Val Phe Ile Ser Leu Ile Gly Gln
 465 470 475 480

Ser Leu Ser Trp Tyr Asn His Phe Tyr Val Ser Val Cys Leu Tyr Gly
 485 490 495

Thr Ala Thr Val Ala Lys Ile Ile Leu Ile His Thr Leu Ala Lys Arg
 500 505 510

Phe Tyr Tyr Met Asn Ala Ser Ala Gln Tyr Leu Gly Glu Val Phe Phe
 515 520 525

Asp Ile Ser Leu Phe Val His Cys Cys Phe Leu Val Thr Leu Thr Tyr
 530 535 540

Gln Gly Leu Cys Ser Ala Phe Ile Ser Ala Val Trp Val Ala Phe Pro
 545 550 555 560

Leu Leu Thr Lys Leu Cys Val His Lys Asp Phe Lys Gln His Gly Ala
 565 570 575

Gln Gly Lys Phe Ile Ala Phe Tyr Leu Leu Gly Met Phe Ile Pro Tyr
 580 585 590

Leu Tyr Ala Leu Tyr Leu Ile Trp Ala Val Phe Glu Met Phe Thr Pro
 595 600 605

Ile Leu Gly Arg Ser Gly Ser Glu Ile Pro Pro Asp Val Val Leu Ala
 610 615 620

Ser Ile Leu Ala Gly Cys Thr Met Ile Leu Ser Ser Tyr Phe Ile Asn
 625 630 635 640

Phe Ile Tyr Leu Ala Lys Ser Thr Lys Lys Thr Met Leu Thr Leu Thr
 645 650 655

Leu Val Cys Ala Ile Thr Phe Leu Leu Val Cys Ser Gly Thr Phe Phe
 660 665 670

Pro Tyr Ser Ser Asn Pro Ala Asn Pro Lys Pro Lys Arg Val Phe Leu
 675 680 685

Gln His Met Thr Arg Thr Phe His Asp Leu Glu Gly Asn Ala Val Lys
 690 695 700

Arg Asp Ser Gly Ile Trp Ile Asn Gly Phe Asp Tyr Thr Gly Ile Ser
 705 710 715 720

EX05-002patentin.txt

His Ile Thr Pro His Ile Pro Glu Ile Asn Asp Ser Ile Arg Ala His
 725 730 735

Cys Glu Glu Asn Ala Pro Leu Cys Gly Phe Pro Trp Tyr Leu Pro Val
 740 745 750

His Phe Leu Ile Arg Lys Asn Trp Tyr Leu Pro Ala Pro Glu Val Ser
 755 760 765

Pro Arg Asn Pro Pro His Phe Arg Leu Ile Ser Lys Glu Gln Thr Pro
 770 775 780

Trp Asp Ser Ile Lys Leu Thr Phe Glu Ala Thr Gly Pro Ser His Met
 785 790 795 800

Ser Phe Tyr Val Arg Ala His Lys Gly Ser Thr Leu Ser Gln Trp Ser
 805 810 815

Leu Gly Asn Gly Thr Pro Val Thr Ser Lys Gly Gly Asp Tyr Phe Val
 820 825 830

Phe Tyr Ser His Gly Leu Gln Ala Ser Ala Trp Gln Phe Trp Ile Glu
 835 840 845

Val Gln Val Ser Glu Glu His Pro Glu Gly Met Val Thr Val Ala Ile
 850 855 860

Ala Ala His Tyr Leu Ser Gly Glu Asp Lys Arg Ser Pro Gln Leu Asp
 865 870 875 880

Ala Leu Lys Glu Lys Phe Pro Asp Trp Thr Phe Pro Ser Ala Trp Val
 885 890 895

Cys Thr Tyr Asp Leu Phe Val Phe
 900

<210> 68
 <211> 747
 <212> PRT
 <213> Homo sapiens

<400> 68

Met Trp Gly Phe Leu Lys Arg Pro Val Val Val Thr Ala Asp Ile Asn
 1 5 10 15

Leu Ser Leu Val Ala Leu Thr Gly Met Gly Leu Leu Ser Arg Leu Trp
 20 25 30

Arg Leu Thr Tyr Pro Arg Ala Val Val Phe Asp Glu Val Tyr Tyr Gly
 35 40 45

Gln Tyr Ile Ser Phe Tyr Met Lys Gln Ile Phe Phe Leu Asp Asp Ser
 Page 128

55

Val Ala Phe Gly Ser Gln Val Thr Leu Arg Asn Val Phe Gly Lys Pro
Page 129

EX05-002patentin.txt

325

330

335

Val Pro Cys Trp Leu His Ser His Gln Asp Thr Tyr Pro Met Ile Tyr
 340 345 350

Glu Asn Gly Arg Gly Ser Ser His Gln Gln Gln Val Thr Cys Tyr Pro
 355 360 365

Phe Lys Asp Val Asn Asn Trp Trp Ile Val Lys Asp Pro Arg Arg His
 370 375 380

Gln Leu Val Val Ser Ser Pro Pro Arg Pro Val Arg His Gly Asp Met
 385 390 395 400

Val Gln Leu Val His Gly Met Thr Thr Arg Ser Leu Asn Thr His Asp
 405 410 415

Val Ala Ala Pro Leu Ser Pro His Ser Gln Glu Val Ser Cys Tyr Ile
 420 425 430

Asp Tyr Asn Ile Ser Met Pro Ala Gln Asn Leu Trp Arg Leu Glu Ile
 435 440 445

Val Asn Arg Gly Ser Asp Thr Asp Val Trp Lys Thr Ile Leu Ser Glu
 450 455 460

Val Arg Phe Val His Val Asn Thr Ser Ala Val Leu Lys Leu Ser Gly
 465 470 475 480

Ala His Leu Pro Asp Trp Gly Tyr Arg Gln Leu Glu Ile Val Gly Glu
 485 490 495

Lys Leu Ser Arg Gly Tyr His Gly Ser Thr Val Trp Asn Val Glu Glu
 500 505 510

His Arg Tyr Gly Ala Ser Gln Glu Gln Arg Glu Arg Glu Arg Glu Leu
 515 520 525

His Ser Pro Ala Gln Val Asp Val Ser Arg Asn Leu Ser Phe Met Ala
 530 535 540

Arg Phe Ser Glu Leu Gln Trp Arg Met Leu Ala Leu Arg Ser Asp Asp
 545 550 555 560

Ser Glu His Lys Tyr Ser Ser Ser Pro Leu Glu Trp Val Thr Leu Asp
 565 570 575

Thr Asn Ile Ala Tyr Trp Leu His Pro Arg Thr Ser Ala Gln Ile His
 580 585 590

Leu Leu Gly Asn Ile Val Ile Trp Val Ser Gly Ser Leu Ala Leu Ala
 Page 130

595 EX05-002patentin.txt
600 605

Ile Tyr Ala Leu Leu Ser Leu Trp Tyr Leu Leu Arg Arg Arg Arg Asn
610 615 620

Val His Asp Leu Pro Gln Asp Ala Trp Leu Arg Trp Val Leu Ala Gly
625 630 635 640

Ala Leu Cys Ala Gly Gly Trp Ala Val Asn Tyr Leu Pro Phe Phe Leu
645 650 655

Met Glu Lys Thr Leu Phe Leu Tyr His Tyr Leu Pro Ala Leu Thr Phe
660 665 670

Gln Ile Leu Leu Leu Pro Val Val Leu Gln His Ile Ser Asp His Leu
675 680 685

Cys Arg Ser Gln Leu Gln Arg Asn Ser Phe Ser Ala Leu Val Val Ala
690 695 700

Trp Tyr Ser Ser Ala Cys His Val Ser Asn Thr Leu Arg Pro Leu Thr
705 710 715 720

Tyr Gly Asp Lys Ser Leu Ser Pro His Glu Leu Lys Ala Leu Arg Trp
725 730 735

Lys Asp Ser Trp Asp Ile Leu Ile Arg Lys His
740 745

<210> 69
<211> 979
<212> PRT
<213> Homo sapiens

<400> 69

Met Arg Arg Pro Arg Arg Pro Gly Gly Leu Gly Gly Ser Gly Gly Leu
1 5 10 15

Arg Leu Leu Leu Cys Leu Leu Leu Leu Ser Ser Arg Pro Gly Gly Cys
20 25 30

Ser Ala Val Ser Ala His Gly Cys Leu Phe Asp Arg Arg Leu Cys Ser
35 40 45

His Leu Glu Val Cys Ile Gln Asp Gly Leu Phe Gly Gln Cys Gln Val
50 55 60

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

Gln Arg Leu Gln Gly Val Leu Arg Gln Leu Met Ser Gln Gly Leu Ser
85 90 95

EX05-002patentin.txt

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

EX05-002patentin.txt

Lys Gly Ala Gly Arg Asn Pro Gly Gly Val Val Asn Val Gly Ala Asp
 370 375 380

Ile Lys Lys Thr Met Glu Gly Pro Val Glu Gly Arg Asp Thr Ala Glu
 385 390 395 400

Leu Pro Ala Arg Thr Ser Pro Met Pro Gly His Pro Thr Ala Ser Pro
 405 410 415

Thr Ser Ser Glu Val Gln Gln Val Pro Ser Pro Val Ser Ser Glu Pro
 420 425 430

Pro Lys Ala Ala Arg Pro Pro Val Thr Pro Val Leu Leu Glu Lys Lys
 435 440 445

Ser Pro Leu Gly Gln Ser Gln Pro Thr Val Ala Gly Gln Pro Ser Ala
 450 455 460

Arg Pro Ala Ala Glu Glu Tyr Gly Tyr Ile Val Thr Asp Gln Lys Pro
 465 470 475 480

Leu Ser Leu Ala Ala Gly Val Lys Leu Leu Glu Ile Leu Ala Glu His
 485 490 495

Val His Met Ser Ser Gly Ser Phe Ile Asn Ile Ser Val Val Gly Pro
 500 505 510

Ala Leu Thr Phe Arg Ile Arg His Asn Glu Gln Asn Leu Ser Leu Ala
 515 520 525

Asp Val Thr Gln Gln Ala Gly Leu Val Lys Ser Glu Leu Glu Ala Gln
 530 535 540

Thr Gly Leu Gln Ile Leu Gln Thr Gly Val Gly Gln Arg Glu Glu Ala
 545 550 555 560

Ala Ala Val Leu Pro Gln Thr Ala His Ser Thr Ser Pro Met Arg Ser
 565 570 575

Val Leu Leu Thr Leu Val Ala Leu Ala Gly Val Ala Gly Leu Leu Val
 580 585 590

Ala Leu Ala Val Ala Leu Cys Val Arg Gln His Ala Arg Gln Gln Asp
 595 600 605

Lys Glu Arg Leu Ala Ala Leu Gly Pro Glu Gly Ala His Gly Asp Thr
 610 615 620

Thr Phe Glu Tyr Gln Asp Leu Cys Arg Gln His Met Ala Thr Lys Ser
 625 630 635 640

EX05-002patentin.txt

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

EX05-002patentin.txt

Ala Gly Arg Thr Gly Thr Tyr Ile Leu Ile Asp Met Val Leu Asn Arg
 915 920 925

Met Ala Lys Gly Val Lys Glu Ile Asp Ile Ala Ala Thr Leu Glu His
 930 935 940

Val Arg Asp Gln Arg Pro Gly Leu Val Arg Ser Lys Asp Gln Phe Glu
 945 950 955 960

Phe Ala Leu Thr Ala Val Ala Glu Glu Val Asn Ala Ile Leu Lys Ala
 965 970 975

Leu Pro Gln

<210> 70
 <211> 1015
 <212> PRT
 <213> Homo sapiens

<400> 70

Met Gly Pro Pro Leu Pro Leu Leu Leu Leu Leu Leu Leu Leu Pro
 1 5 10 15

Pro Arg Val Leu Pro Ala Ala Pro Ser Ser Val Pro Arg Gly Arg Gln
 20 25 30

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

Ser Glu Ala Cys Val Asn Asp Gly Val Phe Gly Arg Cys Gln Lys Val
 50 55 60

Pro Ala Met Asp Phe Tyr Arg Tyr Glu Val Ser Pro Val Ala Leu Gln
 65 70 75 80

Arg Leu Arg Val Ala Leu Gln Lys Leu Ser Gly Thr Gly Phe Thr Trp
 85 90 95

Gln Asp Asp Tyr Thr Gln Tyr Val Met Asp Gln Glu Leu Ala Asp Leu
 100 105 110

Pro Lys Thr Tyr Leu Arg Arg Pro Glu Ala Ser Ser Pro Ala Arg Pro
 115 120 125

Ser Lys His Ser Val Gly Ser Glu Arg Arg Tyr Ser Arg Glu Gly Gly
 130 135 140

Ala Ala Leu Ala Asn Ala Leu Arg Arg His Leu Pro Phe Leu Glu Ala
 145 150 155 160

EX05-002patentin.txt

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

EX05-002patentin.txt

Ser Ser Leu Ser Ser Glu Glu Glu Thr Ala Gly Val Glu Asn Val Lys
 435 440 445
 Ser Gln Thr Tyr Ser Lys Asp Leu Leu Gly Gln Gln Pro His Ser Glu
 450 455 460
 Pro Gly Ala Ala Ala Phe Gly Glu Leu Gln Asn Gln Met Pro Gly Pro
 465 470 475 480
 Ser Lys Glu Glu Gln Ser Leu Pro Ala Gly Ala Gln Glu Ala Leu Ser
 485 490 495
 Asp Gly Leu Gln Leu Glu Val Gln Pro Ser Glu Glu Glu Ala Arg Gly
 500 505 510
 Tyr Ile Val Thr Asp Arg Asp Pro Leu Arg Pro Glu Glu Gly Arg Arg
 515 520 525
 Leu Val Glu Asp Val Ala Arg Leu Leu Gln Val Pro Ser Ser Ala Phe
 530 535 540
 Ala Asp Val Glu Val Leu Gly Pro Ala Val Thr Phe Lys Val Ser Ala
 545 550 555 560
 Asn Val Gln Asn Val Thr Thr Glu Asp Val Glu Lys Ala Thr Val Asp
 565 570 575
 Asn Lys Asp Lys Leu Glu Glu Thr Ser Gly Leu Lys Ile Leu Gln Thr
 580 585 590
 Gly Val Gly Ser Lys Ser Lys Leu Lys Phe Leu Pro Pro Gln Ala Glu
 595 600 605
 Gln Glu Asp Ser Thr Lys Phe Ile Ala Leu Thr Leu Val Ser Leu Ala
 610 615 620
 Cys Ile Leu Gly Val Leu Leu Ala Ser Gly Leu Ile Tyr Cys Leu Arg
 625 630 635 640
 His Ser Ser Gln His Arg Leu Lys Glu Lys Leu Ser Gly Leu Gly Gly
 645 650 655
 Asp Pro Gly Ala Asp Ala Thr Ala Ala Tyr Gln Glu Leu Cys Arg Gln
 660 665 670
 Arg Met Ala Thr Arg Pro Pro Asp Arg Pro Glu Gly Pro His Thr Ser
 675 680 685
 Arg Ile Ser Ser Val Ser Ser Gln Phe Ser Asp Gly Pro Ile Pro Ser
 690 695 700

EX05-002patentin.txt

Pro Ser Ala Arg Ser Ser Ala Ser Ser Trp Ser Glu Glu Pro Val Gln
 705 710 715 720
 Ser Asn Met Asp Ile Ser Thr Gly His Met Ile Leu Ser Tyr Met Glu
 725 730 735
 Asp His Leu Lys Asn Lys Asn Arg Leu Glu Lys Glu Trp Glu Ala Leu
 740 745 750
 Cys Ala Tyr Gln Ala Glu Pro Asn Ser Ser Phe Val Ala Gln Arg Glu
 755 760 765
 Glu Asn Val Pro Lys Asn Arg Ser Leu Ala Val Leu Thr Tyr Asp His
 770 775 780
 Ser Arg Val Leu Leu Lys Ala Glu Asn Ser His Ser His Ser Asp Tyr
 785 790 795 800
 Ile Asn Ala Ser Pro Ile Met Asp His Asp Pro Arg Asn Pro Ala Tyr
 805 810 815
 Ile Ala Thr Gln Gly Pro Leu Pro Ala Thr Val Ala Asp Phe Trp Gln
 820 825 830
 Met Val Trp Glu Ser Gly Cys Val Val Ile Val Met Leu Thr Pro Leu
 835 840 845
 Ala Glu Asn Gly Val Arg Gln Cys Tyr His Tyr Trp Pro Asp Glu Gly
 850 855 860
 Ser Asn Leu Tyr His Ile Tyr Glu Val Asn Leu Val Ser Glu His Ile
 865 870 875 880
 Trp Cys Glu Asp Phe Leu Val Arg Ser Phe Tyr Leu Lys Asn Leu Gln
 885 890 895
 Thr Asn Glu Thr Arg Thr Val Thr Gln Phe His Phe Leu Ser Trp Tyr
 900 905 910
 Asp Arg Gly Val Pro Ser Ser Ser Arg Ser Leu Leu Asp Phe Arg Arg
 915 920 925
 Lys Val Asn Lys Cys Tyr Arg Gly Arg Ser Cys Pro Ile Ile Val His
 930 935 940
 Cys Ser Asp Gly Ala Gly Arg Ser Gly Thr Tyr Val Leu Ile Asp Met
 945 950 955 960
 Val Leu Asn Lys Met Ala Lys Gly Ala Lys Glu Ile Asp Ile Ala Ala
 965 970 975

EX05-002patentin.txt

Thr Leu Glu His Leu Arg Asp Gln Arg Pro Gly Met Val Gln Thr Lys
 980 985 990
 Glu Gln Phe Glu Phe Ala Leu Thr Ala Val Ala Glu Glu Val Asn Ala
 995 1000 1005
 Ile Leu Lys Ala Leu Pro Gln
 1010 1015
 <210> 71
 <211> 1575
 <212> PRT
 <213> Homo sapiens
 <400> 71
 Met Ala Phe Ser Lys Gly Phe Arg Ile Tyr His Lys Leu Asp Pro Pro
 1 5 10 15
 Pro Phe Ser Leu Ile Val Glu Thr Arg His Lys Glu Glu Cys Leu Met
 20 25 30
 Phe Glu Ser Gly Ala Val Ala Val Leu Ser Ser Ala Glu Lys Glu Ala
 35 40 45
 Ile Lys Gly Thr Tyr Ser Lys Val Leu Asp Ala Tyr Gly Leu Leu Gly
 50 55 60
 Val Leu Arg Leu Asn Leu Gly Asp Thr Met Leu His Tyr Leu Val Leu
 65 70 75 80
 Val Thr Gly Cys Met Ser Val Gly Lys Ile Gln Glu Ser Glu Val Phe
 85 90 95
 Arg Val Thr Ser Thr Glu Phe Ile Ser Leu Arg Ile Asp Ser Ser Asp
 100 105 110
 Glu Asp Arg Ile Ser Glu Val Arg Lys Val Leu Asn Ser Gly Asn Phe
 115 120 125
 Tyr Phe Ala Trp Ser Ala Ser Gly Ile Ser Leu Asp Leu Ser Leu Asn
 130 135 140
 Ala His Arg Ser Met Gln Glu Gln Thr Thr Asp Asn Arg Phe Phe Trp
 145 150 155 160
 Asn Gln Ser Leu His Leu His Leu Lys His Tyr Gly Val Asn Cys Asp
 165 170 175
 Asp Trp Leu Leu Arg Leu Met Cys Gly Gly Val Glu Ile Arg Thr Ile
 180 185 190

EX05-002patentin.txt

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

EX05-002patentin.txt

Asn Asn Phe Phe Asp Ser Ser Lys Gln Glu Ala Ile Asp Val Leu Leu
 465 470 475 480

Leu Gly Asn Thr Leu Asn Ser Asp Leu Ala Asp Lys Ala Arg Ala Leu
 485 490 495

Leu Thr Thr Gly Ser Leu Arg Val Ser Glu Gln Thr Leu Gln Ser Ala
 500 505 510

Ser Ser Lys Val Leu Lys Ser Met Cys Glu Asn Phe Tyr Lys Tyr Ser
 515 520 525

Lys Pro Lys Lys Ile Arg Val Cys Val Gly Thr Trp Asn Val Asn Gly
 530 535 540

Gly Lys Gln Phe Arg Ser Ile Ala Phe Lys Asn Gln Thr Leu Thr Asp
 545 550 555 560

Trp Leu Leu Asp Ala Pro Lys Leu Ala Gly Ile Gln Glu Phe Gln Asp
 565 570 575

Lys Arg Ser Lys Pro Thr Asp Ile Phe Ala Ile Gly Phe Glu Glu Met
 580 585 590

Val Glu Leu Asn Ala Gly Asn Ile Val Ser Ala Ser Thr Thr Asn Gln
 595 600 605

Lys Leu Trp Ala Val Glu Leu Gln Lys Thr Ile Ser Arg Asp Asn Lys
 610 615 620

Tyr Val Leu Leu Ala Ser Glu Gln Leu Val Gly Val Cys Leu Phe Val
 625 630 635 640

Phe Ile Arg Pro Gln His Ala Pro Phe Ile Arg Asp Val Ala Val Asp
 645 650 655

Thr Val Lys Thr Gly Met Gly Gly Ala Thr Gly Asn Lys Gly Ala Val
 660 665 670

Ala Ile Arg Met Leu Phe His Thr Thr Ser Leu Cys Phe Val Cys Ser
 675 680 685

His Phe Ala Ala Gly Gln Ser Gln Val Lys Glu Arg Asn Glu Asp Phe
 690 695 700

Ile Glu Ile Ala Arg Lys Leu Ser Phe Pro Met Gly Arg Met Leu Phe
 705 710 715 720

Ser His Asp Tyr Val Phe Trp Cys Gly Asp Phe Asn Tyr Arg Ile Asp
 725 730 735

EX05-002patentin.txt

Leu Pro Asn Glu Glu Val Lys Glu Leu Ile Arg Gln Gln Asn Trp Asp
 740 745 750

Ser Leu Ile Ala Gly Asp Gln Leu Ile Asn Gln Lys Asn Ala Gly Gln
 755 760 765

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

Lys Tyr Asp Leu Phe Ser Asp Asp Tyr Asp Thr Ser Glu Lys Cys Arg
 785 790 795 800

Thr Pro Ala Trp Thr Asp Arg Val Leu Trp Arg Arg Arg Lys Trp Pro
 805 810 815

Phe Asp Arg Ser Ala Glu Asp Leu Asp Leu Leu Asn Ala Ser Phe Gln
 820 825 830

Asp Glu Ser Lys Ile Leu Tyr Thr Trp Thr Pro Gly Thr Leu Leu His
 835 840 845

Tyr Gly Arg Ala Glu Leu Lys Thr Ser Asp His Arg Pro Val Val Ala
 850 855 860

Leu Ile Asp Ile Asp Ile Phe Glu Val Glu Ala Glu Glu Arg Gln Asn
 865 870 875 880

Ile Tyr Lys Glu Val Ile Ala Val Gln Gly Pro Pro Asp Gly Thr Val
 885 890 895

Leu Val Ser Ile Lys Ser Ser Leu Pro Glu Asn Asn Phe Phe Asp Asp
 900 905 910

Ala Leu Ile Asp Glu Leu Leu Gln Gln Phe Ala Ser Phe Gly Glu Val
 915 920 925

Ile Leu Ile Arg Phe Val Glu Asp Lys Met Trp Val Thr Phe Leu Glu
 930 935 940

Gly Ser Ser Ala Leu Asn Val Leu Ser Leu Asn Gly Lys Glu Leu Leu
 945 950 955 960

Asn Arg Thr Ile Thr Ile Ala Leu Lys Ser Pro Asp Trp Ile Lys Asn
 965 970 975

Leu Glu Glu Glu Met Ser Leu Glu Lys Ile Ser Ile Ala Leu Pro Ser
 980 985 990

Ser Thr Ser Ser Thr Leu Leu Gly Glu Asp Ala Glu Val Ala Ala Asp
 995 1000 1005

EX05-002patentin.txt

Phe	Asp	Met	Glu	Gly	Asp	Val	Asp	Asp	Tyr	Ser	Ala	Glu	Val	Glu
	1010					1015					1020			
Glu	Leu	Leu	Pro	Gln	His	Leu	Gln	Pro	Ser	Ser	Ser	Ser	Gly	Leu
	1025					1030					1035			
Gly	Thr	Ser	Pro	Ser	Ser	Ser	Pro	Arg	Thr	Ser	Pro	Cys	Gln	Ser
	1040					1045					1050			
Pro	Thr	Ile	Ser	Glu	Gly	Pro	Val	Pro	Ser	Leu	Pro	Ile	Arg	Pro
	1055					1060					1065			
Ser	Arg	Ala	Pro	Ser	Arg	Thr	Pro	Gly	Pro	Pro	Ser	Ala	Gln	Ser
	1070					1075					1080			
Ser	Pro	Ile	Asp	Ala	Gln	Pro	Ala	Thr	Pro	Leu	Pro	Gln	Lys	Asp
	1085					1090					1095			
Pro	Ala	Gln	Pro	Leu	Glu	Pro	Lys	Arg	Pro	Pro	Pro	Pro	Arg	Pro
	1100					1105					1110			
Val	Ala	Pro	Pro	Thr	Arg	Pro	Ala	Pro	Pro	Gln	Arg	Pro	Pro	Pro
	1115					1120					1125			
Pro	Ser	Gly	Ala	Arg	Ser	Pro	Ala	Pro	Thr	Arg	Lys	Glu	Phe	Gly
	1130					1135					1140			
Gly	Ile	Gly	Ala	Pro	Pro	Ser	Pro	Gly	Val	Ala	Arg	Arg	Glu	Met
	1145					1150					1155			
Glu	Ala	Pro	Lys	Ser	Pro	Gly	Thr	Thr	Arg	Lys	Asp	Asn	Ile	Gly
	1160					1165					1170			
Arg	Ser	Gln	Pro	Ser	Pro	Gln	Ala	Gly	Leu	Ala	Gly	Pro	Gly	Pro
	1175					1180					1185			
Ala	Gly	Tyr	Ser	Thr	Ala	Arg	Pro	Thr	Ile	Pro	Pro	Arg	Ala	Gly
	1190					1195					1200			
Val	Ile	Ser	Ala	Pro	Gln	Ser	His	Ala	Arg	Ala	Ser	Ala	Gly	Arg
	1205					1210					1215			
Leu	Thr	Pro	Glu	Ser	Gln	Ser	Lys	Thr	Ser	Glu	Thr	Ser	Lys	Gly
	1220					1225					1230			
Ser	Thr	Phe	Leu	Pro	Glu	Pro	Leu	Lys	Pro	Gln	Ala	Ala	Phe	Pro
	1235					1240					1245			
Pro	Gln	Ser	Ser	Leu	Pro	Pro	Pro	Ala	Gln	Arg	Leu	Gln	Glu	Pro
	1250					1255					1260			

EX05-002patentin.txt

Leu	Val	Pro	Val	Ala	Ala	Pro	Met	Pro	Gln	Ser	Gly	Pro	Gln	Pro
	1265					1270					1275			
Asn	Leu	Glu	Thr	Pro	Pro	Gln	Pro	Pro	Pro	Arg	Ser	Arg	Ser	Ser
	1280					1285					1290			
His	Ser	Leu	Pro	Ser	Glu	Ala	Ser	Ser	Gln	Pro	Gln	Val	Lys	Thr
	1295					1300					1305			
Asn	Gly	Ile	Ser	Asp	Gly	Lys	Arg	Glu	Ser	Pro	Leu	Lys	Ile	Asp
	1310					1315					1320			
Pro	Phe	Glu	Asp	Leu	Ser	Phe	Asn	Leu	Leu	Ala	Val	Ser	Lys	Ala
	1325					1330					1335			
Gln	Leu	Ser	Val	Gln	Thr	Ser	Pro	Val	Pro	Thr	Pro	Asp	Pro	Lys
	1340					1345					1350			
Arg	Leu	Ile	Gln	Leu	Pro	Ser	Ala	Thr	Gln	Ser	Asn	Val	Asn	Thr
	1355					1360					1365			
Leu	Ser	Ser	Val	Ser	Cys	Met	Pro	Thr	Met	Pro	Pro	Ile	Pro	Ala
	1370					1375					1380			
Arg	Ser	Gln	Ser	Gln	Glu	Asn	Met	Arg	Ser	Ser	Pro	Asn	Pro	Phe
	1385					1390					1395			
Ile	Thr	Gly	Leu	Thr	Arg	Thr	Asn	Pro	Phe	Ser	Asp	Arg	Thr	Ala
	1400					1405					1410			
Ala	Pro	Gly	Asn	Pro	Phe	Arg	Ala	Lys	Ser	Glu	Glu	Ser	Glu	Ala
	1415					1420					1425			
Thr	Ser	Trp	Phe	Ser	Lys	Glu	Glu	Pro	Val	Thr	Ile	Ser	Pro	Phe
	1430					1435					1440			
Pro	Ser	Leu	Gln	Pro	Leu	Gly	His	Asn	Lys	Ser	Arg	Ala	Ser	Ser
	1445					1450					1455			
Ser	Leu	Asp	Gly	Phe	Lys	Asp	Ser	Phe	Asp	Leu	Gln	Gly	Gln	Ser
	1460					1465					1470			
Thr	Leu	Lys	Ile	Ser	Asn	Pro	Lys	Gly	Trp	Val	Thr	Phe	Glu	Glu
	1475					1480					1485			
Glu	Glu	Asp	Phe	Gly	Val	Lys	Gly	Lys	Ser	Lys	Ser	Ala	Cys	Ser
	1490					1495					1500			
Asp	Leu	Leu	Gly	Asn	Gln	Pro	Ser	Ser	Phe	Ser	Gly	Ser	Asn	Leu
	1505					1510					1515			

EX05-002patentin.txt
 Thr Leu Asn Asp Asp Trp Asn Lys Gly Thr Asn Val Ser Phe Cys
 1520 1525 1530

Val Leu Pro Ser Arg Arg Pro Pro Pro Pro Pro Val Pro Leu Leu
 1535 1540 1545

Pro Pro Gly Thr Ser Pro Pro Val Asp Pro Phe Thr Thr Leu Ala
 1550 1555 1560

Ser Lys Ala Ser Pro Thr Leu Asp Phe Thr Glu Arg
 1565 1570 1575

<210> 72
 <211> 1496
 <212> PRT
 <213> Homo sapiens
 <400> 72

Met Ala Leu Ser Lys Gly Leu Arg Leu Leu Gly Arg Leu Gly Ala Glu
 1 5 10 15

Gly Asp Cys Ser Val Leu Leu Glu Ala Arg Gly Arg Asp Asp Cys Leu
 20 25 30

Leu Phe Glu Ala Gly Thr Val Ala Thr Leu Ala Pro Glu Glu Lys Glu
 35 40 45

Val Ile Lys Gly Gln Tyr Gly Lys Leu Thr Asp Ala Tyr Gly Cys Leu
 50 55 60

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

Leu Val Thr Gly Cys Thr Ser Val Gly Arg Ile Pro Asp Ala Glu Ile
 85 90 95

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

Glu Glu Glu Arg Leu Ile Ala Leu Lys Lys Ile Leu Ser Ser Gly Val
 115 120 125

Phe Tyr Phe Ser Trp Pro Asn Asp Gly Ser Arg Phe Asp Leu Thr Val
 130 135 140

Arg Thr Gln Lys Gln Gly Asp Asp Ser Ser Glu Trp Gly Asn Ser Phe
 145 150 155 160

Phe Trp Asn Gln Leu Leu His Val Pro Leu Arg Gln His Gln Val Ser
 165 170 175

Cys Cys Asp Trp Leu Leu Lys Ile Ile Cys Gly Val Val Thr Ile Arg
 Page 145

EX05-002patentin.txt

180

185

190

Thr Val Tyr Ala Ser His Lys Gln Ala Lys Ala Cys Leu Val Ser Arg
195 200 205

Val Ser Cys Glu Arg Thr Gly Thr Arg Phe His Thr Arg Gly Val Asn
210 215 220

Asp Asp Gly His Val Ser Asn Phe Val Glu Thr Glu Gln Met Ile Tyr
225 230 235 240

Met Asp Asp Gly Val Ser Ser Phe Val Gln Ile Arg Gly Ser Val Pro
245 250 255

Leu Phe Trp Glu Gln Pro Gly Leu Gln Val Gly Ser His His Leu Arg
260 265 270

Leu His Arg Gly Leu Glu Ala Asn Ala Pro Ala Phe Asp Arg His Met
275 280 285

Val Leu Leu Lys Glu Gln Tyr Gly Gln Gln Val Val Val Asn Leu Leu
290 300

Gly Ser Arg Gly Gly Glu Glu Val Leu Asn Arg Ala Phe Lys Lys Leu
305 310 315 320

Leu Trp Ala Ser Cys His Ala Gly Asp Thr Pro Met Ile Asn Phe Asp
325 330 335

Phe His Gln Phe Ala Lys Gly Gly Lys Leu Glu Lys Leu Glu Thr Leu
340 345 350

Leu Arg Pro Gln Leu Lys Leu His Trp Glu Asp Phe Asp Val Phe Thr
355 360 365

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

Asn Cys Leu Asp Cys Leu Asp Arg Thr Asn Thr Val Gln Ser Phe Ile
385 390 395 400

Ala Leu Glu Val Leu His Leu Gln Leu Lys Thr Leu Gly Leu Ser Ser
405 410 415

Lys Pro Ile Val Asp Arg Phe Val Glu Ser Phe Lys Ala Met Trp Ser
420 425 430

Leu Asn Gly His Ser Leu Ser Lys Val Phe Thr Gly Ser Arg Ala Leu
435 440 445

Glu Gly Lys Ala Lys Val Gly Lys Leu Lys Asp Gly Ala Arg Ser Met
Page 146

EX05-002patentin.txt

450
 Ser Arg Thr Ile Gln Ser Asn Phe Phe Asp Gly Val Lys Gln Glu Ala
 465 470 475 480
 Ile Lys Leu Leu Leu Val Gly Asp Val Tyr Gly Glu Glu Val Ala Asp
 485 490 495
 Lys Gly Gly Met Leu Leu Asp Ser Thr Ala Leu Leu Val Thr Pro Arg
 500 505 510
 Ile Leu Lys Ala Met Thr Glu Arg Gln Ser Glu Phe Thr Asn Phe Lys
 515 520 525
 Arg Ile Arg Ile Ala Met Gly Thr Trp Asn Val Asn Gly Gly Lys Gln
 530 535 540
 Phe Arg Ser Asn Val Leu Arg Thr Ala Glu Leu Thr Asp Trp Leu Leu
 545 550 555 560
 Asp Ser Pro Gln Leu Ser Gly Ala Thr Asp Ser Gln Asp Asp Ser Ser
 565 570 575
 Pro Ala Asp Ile Phe Ala Val Gly Phe Glu Glu Met Val Glu Leu Ser
 580 585 590
 Ala Gly Asn Ile Val Asn Ala Ser Thr Thr Asn Lys Lys Met Trp Gly
 595 600 605
 Glu Gln Leu Gln Lys Ala Ile Ser Arg Ser His Arg Tyr Ile Leu Leu
 610 615 620
 Thr Ser Ala Gln Leu Val Gly Val Cys Leu Tyr Ile Phe Val Arg Pro
 625 630 635 640
 Tyr His Val Pro Phe Ile Arg Asp Val Ala Ile Asp Thr Val Lys Thr
 645 650 655
 Gly Met Gly Gly Lys Ala Gly Asn Lys Gly Ala Val Gly Ile Arg Phe
 660 665 670
 Gln Phe His Ser Thr Ser Phe Cys Phe Ile Cys Ser His Leu Thr Ala
 675 680 685
 Gly Gln Ser Gln Val Lys Glu Arg Asn Glu Asp Tyr Lys Glu Ile Thr
 690 695 700
 Gln Lys Leu Cys Phe Pro Met Gly Arg Asn Val Phe Ser His Asp Tyr
 705 710 715 720
 Val Phe Trp Cys Gly Asp Phe Asn Tyr Arg Ile Asp Leu Thr Tyr Glu

EX05-002patentin.txt
730

725

735

Glu Val Phe Tyr Phe Val Lys Arg Gln Asp Trp Lys Lys Leu Leu Glu
740 745 750

Phe Asp Gln Leu Gln Leu Gln Lys Ser Ser Gly Lys Ile Phe Lys Asp
755 760 765

Phe His Glu Gly Ala Ile Asn Phe Gly Pro Thr Tyr Lys Tyr Asp Val
770 775 780

Gly Ser Ala Ala Tyr Asp Thr Ser Asp Lys Cys Arg Thr Pro Ala Trp
785 790 795 800

Thr Asp Arg Val Leu Trp Trp Arg Lys Lys His Pro Phe Asp Lys Thr
805 810 815

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

Val Arg His Thr Trp Ser Pro Gly Ala Leu Gln Tyr Tyr Gly Arg Ala
835 840 845

Glu Leu Gln Ala Ser Asp His Arg Pro Val Leu Ala Ile Val Glu Val
850 855 860

Glu Val Gln Glu Val Asp Val Gly Ala Arg Glu Arg Val Phe Gln Glu
865 870 875 880

Val Ser Ser Phe Gln Gly Pro Leu Asp Ala Thr Val Val Val Asn Leu
885 890 895

Gln Ser Pro Thr Leu Glu Glu Lys Asn Glu Phe Pro Glu Asp Leu Arg
900 905 910

Thr Glu Leu Met Gln Thr Leu Gly Ser Tyr Gly Thr Ile Val Leu Val
915 920 925

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

Ala Leu Ser Val Leu Asp Val Asp Gly Met Lys Val Lys Gly Arg Ala
945 950 955 960

Val Lys Ile Arg Pro Lys Thr Lys Asp Trp Leu Lys Gly Leu Arg Glu
965 970 975

Glu Ile Ile Arg Lys Arg Asp Ser Met Ala Pro Val Ser Pro Thr Ala
980 985 990

Asn Ser Cys Leu Leu Glu Glu Asn Phe Asp Phe Thr Ser Leu Asp Tyr
Page 148

EX05-002patentin.txt

995	1000	1005
Glu Ser 1010	Glu Gly Asp Ile 1015	Glu Asp Asp Glu Asp Tyr Leu Val 1020
Asp Glu 1025	Phe Asn Gln Pro Gly 1030	Val Ser Asp Ser Glu Leu Gly Gly 1035
Asp Asp 1040	Leu Ser Asp Val Pro 1045	Gly Pro Thr Ala Leu Ala Pro Pro 1050
Ser Lys 1055	Ser Pro Ala Leu Thr 1060	Lys Lys Lys Gln His Pro Thr Tyr 1065
Lys Asp 1070	Asp Ala Asp Leu Val 1075	Glu Leu Lys Arg Glu Leu Glu Ala 1080
Val Gly 1085	Glu Phe Arg His Arg 1090	Ser Pro Ser Arg Ser Leu Ser Val 1095
Pro Asn 1100	Arg Pro Arg Pro Pro 1105	Gln Pro Pro Gln Arg Pro Pro Pro 1110
Pro Thr 1115	Gly Leu Met Val Lys 1120	Lys Ser Ala Ser Asp Ala Ser Ile 1125
Ser Ser 1130	Gly Thr His Gly Gln 1135	Tyr Ser Ile Leu Gln Thr Ala Arg 1140
Leu Leu 1145	Pro Gly Ala Pro Gln 1150	Gln Pro Pro Lys Ala Arg Thr Gly 1155
Ile Ser 1160	Lys Pro Tyr Asn Val 1165	Lys Gln Ile Lys Thr Thr Asn Ala 1170
Gln Glu 1175	Ala Glu Ala Ala Ile 1180	Arg Cys Leu Leu Glu Ala Arg Gly 1185
Gly Ala 1190	Ser Glu Glu Ala Leu 1195	Ser Ala Val Ala Pro Arg Asp Leu 1200
Glu Ala 1205	Ser Ser Glu Pro Glu 1210	Pro Thr Pro Gly Ala Ala Lys Pro 1215
Glu Thr 1220	Pro Gln Ala Pro Pro 1225	Leu Leu Pro Arg Arg Pro Pro Pro 1230
Arg Val 1235	Pro Ala Ile Lys Lys 1240	Pro Thr Leu Arg Arg Thr Gly Lys 1245
Pro Leu	Ser Pro Glu Glu Gln	Phe Glu Gln Gln Thr Val His Phe

EX05-002patentin.txt

1250		1255		1260
Thr Ile Gly Pro Pro Glu Thr	Ser Val Glu Ala Pro	Pro Val Val		
1265		1270		1275
Thr Ala Pro Arg Val Pro	Pro Val Pro Lys Pro	Arg Thr Phe Gln		
1280		1285		1290
Pro Gly Lys Ala Ala Glu	Arg Pro Ser His Arg	Lys Pro Ala Ser		
1295		1300		1305
Asp Glu Ala Pro Pro Gly	Ala Gly Ala Ser Val	Pro Pro Pro Leu		
1310		1315		1320
Glu Ala Pro Pro Leu Val	Pro Lys Val Pro Pro	Arg Arg Lys Lys		
1325		1330		1335
Ser Ala Pro Ala Ala Phe	His Leu Gln Val Leu	Gln Ser Asn Ser		
1340		1345		1350
Gln Leu Leu Gln Gly Leu	Thr Tyr Asn Ser Ser	Asp Ser Pro Ser		
1355		1360		1365
Gly His Pro Pro Ala Ala	Gly Thr Val Phe Pro	Gln Gly Asp Phe		
1370		1375		1380
Leu Ser Thr Ser Ser Ala	Thr Ser Pro Asp Ser	Asp Gly Thr Lys		
1385		1390		1395
Ala Met Lys Pro Glu Ala	Ala Pro Leu Leu Gly	Asp Tyr Gln Asp		
1400		1405		1410
Pro Phe Trp Asn Leu Leu	His His Pro Lys Leu	Leu Asn Asn Thr		
1415		1420		1425
Trp Leu Ser Lys Ser Ser	Asp Pro Leu Asp Ser	Gly Thr Arg Ser		
1430		1435		1440
Pro Lys Arg Asp Pro Ile	Asp Pro Val Ser Ala	Gly Ala Ser Ala		
1445		1450		1455
Ala Lys Ala Glu Leu Pro	Pro Asp His Glu His	Lys Thr Leu Gly		
1460		1465		1470
His Trp Val Thr Ile Ser	Asp Gln Glu Lys Arg	Thr Ala Leu Gln		
1475		1480		1485
Val Phe Asp Pro Leu Ala	Lys Thr			
1490		1495		

EX05-002patentin.txt

<211> 147
 <212> PRT
 <213> Homo sapiens

<400> 73

Met Ala Leu Lys Arg Ile Asn Lys Glu Leu Ser Asp Leu Ala Arg Asp
 1 5 10 15

Pro Pro Ala Gln Cys Ser Ala Gly Pro Val Gly Asp Asp Met Phe His
 20 25 30

Trp Gln Ala Thr Ile Met Gly Pro His Asp Arg Pro Tyr Gln Gly Gly
 35 40 45

Val Phe Phe Trp Thr Ile Arg Phe Pro Thr Asp Tyr Pro Phe Lys Pro
 50 55 60

Ser Lys Val Ala Phe Thr Thr Arg Ile Tyr His Pro Asn Ile Asn Ser
 65 70 75 80

Asn Gly Ser Ile Phe Leu Asp Ile Leu Arg Ser Gln Trp Ser Pro Ala
 85 90 95

Leu Thr Leu Ser Lys Val Leu Leu Ser Ile Cys Ser Leu Leu Cys Asp
 100 105 110

Pro Asn Pro Asp Asp Pro Leu Val Pro Glu Ile Ala Arg Ile Tyr Lys
 115 120 125

Thr Asp Arg Asp Lys Tyr Asn Arg Ile Ser Arg Glu Trp Thr Gln Lys
 130 135 140

Tyr Ala Met
 145

<210> 74
 <211> 147
 <212> PRT
 <213> Homo sapiens

<400> 74

Met Ala Leu Lys Arg Ile Gln Lys Glu Leu Thr Asp Leu Gln Arg Asp
 1 5 10 15

Pro Pro Ala Gln Cys Ser Ala Gly Pro Val Gly Asp Asp Leu Phe His
 20 25 30

Trp Gln Ala Thr Ile Met Gly Pro Asn Asp Ser Pro Tyr Gln Gly Gly
 35 40 45

Val Phe Phe Leu Thr Ile His Phe Pro Thr Asp Tyr Pro Phe Lys Pro
 50 55 60

EX05-002patentin.txt

Pro Lys Val Ala Phe Thr Thr Lys Ile Tyr His Pro Asn Ile Asn Ser
65 70 75 80

Asn Gly Ser Ile Cys Leu Asp Ile Leu Arg Ser Gln Trp Ser Pro Ala
85 90 95

Leu Thr Val Ser Lys Val Leu Leu Ser Ile Cys Ser Leu Leu Cys Asp
100 105 110

Pro Asn Pro Asp Asp Pro Leu Val Pro Glu Ile Ala His Thr Tyr Lys
115 120 125

Ala Asp Arg Glu Lys Tyr Asn Arg Leu Ala Arg Glu Trp Thr Gln Lys
130 135 140

Tyr Ala Met
145

<210> 75
<211> 118
<212> PRT
<213> Homo sapiens

<400> 75

Met Phe His Trp Gln Ala Thr Ile Met Gly Pro Asn Asp Ser Pro Tyr
1 5 10 15

Gln Gly Gly Val Phe Phe Leu Thr Ile His Phe Pro Thr Asp Tyr Pro
20 25 30

Phe Lys Pro Pro Lys Val Ala Phe Thr Thr Arg Ile Tyr His Pro Asn
35 40 45

Ile Asn Ser Asn Gly Ser Ile Cys Leu Asp Ile Leu Arg Ser Gln Trp
50 55 60

Ser Pro Ala Leu Thr Ile Ser Lys Val Leu Leu Ser Ile Cys Ser Leu
65 70 75 80

Leu Cys Asp Pro Asn Pro Asp Asp Pro Leu Val Pro Glu Ile Ala Arg
85 90 95

Ile Tyr Lys Thr Asp Arg Glu Lys Tyr Asn Arg Ile Ala Arg Glu Trp
100 105 110

Thr Gln Lys Tyr Ala Met
115

<210> 76
<211> 148
<212> PRT
<213> Homo sapiens

EX05-002patentin.txt

<400> 76

Met Ala Leu Lys Arg Ile Asn Lys Glu Leu Ser Asp Leu Ala Arg Asp
 1 5 10 15

Pro Pro Ala Gln Cys Ser Ala Gly Pro Val Gly Asp Asp Met Phe His
 20 25 30

Trp Gln Ala Thr Ile Met Gly Pro Asn Asp Ser Pro Tyr Gln Gly Gly
 35 40 45

Val Phe Phe Leu Thr Ile His Phe Pro Thr Asp Tyr Pro Phe Lys Pro
 50 55 60

Pro Lys Val Ala Phe Thr Thr Arg Ile Tyr His Pro Asn Ile Asn Ser
 65 70 75 80

Asn Gly Ser Ile Cys Leu Asp Ile Leu Arg Ser Gln Trp Ser Pro Ala
 85 90 95

Leu Thr Ile Ser Lys Val Leu Leu Ser Ile Cys Ser Leu Leu Cys Asp
 100 105 110

Pro Asn Pro Asp Asp Pro Leu Val Pro Glu Ile Ala Arg Ile Tyr Lys
 115 120 125

Thr Asp Arg Asp Lys Tyr Asn Arg Leu Ala Arg Glu Trp Thr Glu Lys
 130 135 140

Tyr Ala Met Leu
 145

<210> 77

<211> 451

<212> PRT

<213> Homo sapiens

<400> 77

Met Ala His Asp Leu Leu Phe Arg Leu Phe Pro Leu Leu Ala Leu Gly
 1 5 10 15

Val Pro Leu Gln Ser Asn Arg Leu Gly Pro Thr Ser Arg Leu Arg Tyr
 20 25 30

Ser Arg Phe Leu Asp Pro Ser Asn Val Ile Phe Leu Arg Trp Asp Phe
 35 40 45

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

Gly Trp Val Gly Phe Gly Val Thr Asn Arg Tyr Thr Asn Val Gly Ser
 65 70 75 80

EX05-002patentin.txt

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

EX05-002patentin.txt

Gln Tyr Arg Asn Gly Thr Gln Leu Arg Lys Ile Cys Lys Asp Asp Ser
 355 360 365

Tyr Asp Phe Asn Leu Gln Glu Thr Arg Asp Leu Pro Ser Arg Val Glu
 370 375 380

Ile Lys Pro Gly Asp Glu Leu Leu Val Glu Cys His Tyr Gln Thr Leu
 385 390 395 400

Asp Arg Asp Ser Met Thr Phe Gly Gly Pro Ser Thr Ile Asn Glu Met
 405 410 415

Cys Leu Ile Phe Leu Phe Tyr Tyr Pro Gln Asn Asn Ile Ser Ser Cys
 420 425 430

Met Gly Tyr Pro Asp Ile Ile Tyr Val Ala His Glu Leu Gly Glu Glu
 435 440 445

Ala Ser Glu
 450

<210> 78
 <211> 613
 <212> PRT
 <213> Homo sapiens

<400> 78

Met Cys Cys Trp Pro Leu Leu Leu Leu Trp Gly Leu Leu Pro Gly Thr
 1 5 10 15

Ala Ala Gly Gly Ser Gly Arg Thr Tyr Pro His Arg Thr Leu Leu Asp
 20 25 30

Ser Glu Gly Lys Tyr Trp Leu Gly Trp Ser Gln Arg Gly Ser Gln Ile
 35 40 45

Ala Phe Arg Leu Gln Val Arg Thr Ala Gly Tyr Val Gly Phe Gly Phe
 50 55 60

Ser Pro Thr Gly Ala Met Ala Ser Ala Asp Ile Val Val Gly Gly Val
 65 70 75 80

Ala His Gly Arg Pro Tyr Leu Gln Asp Tyr Phe Thr Asn Ala Asn Arg
 85 90 95

Glu Leu Lys Lys Asp Ala Gln Gln Asp Tyr His Leu Glu Tyr Ala Met
 100 105 110

Glu Asn Ser Thr His Thr Ile Ile Glu Phe Thr Arg Glu Leu His Thr
 115 120 125

EX05-002patentin.txt

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

EX05-002patentin.txt

His Phe Arg Lys Gly Lys Glu Met Lys Leu Leu Ala Tyr Asp Asp Asp
 405 410 415

Phe Asp Phe Asn Phe Gln Glu Phe Gln Tyr Leu Lys Glu Glu Gln Thr
 420 425 430

Ile Leu Pro Gly Asp Asn Leu Ile Thr Glu Cys Arg Tyr Asn Thr Lys
 435 440 445

Asp Arg Ala Glu Met Thr Trp Gly Gly Leu Ser Thr Arg Ser Glu Met
 450 455 460

Cys Leu Ser Tyr Leu Leu Tyr Tyr Pro Arg Ile Asn Leu Thr Arg Cys
 465 470 475 480

Ala Ser Ile Pro Asp Ile Met Glu Gln Leu Gln Phe Ile Gly Val Lys
 485 490 495

Glu Ile Tyr Arg Pro Val Thr Thr Trp Pro Phe Ile Ile Lys Ser Pro
 500 505 510

Lys Gln Tyr Lys Asn Leu Ser Phe Met Asp Ala Met Asn Lys Phe Lys
 515 520 525

Trp Thr Lys Lys Glu Gly Leu Ser Phe Asn Lys Leu Val Leu Ser Leu
 530 535 540

Pro Val Asn Val Arg Cys Ser Lys Thr Asp Asn Ala Glu Trp Ser Ile
 545 550 555 560

Gln Gly Met Thr Ala Leu Pro Pro Asp Ile Glu Arg Pro Tyr Lys Ala
 565 570 575

Glu Pro Leu Val Cys Gly Thr Ser Ser Ser Ser Ser Leu His Arg Asp
 580 585 590

Phe Ser Ile Asn Leu Leu Val Cys Leu Leu Leu Leu Ser Cys Thr Leu
 595 600 605

Ser Thr Lys Ser Leu
 610

<210> 79
 <211> 1054
 <212> PRT
 <213> Homo sapiens

<400> 79

Gly Cys Ser Ser Gly Thr Gly Val Arg Ala Leu Trp Arg Glu Glu Lys
 1 5 10 15

EX05-002patentin.txt

Pro Gly Gly Gly Arg Arg Val Lys Arg Arg Asn Pro Gly Arg Gln Ala
 20 25 30

Val Gly His Thr Glu Glu Asp Pro Pro Arg Val Gly Thr Pro Trp Lys
 35 40 45

Glu His Thr Gly Pro Gly Pro Gln Glu Gly Ser Thr Met Glu Ala Ala
 50 55 60

His Ala Lys Thr Thr Glu Glu Cys Leu Ala Tyr Phe Gly Val Gly Glu
 65 70 75 80

Thr Thr Gly Leu Thr Pro Asp Gln Val Lys Arg Asn Leu Glu Lys Tyr
 85 90 95

Gly Leu Asn Glu Leu Pro Ala Glu Glu Gly Lys Thr Leu Trp Glu Leu
 100 105 110

Val Ile Glu Gln Phe Glu Asp Leu Leu Val Arg Ile Leu Leu Leu Ala
 115 120 125

Ala Cys Ile Ser Phe Val Leu Ala Trp Phe Glu Glu Gly Glu Glu Thr
 130 135 140

Ile Thr Ala Phe Val Glu Pro Phe Val Ile Leu Leu Ile Leu Ile Ala
 145 150 155 160

Asn Ala Ile Val Gly Val Trp Gln Glu Arg Asn Ala Glu Asn Ala Ile
 165 170 175

Glu Ala Leu Lys Glu Tyr Glu Pro Glu Met Gly Lys Val Tyr Arg Ala
 180 185 190

Asp Arg Lys Ser Val Gln Arg Ile Lys Ala Arg Asp Ile Val Pro Gly
 195 200 205

Asp Ile Val Glu Val Ala Val Gly Asp Lys Val Pro Ala Asp Ile Arg
 210 215 220

Ile Leu Ala Ile Lys Ser Thr Thr Leu Arg Val Asp Gln Ser Ile Leu
 225 230 235 240

Thr Gly Glu Ser Val Ser Val Ile Lys His Thr Glu Pro Val Pro Asp
 245 250 255

Pro Arg Ala Val Asn Gln Asp Lys Lys Asn Met Leu Phe Ser Gly Thr
 260 265 270

Asn Ile Ala Ala Gly Lys Ala Leu Gly Ile Val Ala Thr Thr Gly Val
 275 280 285

EX05-002patentin.txt

Gly Thr Glu Ile Gly Arg Ile Arg Asp Gln Met Ala Ala Thr Glu Gln
 290 295 300

Asp Lys Thr Pro Leu Gln Gln Lys Leu Asp Glu Phe Gly Glu Gln Leu
 305 310 315 320

Ser Lys Val Ile Ser Leu Ile Cys Val Ala Val Trp Leu Ile Asn Ile
 325 330 335

Gly His Phe Asn Asp Pro Val His Gly Gly Ser Trp Phe Arg Gly Ala
 340 345 350

Ile Tyr Tyr Phe Lys Ile Ala Val Ala Leu Ala Val Ala Ala Ile Pro
 355 360 365

Glu Gly Leu Pro Ala Val Ile Thr Thr Cys Leu Ala Leu Gly Thr Arg
 370 375 380

Arg Met Ala Lys Lys Asn Ala Ile Val Arg Ser Leu Pro Ser Val Glu
 385 390 395 400

Thr Leu Gly Cys Thr Ser Val Ile Cys Ser Asp Lys Thr Gly Thr Leu
 405 410 415

Thr Thr Asn Gln Met Ser Val Cys Lys Met Phe Ile Ile Asp Lys Val
 420 425 430

Asp Gly Asp Ile Cys Leu Leu Asn Glu Phe Ser Ile Thr Gly Ser Thr
 435 440 445

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

Gly Gln Tyr Asp Gly Leu Val Glu Leu Ala Thr Ile Cys Ala Leu Cys
 465 470 475 480

Asn Asp Ser Ser Leu Asp Phe Asn Glu Ala Lys Gly Val Tyr Glu Lys
 485 490 495

Val Gly Glu Ala Thr Glu Thr Ala Leu Thr Thr Leu Val Glu Lys Met
 500 505 510

Asn Val Phe Asn Thr Asp Val Arg Ser Leu Ser Lys Val Glu Arg Ala
 515 520 525

Asn Ala Cys Asn Ser Val Ile Arg Gln Leu Met Lys Lys Glu Phe Thr
 530 535 540

Leu Glu Phe Ser Arg Asp Arg Lys Ser Met Ser Val Tyr Cys Ser Pro
 545 550 555 560

EX05-002patentin.txt

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

EX05-002patentin.txt

Val Cys Ile Phe Leu Thr Ala Ala Leu Gly Leu Pro Glu Ala Leu Ile
 835 840 845

Pro Val Gln Leu Leu Trp Val Asn Leu Val Thr Asp Gly Leu Pro Ala
 850 855 860

Thr Ala Leu Gly Phe Asn Pro Pro Asp Leu Asp Ile Met Asp Arg Pro
 865 870 875 880

Pro Arg Ser Pro Lys Glu Pro Leu Ile Ser Gly Trp Leu Phe Phe Arg
 885 890 895

Tyr Met Ala Ile Gly Gly Tyr Val Gly Ala Ala Thr Val Gly Ala Ala
 900 905 910

Ala Trp Trp Phe Leu Tyr Ala Glu Asp Gly Pro His Val Asn Tyr Ser
 915 920 925

Gln Leu Thr His Phe Met Gln Cys Thr Glu Asp Asn Thr His Phe Glu
 930 935 940

Gly Ile Asp Cys Glu Val Phe Glu Ala Pro Glu Pro Met Thr Met Ala
 945 950 955 960

Leu Ser Val Leu Val Thr Ile Glu Met Cys Asn Ala Leu Asn Ser Leu
 965 970 975

Ser Glu Asn Gln Ser Leu Leu Arg Met Pro Pro Trp Val Asn Ile Trp
 980 985 990

Leu Leu Gly Ser Ile Cys Leu Ser Met Ser Leu His Phe Leu Ile Leu
 995 1000 1005

Tyr Val Asp Pro Leu Pro Met Ile Phe Lys Leu Arg Ala Leu Asp
 1010 1015 1020

Leu Thr Gln Trp Leu Met Val Leu Lys Ile Ser Leu Pro Val Ile
 1025 1030 1035

Gly Leu Asp Glu Ile Leu Lys Phe Val Ala Arg Asn Tyr Leu Glu
 1040 1045 1050

Gly

<210> 80
 <211> 1042
 <212> PRT
 <213> Homo sapiens

<400> 80

Met Glu Asn Ala His Thr Lys Thr Val Glu Glu Val Leu Gly His Phe
 Page 161

1

5

10

15

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

Leu Leu Glu Leu Val Ile Glu Gln Phe Glu Asp Leu Leu Val Arg Ile
50 55 60

Leu Leu Leu Ala Ala Cys Ile Ser Phe Val Leu Ala Trp Phe Glu Glu
65 70 75 80

Gly Glu Glu Thr Ile Thr Ala Phe Val Glu Pro Phe Val Ile Leu Leu
85 90 95

Ile Leu Val Ala Asn Ala Ile Val Gly Val Trp Gln Glu Arg Asn Ala
100 105 110

Glu Asn Ala Ile Glu Ala Leu Lys Glu Tyr Glu Pro Glu Met Gly Lys
115 120 125

Val Tyr Arg Gln Asp Arg Lys Ser Val Gln Arg Ile Lys Ala Lys Asp
130 135 140

Ile Val Pro Gly Asp Ile Val Glu Ile Ala Val Gly Asp Lys Val Pro
145 150 155 160

Ala Asp Ile Arg Leu Thr Ser Ile Lys Ser Thr Thr Leu Arg Val Asp
165 170 175

Gln Ser Ile Leu Thr Gly Glu Ser Val Ser Val Ile Lys His Thr Asp
180 185 190

Pro Val Pro Asp Pro Arg Ala Val Asn Gln Asp Lys Lys Asn Met Leu
195 200 205

Phe Ser Gly Thr Asn Ile Ala Ala Gly Lys Ala Met Gly Val Val Val
210 215 220

Ala Thr Gly Val Asn Thr Glu Ile Gly Lys Ile Arg Asp Glu Met Val
225 230 235 240

Ala Thr Glu Gln Glu Arg Thr Pro Leu Gln Gln Lys Leu Asp Glu Phe
245 250 255

Gly Glu Gln Leu Ser Lys Val Ile Ser Leu Ile Cys Ile Ala Val Trp
260 265 270

Ile Ile Asn Ile Gly His Phe Asn Asp Pro Val His Gly Gly Ser Trp
Page 162

Page 163

545 550 555 560

Asn Lys Pro Pro Arg Asn Pro Lys Glu Pro Leu Ile Ser Gly Trp Leu
Page 164

EX05-002patentin.txt

820

825

830

Phe Phe Arg Tyr Leu Ala Ile Gly Cys Tyr Val Gly Ala Ala Thr Val
 835 840 845

Gly Ala Ala Ala Trp Trp Phe Ile Ala Ala Asp Gly Gly Pro Arg Val
 850 855 860

Ser Phe Tyr Gln Leu Ser His Phe Leu Gln Cys Lys Glu Asp Asn Pro
 865 870 875 880

Asp Phe Glu Gly Val Asp Cys Ala Ile Phe Glu Ser Pro Tyr Pro Met
 885 890 895

Thr Met Ala Leu Ser Val Leu Val Thr Ile Glu Met Cys Asn Ala Leu
 900 905 910

Asn Ser Leu Ser Glu Asn Gln Ser Leu Leu Arg Met Pro Pro Trp Glu
 915 920 925

Asn Ile Trp Leu Val Gly Ser Ile Cys Leu Ser Met Ser Leu His Phe
 930 935 940

Leu Ile Leu Tyr Val Glu Pro Leu Pro Leu Ile Phe Gln Ile Thr Pro
 945 950 955 960

Leu Asn Val Thr Gln Trp Leu Met Val Leu Lys Ile Ser Leu Pro Val
 965 970 975

Ile Leu Met Asp Glu Thr Leu Lys Phe Val Ala Arg Asn Tyr Leu Glu
 980 985 990

Pro Gly Lys Glu Cys Val Gln Pro Ala Thr Lys Ser Cys Ser Phe Ser
 995 1000 1005

Ala Cys Thr Asp Gly Ile Ser Trp Pro Phe Val Leu Leu Ile Met
 1010 1015 1020

Pro Leu Val Ile Trp Val Tyr Ser Thr Asp Thr Asn Phe Ser Asp
 1025 1030 1035

Met Phe Trp Ser
 1040

<210> 81
 <211> 1052
 <212> PRT
 <213> Homo sapiens

<400> 81

Met Glu Ala Ala His Leu Leu Pro Ala Ala Asp Val Leu Arg His Phe
 1 5 10 15

EX05-002patentin.txt

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

EX05-002patentin.txt

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

EX05-002patentin.txt

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

EX05-002patentin.txt

Leu Phe Phe Arg Tyr Leu Ala Ile Gly Val Tyr Val Gly Leu Ala Thr
 835 840 845
 Val Ala Ala Ala Thr Trp Trp Phe Val Tyr Asp Ala Glu Gly Pro His
 850 855 860
 Ile Asn Phe Tyr Gln Leu Arg Asn Phe Leu Lys Cys Ser Glu Asp Asn
 865 870 875 880
 Pro Leu Phe Ala Gly Ile Asp Cys Glu Val Phe Glu Ser Arg Phe Pro
 885 890 895
 Thr Thr Met Ala Leu Ser Val Leu Val Thr Ile Glu Met Cys Asn Ala
 900 905 910
 Leu Asn Ser Val Ser Glu Asn Gln Ser Leu Leu Arg Met Pro Pro Trp
 915 920 925
 Met Asn Pro Trp Leu Leu Val Ala Val Ala Met Ser Met Ala Leu His
 930 935 940
 Phe Leu Ile Leu Leu Val Pro Pro Leu Pro Leu Ile Phe Gln Val Thr
 945 950 955 960
 Pro Leu Ser Gly Arg Gln Trp Val Val Val Leu Gln Ile Ser Leu Pro
 965 970 975
 Val Ile Leu Leu Asp Glu Ala Leu Lys Tyr Leu Ser Arg Asn His Met
 980 985 990
 His Ala Cys Leu Tyr Pro Gly Leu Leu Arg Thr Val Ser Gln Ala Trp
 995 1000 1005
 Ser Arg Gln Pro Leu Thr Thr Ser Trp Thr Pro Asp His Thr Gly
 1010 1015 1020
 Leu Ala Ser Leu Gly Gln Gly His Ser Ile Val Ser Leu Ser Glu
 1025 1030 1035
 Leu Leu Arg Glu Gly Gly Ser Arg Glu Glu Met Ser Gln Lys
 1040 1045 1050
 <210> 82
 <211> 724
 <212> PRT
 <213> Homo sapiens
 <400> 82
 Met Pro Arg Asn Ser Gly Ala Gly Tyr Gly Cys Pro His Gly Asp Pro
 1 5 10 15

EX05-002patentin.txt

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

EX05-002patentin.txt

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

EX05-002patentin.txt

Tyr Ile Thr Gly Arg Leu Lys Glu Leu Ile Ile Thr Ala Gly Gly Glu
565 570 575

Asn Val Pro Pro Val Pro Ile Glu Glu Ala Val Lys Met Glu Leu Pro
580 585 590

Ile Ile Ser Asn Ala Met Leu Ile Gly Asp Gln Arg Lys Phe Leu Ser
595 600 605

Met Leu Leu Thr Leu Lys Cys Thr Leu Asp Pro Asp Thr Ser Asp Gln
610 615 620

Thr Asp Asn Leu Thr Glu Gln Ala Met Glu Phe Cys Gln Arg Val Gly
625 630 635 640

Ser Arg Ala Thr Thr Val Ser Glu Ile Ile Glu Lys Lys Asp Glu Ala
645 650 655

Val Tyr Gln Ala Ile Glu Glu Gly Ile Arg Arg Val Asn Met Asn Ala
660 665 670

Ala Ala Arg Pro Tyr His Ile Gln Lys Trp Ala Ile Leu Glu Arg Asp
675 680 685

Phe Ser Ile Ser Gly Gly Glu Leu Gly Pro Thr Met Lys Leu Lys Arg
690 700

Leu Thr Val Leu Glu Lys Tyr Lys Gly Ile Ile Asp Ser Phe Tyr Gln
705 710 715 720

Glu Gln Lys Met

<210> 83
<211> 666
<212> PRT
<213> Homo sapiens

<400> 83

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

Asp Met Asn Lys Thr Glu Val Thr Pro Arg Leu Trp Thr Thr Cys Arg
20 25 30

Asp Gly Glu Val Leu Leu Arg Leu Ser Lys His Gly Pro Gly His Glu
35 40 45

Thr Pro Met Thr Ile Pro Glu Phe Phe Arg Glu Ser Val Asn Arg Phe
50 55 60

EX05-002patentin.txt

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

EX05-002patentin.txt

Lys Ser Met Gly Leu Lys Lys Lys Ala Phe Val Trp Ala Arg Asn Ile
 340 345 350

Gly Phe Lys Val Asn Ser Lys Lys Met Leu Gly Lys Tyr Asn Thr Pro
 355 360 365

Val Ser Tyr Arg Met Ala Lys Thr Leu Val Phe Ser Lys Val Lys Thr
 370 375 380

Ser Leu Gly Leu Asp His Cys His Ser Phe Ile Ser Gly Thr Ala Pro
 385 390 395 400

Leu Asn Gln Glu Thr Ala Glu Phe Phe Leu Ser Leu Asp Ile Pro Ile
 405 410 415

Gly Glu Leu Tyr Gly Leu Ser Glu Ser Ser Gly Pro His Thr Ile Ser
 420 425 430

Asn Gln Asn Asn Tyr Arg Leu Leu Ser Cys Gly Lys Ile Leu Thr Gly
 435 440 445

Cys Lys Asn Met Leu Phe Gln Gln Asn Lys Asp Gly Ile Gly Glu Ile
 450 455 460

Cys Leu Trp Gly Arg His Ile Phe Met Gly Tyr Leu Glu Ser Glu Thr
 465 470 475 480

Glu Thr Thr Glu Ala Ile Asp Asp Glu Gly Trp Leu His Ser Gly Asp
 485 490 495

Leu Gly Gln Leu Asp Gly Leu Gly Phe Leu Tyr Val Thr Gly His Ile
 500 505 510

Lys Glu Ile Leu Ile Thr Ala Gly Gly Glu Asn Val Pro Pro Ile Pro
 515 520 525

Val Glu Thr Leu Val Lys Lys Lys Ile Pro Ile Ile Ser Asn Ala Met
 530 535 540

Leu Val Gly Asp Lys Leu Lys Phe Leu Ser Met Leu Leu Thr Leu Lys
 545 550 555 560

Cys Glu Met Asn Gln Met Ser Gly Glu Pro Leu Asp Lys Leu Asn Phe
 565 570 575

Glu Ala Ile Asn Phe Cys Arg Asp Leu Asp Ser Gln Ala Ser Thr Val
 580 585 590

Thr Glu Ile Val Lys Gln Gln Asp Pro Leu Val Tyr Lys Ala Ile Gln
 595 600 605

EX05-002patentin.txt

Gln Gly Ile Asn Ala Val Asn Gln Glu Ala Met Asn Asn Ala Gln Lys
 610 615 620

Ile Gln Lys Trp Val Ile Leu Glu Lys Asp Phe Ser Ile Tyr Gly Gly
 625 630 635 640

Glu Leu Gly Pro Met Met Lys Leu Lys Arg His Phe Val Ala Gln Lys
 645 650 655

Tyr Lys Lys Gln Ile Asp His Met Tyr His
 660 665

<210> 84
 <211> 274
 <212> PRT
 <213> Homo sapiens

<400> 84

Met Ala Ser Asp Ser Gly Asn Gln Gly Thr Leu Cys Thr Leu Glu Phe
 1 5 10 15

Ala Val Gln Met Thr Cys Gln Ser Cys Val Asp Ala Val Arg Lys Ser
 20 25 30

Leu Gln Gly Val Ala Gly Val Gln Asp Val Glu Val His Leu Glu Asp
 35 40 45

Gln Met Val Leu Val His Thr Thr Leu Pro Ser Gln Glu Val Gln Ala
 50 55 60

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

Gly Gln Leu Gln Asn Leu Gly Ala Ala Val Ala Ile Leu Gly Gly Pro
 85 90 95

Gly Thr Val Gln Gly Val Val Arg Phe Leu Gln Leu Thr Pro Glu Arg
 100 105 110

Cys Leu Ile Asp Gly Thr Ile Asp Gly Leu Glu Pro Gly Leu His Gly
 115 120 125

Leu His Val His Gln Tyr Gly Asp Leu Thr Asn Asn Cys Asn Ser Cys
 130 135 140

Gly Asn His Phe Asn Pro Asp Gly Ala Ser His Gly Gly Pro Gln Asp
 145 150 155 160

Ser Asp Arg His Arg Gly Asp Leu Gly Asn Val Arg Ala Asp Ala Asp
 165 170 175

Gly Arg Ala Ile Phe Arg Met Glu Asp Glu Gln Leu Lys Val Trp Asp
 Page 175

EX05-002patentin.txt

180

185

190

Val Ile Gly Arg Ser Leu Ile Ile Asp Glu Gly Glu Asp Asp Leu Gly
 195 200 205

Arg Gly Gly His Pro Leu Ser Lys Ile Thr Gly Asn Ser Gly Glu Arg
 210 215 220

Leu Ala Cys Gly Ile Ile Ala Arg Ser Ala Gly Leu Phe Gln Asn Pro
 225 230 235 240

Lys Gln Ile Cys Ser Cys Asp Gly Leu Thr Ile Trp Glu Glu Arg Gly
 245 250 255

Arg Pro Ile Ala Gly Lys Gly Arg Lys Glu Ser Ala Gln Pro Pro Ala
 260 265 270

His Leu

<210> 85
 <211> 604
 <212> PRT
 <213> Homo sapiens

<400> 85

Met Arg Gly Ala Ala Arg Leu Gly Arg Pro Gly Arg Ser Cys Leu Pro
 1 5 10 15

Gly Pro Ala Leu Arg Ala Ala Ala Ala Pro Ala Leu Leu Leu Ala Arg
 20 25 30

Cys Ala Val Ala Ala Ala Ala Gly Leu Arg Ala Ala Ala Arg Pro Arg
 35 40 45

Pro Pro Glu Leu Gln Ser Ala Ser Ala Gly Pro Ser Val Ser Leu Tyr
 50 55 60

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

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

Leu Leu Val Pro Ser Glu Thr Asn Phe Leu His Phe Thr Trp His Ala
 100 105 110

Lys Ser Lys Val Glu Tyr Lys Leu Gly Phe Gln Val Asp Asn Val Leu
 115 120 125

Ala Met Asp Met Pro Gln Val Asn Ile Ser Val Gln Gly Glu Val Pro
 130 135 140

EX05-002patentin.txt

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

EX05-002patentin.txt

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

<210> 86
 <211> 538
 <212> PRT
 <213> Homo sapiens

<400> 86

Met Thr Thr Pro Gly Lys Glu Asn Phe Arg Leu Lys Ser Tyr Lys Asn
 1 5 10 15
 Lys Ser Leu Asn Pro Asp Glu Met Arg Arg Arg Arg Glu Glu Glu Gly
 20 25 30
 Leu Gln Leu Arg Lys Gln Lys Arg Glu Glu Gln Leu Phe Lys Arg Arg
 35 40 45

EX05-002patentin.txt

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

EX05-002patentin.txt

Gly Asn Ile Val Thr Gly Asp Asp Ile Gln Thr Gln Val Ile Leu Asn
 325 330 335

Cys Ser Ala Leu Gln Ser Leu Leu His Leu Leu Ser Ser Pro Lys Glu
 340 345 350

Ser Ile Lys Lys Glu Ala Cys Trp Thr Ile Ser Asn Ile Thr Ala Gly
 355 360 365

Asn Arg Ala Gln Ile Gln Thr Val Ile Asp Ala Asn Ile Phe Pro Ala
 370 375 380

Leu Ile Ser Ile Leu Gln Thr Ala Glu Phe Arg Thr Arg Lys Glu Ala
 385 390 395 400

Ala Trp Ala Ile Thr Asn Ala Thr Ser Gly Gly Ser Ala Glu Gln Ile
 405 410 415

Lys Tyr Leu Val Glu Leu Gly Cys Ile Lys Pro Leu Cys Asp Leu Leu
 420 425 430

Thr Val Met Asp Ser Lys Ile Val Gln Val Ala Leu Asn Gly Leu Glu
 435 440 445

Asn Ile Leu Arg Leu Gly Glu Gln Glu Ala Lys Arg Asn Gly Thr Gly
 450 455 460

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

Ile Glu Phe Leu Gln Ser His Glu Asn Gln Glu Ile Tyr Gln Lys Ala
 485 490 495

Phe Asp Leu Ile Glu His Tyr Phe Gly Thr Glu Asp Glu Asp Ser Ser
 500 505 510

Ile Ala Pro Gln Val Asp Leu Asn Gln Gln Gln Tyr Ile Phe Gln Gln
 515 520 525

Cys Glu Ala Pro Met Glu Gly Phe Gln Leu
 530 535

<210> 87
 <211> 539
 <212> PRT
 <213> Homo sapiens

<400> 87

Met Asp Ala Met Ala Ser Pro Gly Lys Asp Asn Tyr Arg Met Lys Ser
 1 5 10 15

EX05-002patentin.txt

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

EX05-002patentin.txt

Lys Ile Gln Ala Val Ile Asp Ser Gly Val Cys Arg Arg Leu Val Glu
 290 295 300

Leu Leu Met His Asn Asp Tyr Lys Val Val Ser Pro Ala Leu Arg Ala
 305 310 315 320

Val Gly Asn Ile Val Thr Gly Asp Asp Ile Gln Thr Gln Val Ile Leu
 325 330 335

Asn Cys Ser Ala Leu Pro Cys Leu Leu His Leu Leu Ser Ser Pro Lys
 340 345 350

Glu Ser Ile Arg Lys Glu Ala Cys Trp Thr Val Ser Asn Ile Thr Ala
 355 360 365

Gly Asn Arg Ala Gln Ile Gln Ala Val Ile Asp Ala Asn Ile Phe Pro
 370 375 380

Val Leu Ile Glu Ile Leu Gln Lys Ala Glu Phe Arg Thr Arg Lys Glu
 385 390 395 400

Ala Ala Trp Ala Ile Thr Asn Ala Thr Ser Gly Gly Thr Pro Glu Gln
 405 410 415

Ile Arg Tyr Leu Val Ala Leu Gly Cys Ile Lys Pro Leu Cys Asp Leu
 420 425 430

Leu Thr Val Met Asp Ser Lys Ile Val Gln Val Ala Leu Asn Gly Leu
 435 440 445

Glu Asn Ile Leu Arg Leu Gly Glu Gln Glu Ser Lys Gln Asn Gly Ile
 450 455 460

Gly Ile Asn Pro Tyr Cys Ala Leu Ile Glu Glu Ala Tyr Gly Leu Asp
 465 470 475 480

Lys Ile Glu Phe Leu Gln Ser His Glu Asn Gln Glu Ile Tyr Gln Lys
 485 490 495

Ala Phe Asp Leu Ile Glu His Tyr Phe Gly Val Glu Glu Asp Asp Pro
 500 505 510

Ser Ile Val Pro Gln Val Asp Glu Asn Gln Gln Gln Phe Ile Phe Gln
 515 520 525

Gln Gln Glu Ala Pro Met Asp Gly Phe Gln Leu
 530 535

<210> 88
 <211> 536
 <212> PRT
 <213> Homo sapiens

EX05-002patentin.txt

<400> 88

Met Glu Thr Met Ala Ser Pro Gly Lys Asp Asn Tyr Arg Met Lys Ser
 1 5 10 15

Tyr Lys Asn Asn Ala Leu Asn Pro Glu Glu Met Arg Arg Arg Arg Glu
 20 25 30

Glu Glu Gly Ile Gln Leu Arg Lys Gln Lys Arg Glu Gln Gln Leu Phe
 35 40 45

Lys Arg Arg Asn Val Glu Leu Ile Asn Glu Glu Ala Ala Met Phe Asp
 50 55 60

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

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

Gln Leu Ala Thr Thr Gln Lys Phe Arg Lys Leu Leu Ser Lys Glu Pro
 100 105 110

Ser Pro Pro Ile Asp Glu Val Ile Asn Thr Pro Arg Val Val Asp Arg
 115 120 125

Phe Val Glu Phe Leu Lys Arg Asn Glu Asn Cys Thr Leu Gln Phe Glu
 130 135 140

Ala Ala Trp Ala Leu Thr Asn Ile Ala Ser Gly Thr Ser Gln Gln Thr
 145 150 155 160

Lys Ile Val Ile Glu Ala Gly Ala Val Pro Ile Phe Ile Glu Leu Leu
 165 170 175

Asn Ser Asp Phe Glu Asp Val Gln Glu Gln Ala Val Trp Ala Leu Gly
 180 185 190

Asn Ile Ala Gly Asp Ser Ser Val Cys Arg Asp Tyr Val Leu Asn Cys
 195 200 205

Ser Ile Leu Asn Pro Leu Leu Thr Leu Leu Thr Lys Ser Thr Arg Leu
 210 215 220

Thr Met Thr Arg Asn Ala Val Trp Ala Leu Ser Asn Leu Cys Arg Gly
 225 230 235 240

Lys Asn Pro Pro Pro Glu Phe Ala Lys Val Ser Pro Cys Leu Pro Val
 245 250 255

Leu Ser Arg Leu Leu Phe Ser Ser Asp Ser Asp Leu Leu Ala Asp Ala
 Page 183

EX05-002patentin.txt

260

265

270

Cys Trp Ala₂₇₅ Leu Ser Tyr Leu Ser₂₈₀ Asp Gly Pro Asn Glu₂₈₅ Lys Ile Gln

Ala Val₂₉₀ Ile Asp Ser Gly Val₂₉₅ Cys Arg Arg Leu Val₃₀₀ Glu Leu Leu Met

His₃₀₅ Asn Asp Tyr Lys Val₃₁₀ Ala Ser Pro Ala Leu₃₁₅ Arg Ala Val Gly Asn₃₂₀

Ile Val Thr Gly Asp₃₂₅ Asp Ile Gln Thr Gln₃₃₀ Val Ile Leu Asn Cys₃₃₅ Ser

Ala Leu Pro Cys₃₄₀ Leu Leu His Leu₃₄₅ Ser Ser Pro Lys Glu₃₅₀ Ser Ile

Arg Lys Glu₃₅₅ Ala Cys Trp Thr Ile₃₆₀ Ser Asn Ile Thr Ala₃₆₅ Gly Asn Arg

Ala Gln₃₇₀ Ile Gln Ala Val Ile₃₇₅ Asp Ala Asn Ile Phe₃₈₀ Pro Val Leu Ile

Glu₃₈₅ Ile Leu Gln Lys Ala₃₉₀ Glu Phe Arg Thr Arg₃₉₅ Lys Glu Ala Ala Trp₄₀₀

Ala Ile Thr Asn Ala₄₀₅ Thr Ser Gly Gly Thr₄₁₀ Pro Glu Gln Ile Arg₄₁₅ Tyr

Leu Val Ser Leu₄₂₀ Gly Cys Ile Lys Pro₄₂₅ Leu Cys Asp Leu₄₃₀ Leu Thr Val

Met Asp Ser₄₃₅ Lys Ile Val Gln Val₄₄₀ Ala Leu Asn Gly Leu₄₄₅ Glu Asn Ile

Leu Arg₄₅₀ Leu Gly Glu Gln Glu₄₅₅ Gly Lys Arg Ser Gly₄₆₀ Ser Gly Val Asn

Pro Tyr Cys Gly Leu Ile₄₇₀ Glu Glu Ala Tyr Gly₄₇₅ Leu Asp Lys Ile Glu₄₈₀

Phe Leu Gln Ser His₄₈₅ Glu Asn Gln Glu Ile₄₉₀ Tyr Gln Lys Ala Phe₄₉₅ Asp

Leu Ile Glu His₅₀₀ Tyr Phe Gly Val Glu₅₀₅ Asp Asp Asp Ser Ser₅₁₀ Leu Ala

Pro Gln Val₅₁₅ Asp Glu Thr Gln Gln₅₂₀ Gln Phe Ile Phe Gln₅₂₅ Gln Pro Glu

Ala Pro Met Glu Gly Phe Gln Leu

EX05-002patentin.txt

530

535

<210> 89
 <211> 770
 <212> PRT
 <213> Homo sapiens

<400> 89

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

Gly Met Ser Thr Tyr Lys Arg Ala Thr Leu Asp Glu Glu Asp Leu Val
 20 25 30

Asp Ser Leu Ser Glu Gly Asp Ala Tyr Pro Asn Gly Leu Gln Val Asn
 35 40 45

Phe His Ser Pro Arg Ser Gly Gln Arg Cys Trp Ala Ala Arg Thr Gln
 50 55 60

Val Glu Lys Arg Leu Val Val Leu Val Val Leu Leu Ala Ala Gly Leu
 65 70 75 80

Val Ala Cys Leu Ala Ala Leu Gly Ile Gln Tyr Gln Thr Arg Ser Pro
 85 90 95

Ser Val Cys Leu Ser Glu Ala Cys Val Ser Val Thr Ser Ser Ile Leu
 100 105 110

Ser Ser Met Asp Pro Thr Val Asp Pro Cys His Asp Phe Phe Ser Tyr
 115 120 125

Ala Cys Gly Gly Trp Ile Lys Ala Asn Pro Val Pro Asp Gly His Ser
 130 135 140

Arg Trp Gly Thr Phe Ser Asn Leu Trp Glu His Asn Gln Ala Ile Ile
 145 150 155 160

Lys His Leu Leu Glu Asn Ser Thr Ala Ser Val Ser Glu Ala Glu Arg
 165 170 175

Lys Ala Gln Val Tyr Tyr Arg Ala Cys Met Asn Glu Thr Arg Ile Glu
 180 185 190

Glu Leu Arg Ala Lys Pro Leu Met Glu Leu Ile Glu Arg Leu Gly Gly
 195 200 205

Trp Asn Ile Thr Gly Pro Trp Ala Lys Asp Asn Phe Gln Asp Thr Leu
 210 215 220

Gln Val Val Thr Ala His Tyr Arg Thr Ser Pro Phe Phe Ser Val Tyr
 225 230 235 240

EX05-002patentin.txt

Val Ser Ala Asp Ser₂₄₅ Lys Asn Ser Asn₂₅₀ Asn Val Ile Gln Val₂₅₅ Asp
 Gln Ser Gly Leu₂₆₀ Gly Leu Pro Ser Arg₂₆₅ Asp Tyr Tyr Leu Asn₂₇₀ Lys Thr
 Glu Asn Glu₂₇₅ Lys Val Leu Thr Gly₂₈₀ Tyr Leu Asn Tyr Met₂₈₅ Val Gln Leu
 Gly Lys₂₉₀ Leu Leu Gly Gly₂₉₅ Asp Glu Glu Ala Ile₃₀₀ Arg Pro Gln Met
 Gln Gln Ile Leu Asp Phe₃₁₀ Glu Thr Ala Leu Ala₃₁₅ Asn Ile Thr Ile Pro₃₂₀
 Gln Glu Lys Arg Arg₃₂₅ Asp Glu Glu Leu Ile₃₃₀ Tyr His Lys Val Thr Ala₃₃₅
 Ala Glu Leu Gln₃₄₀ Thr Leu Ala Pro Ala₃₄₅ Ile Asn Trp Leu Pro₃₅₀ Phe Leu
 Asn Thr Ile₃₅₅ Phe Tyr Pro Val Glu₃₆₀ Ile Asn Glu Ser Glu₃₆₅ Pro Ile Val
 Val Tyr₃₇₀ Asp Lys Glu Tyr Leu₃₇₅ Glu Gln Ile Ser Thr₃₈₀ Leu Ile Asn Thr
 Thr Asp Arg Cys Leu Leu₃₉₀ Asn Asn Tyr Met Ile₃₉₅ Trp Asn Leu Val Arg₄₀₀
 Lys Thr Ser Ser₄₀₅ Phe Leu Asp Gln Arg Phe₄₁₀ Gln Asp Ala Asp Glu Lys₄₁₅
 Phe Met Glu Val₄₂₀ Met Tyr Gly Thr Lys₄₂₅ Lys Thr Cys Leu Pro Arg Trp₄₃₀
 Lys Phe Cys₄₃₅ Val Ser Asp Thr Glu₄₄₀ Asn Asn Leu Gly Phe₄₄₅ Ala Leu Gly
 Pro Met₄₅₀ Phe Val Lys Ala Thr₄₅₅ Phe Ala Glu Asp Ser₄₆₀ Lys Ser Ile Ala
 Thr Glu Ile Ile Leu Glu₄₇₀ Ile Lys Lys Ala Phe₄₇₅ Glu Glu Ser Leu Ser₄₈₀
 Thr Leu Lys Trp Met₄₈₅ Asp Glu Glu Thr Arg₄₉₀ Lys Ser Ala Lys Glu Lys₄₉₅
 Ala Asp Ala Ile₅₀₀ Tyr Asn Met Ile Gly₅₀₅ Tyr Pro Asn Phe Ile₅₁₀ Met Asp

EX05-002patentin.txt

Pro Lys Glu Leu Asp Lys Val Phe Asn Asp Tyr Thr Ala Val Pro Asp
 515 520 525
 Leu Tyr Phe Glu Asn Ala Met Arg Phe Phe Asn Phe Ser Trp Arg Val
 530 535 540
 Thr Ala Asp Gln Leu Arg Lys Ala Pro Asn Arg Asp Gln Trp Ser Met
 545 550 555 560
 Thr Pro Pro Met Val Asn Ala Tyr Tyr Ser Pro Thr Lys Asn Glu Ile
 565 570 575
 Val Phe Pro Ala Gly Ile Leu Gln Ala Pro Phe Tyr Thr Arg Ser Ser
 580 585 590
 Pro Lys Ala Leu Asn Phe Gly Gly Ile Gly Val Val Val Gly His Glu
 595 600 605
 Leu Thr His Ala Phe Asp Asp Gln Gly Arg Glu Tyr Asp Lys Asp Gly
 610 615 620
 Asn Leu Arg Pro Trp Trp Lys Asn Ser Ser Val Glu Ala Phe Lys Arg
 625 630 635 640
 Gln Thr Glu Cys Met Val Glu Gln Tyr Ser Asn Tyr Ser Val Asn Gly
 645 650 655
 Glu Pro Val Asn Gly Arg His Thr Leu Gly Glu Asn Ile Ala Asp Asn
 660 665 670
 Gly Gly Leu Lys Ala Ala Tyr Arg Ala Tyr Gln Asn Trp Val Lys Lys
 675 680 685
 Asn Gly Ala Glu His Ser Leu Pro Thr Leu Gly Leu Thr Asn Asn Gln
 690 695 700
 Leu Phe Phe Leu Gly Phe Ala Gln Val Trp Cys Ser Val Arg Thr Pro
 705 710 715 720
 Glu Ser Ser His Glu Gly Leu Ile Thr Asp Pro His Ser Pro Ser Arg
 725 730 735
 Phe Arg Val Ile Gly Ser Leu Ser Asn Ser Lys Glu Phe Ser Glu His
 740 745 750
 Phe Arg Cys Pro Pro Gly Ser Pro Met Asn Pro Pro His Lys Cys Glu
 755 760 765
 Val Trp
 770

EX05-002patentin.txt

<210> 90
 <211> 765
 <212> PRT
 <213> Homo sapiens

<400> 90

Met Asn Val Ala Leu Gln Glu Leu Gly Ala Gly Ser Asn Met Val Glu
 1 5 10 15

Tyr Lys Arg Ala Thr Leu Arg Asp Glu Asp Ala Pro Glu Thr Pro Val
 20 25 30

Glu Gly Gly Ala Ser Pro Asp Ala Met Glu Val Gly Phe Gln Lys Gly
 35 40 45

Thr Arg Gln Leu Leu Gly Ser Arg Thr Gln Leu Glu Leu Val Leu Ala
 50 55 60

Gly Ala Ser Leu Leu Leu Ala Ala Leu Leu Leu Gly Cys Leu Val Ala
 65 70 75 80

Leu Gly Val Gln Tyr His Arg Asp Pro Ser His Ser Thr Cys Leu Thr
 85 90 95

Glu Ala Cys Ile Arg Val Ala Gly Lys Ile Leu Glu Ser Leu Asp Arg
 100 105 110

Gly Val Ser Pro Cys Glu Asp Phe Tyr Gln Phe Ser Cys Gly Gly Trp
 115 120 125

Ile Arg Arg Asn Pro Leu Pro Asp Gly Arg Ser Arg Trp Asn Thr Phe
 130 135 140

Asn Ser Leu Trp Asp Gln Asn Gln Ala Ile Leu Lys His Leu Leu Glu
 145 150 155 160

Asn Thr Thr Phe Asn Ser Ser Ser Glu Ala Glu Gln Lys Thr Gln Arg
 165 170 175

Phe Tyr Leu Ser Cys Leu Gln Val Glu Arg Ile Glu Glu Leu Gly Ala
 180 185 190

Gln Pro Leu Arg Asp Leu Ile Glu Lys Ile Gly Gly Trp Asn Ile Thr
 195 200 205

Gly Pro Trp Asp Gln Asp Asn Phe Met Glu Val Leu Lys Ala Val Ala
 210 215 220

Gly Thr Tyr Arg Ala Thr Pro Phe Phe Thr Val Tyr Ile Ser Ala Asp
 225 230 235 240

EX05-002patentin.txt

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

EX05-002patentin.txt

Asp Val Tyr Asp Gly Tyr Glu Ile Ser Glu Asp Ser Phe Phe Gln Asn
 515 520 525

Met Leu Asn Leu Tyr Asn Phe Ser Ala Lys Val Met Ala Asp Gln Leu
 530 535 540

Arg Lys Pro Pro Ser Arg Asp Gln Trp Ser Met Thr Pro Gln Thr Val
 545 550 555 560

Asn Ala Tyr Tyr Leu Pro Thr Lys Asn Glu Ile Val Phe Pro Ala Gly
 565 570 575

Ile Leu Gln Ala Pro Phe Tyr Ala Arg Asn His Pro Lys Ala Leu Asn
 580 585 590

Phe Gly Gly Ile Gly Val Val Met Gly His Glu Leu Thr His Ala Phe
 595 600 605

Asp Asp Gln Gly Arg Glu Tyr Asp Lys Glu Gly Asn Leu Arg Pro Trp
 610 615 620

Trp Gln Asn Glu Ser Leu Ala Ala Phe Arg Asn His Thr Ala Cys Met
 625 630 635 640

Glu Glu Gln Tyr Asn Gln Tyr Gln Val Asn Gly Glu Arg Leu Asn Gly
 645 650 655

Arg Gln Thr Leu Gly Glu Asn Ile Ala Asp Asn Gly Gly Leu Lys Ala
 660 665 670

Ala Tyr Asn Ala Tyr Lys Ala Trp Leu Arg Lys His Gly Glu Glu Gln
 675 680 685

Gln Leu Pro Ala Val Gly Leu Thr Asn His Gln Leu Phe Phe Val Gly
 690 695 700

Phe Ala Gln Val Trp Cys Ser Val Arg Thr Pro Glu Ser Ser His Glu
 705 710 715 720

Gly Leu Val Thr Asp Pro His Ser Pro Ala Arg Phe Arg Val Leu Gly
 725 730 735

Thr Leu Ser Asn Ser Arg Asp Phe Leu Arg His Phe Gly Cys Pro Val
 740 745 750

Gly Ser Pro Met Asn Pro Gly Gln Leu Cys Glu Val Trp
 755 760 765

<210> 91
 <211> 775
 <212> PRT

EX05-002patentin.txt

<213> Homo sapiens

<400> 91

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

EX05-002patentin.txt

Ser Arg Tyr Val Ile Arg Ile Asp Gln Asp Gly Leu Thr Leu Pro Glu
 260 265 270

Arg Thr Leu Tyr Leu Ala Gln Asp Glu Asp Ser Glu Lys Val Leu Ala
 275 280 285

Ala Tyr Arg Val Phe Met Glu Arg Val Leu Ser Leu Leu Gly Ala Asp
 290 295 300

Ala Val Glu Gln Lys Ala Gln Glu Ile Leu Gln Val Glu Gln Gln Leu
 305 310 315 320

Ala Asn Ile Thr Val Ser Glu Tyr Asp Asp Leu Arg Arg Asp Val Ser
 325 330 335

Ser Met Tyr Asn Lys Val Thr Leu Gly Gln Leu Gln Lys Ile Thr Pro
 340 345 350

His Leu Arg Trp Lys Trp Leu Leu Asp Gln Ile Phe Gln Glu Asp Phe
 355 360 365

Ser Glu Glu Glu Glu Val Val Leu Leu Ala Thr Asp Tyr Met Gln Gln
 370 375 380

Val Ser Gln Leu Ile Arg Ser Thr Pro His Arg Val Leu His Asn Tyr
 385 390 395 400

Leu Val Trp Arg Val Val Val Val Leu Ser Glu His Leu Ser Pro Pro
 405 410 415

Phe Arg Glu Ala Leu His Glu Leu Ala Gln Glu Met Glu Gly Ser Asp
 420 425 430

Lys Pro Gln Glu Leu Ala Arg Val Cys Leu Gly Gln Ala Asn Arg His
 435 440 445

Phe Gly Met Ala Leu Gly Ala Leu Phe Val His Glu His Phe Ser Ala
 450 455 460

Ala Ser Lys Ala Lys Val Gln Gln Leu Val Glu Asp Ile Lys Tyr Ile
 465 470 475 480

Leu Gly Gln Arg Leu Glu Glu Leu Asp Trp Met Asp Ala Glu Thr Arg
 485 490 495

Ala Ala Ala Arg Ala Lys Leu Gln Tyr Met Met Val Met Val Gly Tyr
 500 505 510

Pro Asp Phe Leu Leu Lys Pro Asp Ala Val Asp Lys Glu Tyr Glu Phe
 515 520 525

EX05-002patentin.txt

Glu Val His Glu Lys Thr Tyr Phe Lys Asn Ile Leu Asn Ser Ile Arg
 530 535 540

Phe Ser Ile Gln Leu Ser Val Lys Lys Ile Arg Gln Glu Val Asp Lys
 545 550 555 560

Ser Thr Trp Leu Leu Pro Pro Gln Ala Leu Asn Ala Tyr Tyr Leu Pro
 565 570 575

Asn Lys Asn Gln Met Val Phe Pro Ala Gly Ile Leu Gln Pro Thr Leu
 580 585 590

Tyr Asp Pro Asp Phe Pro Gln Ser Leu Asn Tyr Gly Gly Ile Gly Thr
 595 600 605

Ile Ile Gly His Glu Leu Thr His Gly Tyr Asp Asp Trp Gly Gly Gln
 610 615 620

Tyr Asp Arg Ser Gly Asn Leu Leu His Trp Trp Thr Glu Ala Ser Tyr
 625 630 635 640

Ser Arg Phe Leu Arg Lys Ala Glu Cys Ile Val Arg Leu Tyr Asp Asn
 645 650 655

Phe Thr Val Tyr Asn Gln Arg Val Asn Gly Lys His Thr Leu Gly Glu
 660 665 670

Asn Ile Ala Asp Met Gly Gly Leu Lys Leu Ala Tyr His Ala Tyr Gln
 675 680 685

Lys Trp Val Arg Glu His Gly Pro Glu His Pro Leu Pro Arg Leu Lys
 690 695 700

Tyr Thr His Asp Gln Leu Phe Phe Ile Ala Phe Ala Gln Asn Trp Cys
 705 710 715 720

Ile Lys Arg Arg Ser Gln Ser Ile Tyr Leu Gln Val Leu Thr Asp Lys
 725 730 735

His Ala Pro Glu His Tyr Arg Val Leu Gly Ser Val Ser Gln Phe Glu
 740 745 750

Glu Phe Gly Arg Val Leu His Cys Pro Lys Val Ser Pro Met Asn Pro
 755 760 765

Ala His Lys Cys Ser Val Trp
 770 775

<210> 92
 <211> 732
 <212> PRT
 <213> Homo sapiens

EX05-002patentin.txt

<400> 92

Met Glu Gly Gly Asp Gln Ser Glu Glu Glu Pro Arg Glu Arg Ser Gln
 1 5 10 15

Ala Gly Gly Met Gly Thr Leu Trp Ser Gln Glu Ser Thr Pro Glu Glu
 20 25 30

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

Leu Thr Ala Ile Leu Ile Leu Gly Leu Leu Leu Cys Phe Ser Val Leu
 50 55 60

Leu Phe Tyr Asn Phe Gln Asn Cys Gly Pro Arg Pro Cys Glu Thr Ser
 65 70 75 80

Val Cys Leu Asp Leu Arg Asp His Tyr Leu Ala Ser Gly Asn Thr Ser
 85 90 95

Val Ala Pro Cys Thr Asp Phe Phe Ser Phe Ala Cys Gly Arg Ala Lys
 100 105 110

Glu Thr Asn Asn Ser Phe Gln Glu Leu Ala Thr Lys Asn Lys Asn Arg
 115 120 125

Leu Arg Arg Ile Leu Glu Val Gln Asn Ser Trp His Pro Gly Ser Gly
 130 135 140

Glu Glu Lys Ala Phe Gln Phe Tyr Asn Ser Cys Met Asp Thr Leu Ala
 145 150 155 160

Ile Glu Ala Ala Gly Thr Gly Pro Leu Arg Gln Val Ile Glu Glu Leu
 165 170 175

Gly Gly Trp Arg Ile Ser Gly Lys Trp Thr Ser Leu Asn Phe Asn Arg
 180 185 190

Thr Leu Arg Leu Leu Met Ser Gln Tyr Gly His Phe Pro Phe Phe Arg
 195 200 205

Ala Tyr Leu Gly Pro His Pro Ala Ser Pro His Thr Pro Val Ile Gln
 210 215 220

Ile Asp Gln Pro Glu Phe Asp Val Pro Leu Lys Gln Asp Gln Glu Gln
 225 230 235 240

Lys Ile Tyr Ala Gln Ile Phe Arg Glu Tyr Leu Thr Tyr Leu Asn Gln
 245 250 255

Leu Gly Thr Leu Leu Gly Gly Asp Pro Ser Lys Val Gln Glu His Ser
 Page 194

EX05-002patentin.txt

260

265

270

Ser Leu Ser Ile Ser Ile Thr Ser Arg Leu Phe Gln Phe Leu Arg Pro
 275 280 285

Leu Glu Gln Arg Arg Ala Gln Gly Lys Leu Phe Gln Met Val Thr Ile
 290 295 300

Asp Gln Leu Lys Glu Met Ala Pro Ala Ile Asp Trp Leu Ser Cys Leu
 305 310 315 320

Gln Ala Thr Phe Thr Pro Met Ser Leu Ser Pro Ser Gln Ser Leu Val
 325 330 335

Val His Asp Val Glu Tyr Leu Lys Asn Met Ser Gln Leu Val Glu Glu
 340 345 350

Met Leu Leu Lys Gln Arg Asp Phe Leu Gln Ser His Met Ile Leu Gly
 355 360 365

Leu Val Val Thr Leu Ser Pro Ala Leu Asp Ser Gln Phe Gln Glu Ala
 370 375 380

Arg Arg Lys Leu Ser Gln Lys Leu Arg Glu Leu Thr Glu Gln Pro Pro
 385 390 395 400

Met Pro Ala Arg Pro Arg Trp Met Lys Cys Val Glu Glu Thr Gly Thr
 405 410 415

Phe Phe Glu Pro Thr Leu Ala Ala Leu Phe Val Arg Glu Ala Phe Gly
 420 425 430

Pro Ser Thr Arg Ser Ala Ala Met Lys Leu Phe Thr Ala Ile Arg Asp
 435 440 445

Ala Leu Ile Thr Arg Leu Arg Asn Leu Pro Trp Met Asn Glu Glu Thr
 450 455 460

Gln Asn Met Ala Gln Asp Lys Val Ala Gln Leu Gln Val Glu Met Gly
 465 470 475 480

Ala Ser Glu Trp Ala Leu Lys Pro Glu Leu Ala Arg Gln Glu Tyr Asn
 485 490 495

Asp Ile Gln Leu Gly Ser Ser Phe Leu Gln Ser Val Leu Ser Cys Val
 500 505 510

Arg Ser Leu Arg Ala Arg Ile Val Gln Ser Phe Leu Gln Pro His Pro
 515 520 525

Gln His Arg Trp Lys Val Ser Pro Trp Asp Val Asn Ala Tyr Tyr Ser
 Page 195

EX05-002patentin.txt

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

<210> 93
 <211> 750
 <212> PRT
 <213> Homo sapiens

<400> 93

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

EX05-002patentin.txt

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

EX05-002patentin.txt

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

EX05-002patentin.txt

Asn Gly Arg Asn Phe Asn Lys Asp Gly Asp Leu Val Asp Trp Trp Thr
 595 600 605

Gln Gln Ser Ala Ser Asn Phe Lys Glu Gln Ser Gln Cys Met Val Tyr
 610 615 620

Gln Tyr Gly Asn Phe Ser Trp Asp Leu Ala Gly Gly Gln His Leu Asn
 625 630 635 640

Gly Ile Asn Thr Leu Gly Glu Asn Ile Ala Asp Asn Gly Gly Leu Gly
 645 650 655

Gln Ala Tyr Arg Ala Tyr Gln Asn Tyr Ile Lys Lys Asn Gly Glu Glu
 660 665 670

Lys Leu Leu Pro Gly Leu Asp Leu Asn His Lys Gln Leu Phe Phe Leu
 675 680 685

Asn Phe Ala Gln Val Trp Cys Gly Thr Tyr Arg Pro Glu Tyr Ala Val
 690 695 700

Asn Ser Ile Lys Thr Asp Val His Ser Pro Gly Asn Phe Arg Ile Ile
 705 710 715 720

Gly Thr Leu Gln Asn Ser Ala Glu Phe Ser Glu Ala Phe His Cys Arg
 725 730 735

Lys Asn Ser Tyr Met Asn Pro Glu Lys Lys Cys Arg Val Trp
 740 745 750

<210> 94
 <211> 770
 <212> PRT
 <213> Homo sapiens

<400> 94

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

Glu Gly Gly Leu Leu Leu Leu Leu Leu Val Thr Ala Ala Leu Val
 20 25 30

Ala Leu Gly Val Leu Tyr Ala Asp Arg Arg Gly Lys Gln Leu Pro Arg
 35 40 45

Leu Ala Ser Arg Leu Cys Phe Leu Gln Glu Glu Arg Thr Phe Val Lys
 50 55 60

Arg Lys Pro Arg Gly Ile Pro Glu Ala Gln Glu Val Ser Glu Val Cys
 65 70 75 80

EX05-002patentin.txt

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

EX05-002patentin.txt

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

EX05-002patentin.txt

Asp Trp Trp Ser Asn Phe Ser Thr Gln His Phe Arg Glu Gln Ser Glu
625 630 635 640

Cys Met Ile Tyr Gln Tyr Gly Asn Tyr Ser Trp Asp Leu Ala Asp Glu
645 650 655

Gln Asn Val Asn Gly Phe Asn Thr Leu Gly Glu Asn Ile Ala Asp Asn
660 665 670

Gly Gly Val Arg Gln Ala Tyr Lys Ala Tyr Leu Lys Trp Met Ala Glu
675 680 685

Gly Gly Lys Asp Gln Gln Leu Pro Gly Leu Asp Leu Thr His Glu Gln
690 695 700

Leu Phe Phe Ile Asn Tyr Ala Gln Val Trp Cys Gly Ser Tyr Arg Pro
705 710 715 720

Glu Phe Ala Ile Gln Ser Ile Lys Thr Asp Val His Ser Pro Leu Lys
725 730 735

Tyr Arg Val Leu Gly Ser Leu Gln Asn Leu Ala Ala Phe Ala Asp Thr
740 745 750

Phe His Cys Ala Arg Gly Thr Pro Met His Pro Lys Glu Arg Cys Arg
755 760 765

Val Trp
770

<210> 95
<211> 749
<212> PRT
<213> Homo sapiens

<400> 95

Met Glu Ala Glu Thr Gly Ser Ser Val Glu Thr Gly Lys Lys Ala Asn
1 5 10 15

Arg Gly Thr Arg Ile Ala Leu Val Val Phe Val Gly Gly Thr Leu Val
20 25 30

Leu Gly Thr Ile Leu Phe Leu Val Ser Gln Gly Leu Leu Ser Leu Gln
35 40 45

Ala Lys Gln Glu Tyr Cys Leu Lys Pro Glu Cys Ile Glu Ala Ala Ala
50 55 60

Ala Ile Leu Ser Lys Val Asn Leu Ser Val Asp Pro Cys Asp Asn Phe
65 70 75 80

EX05-002patentin.txt

Phe Arg Phe Ala Cys Asp Gly Trp Ile Ser Asn Asn Pro Ile Pro Glu
 85 90 95

Asp Met Pro Ser Tyr Gly Val Tyr Pro Trp Leu Arg His Asn Val Asp
 100 105 110

Leu Lys Leu Lys Glu Leu Leu Glu Lys Ser Ile Ser Arg Arg Arg Asp
 115 120 125

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

Glu Lys Ala Ile Glu Lys Ala Asp Ala Lys Pro Leu Leu His Ile Leu
 145 150 155 160

Arg His Ser Pro Phe Arg Trp Pro Val Leu Glu Ser Asn Ile Gly Pro
 165 170 175

Glu Gly Val Trp Ser Glu Arg Lys Phe Ser Leu Leu Gln Thr Leu Ala
 180 185 190

Thr Phe Arg Gly Gln Tyr Ser Asn Ser Val Phe Ile Arg Leu Tyr Val
 195 200 205

Ser Pro Asp Asp Lys Ala Ser Asn Glu His Ile Leu Lys Leu Asp Gln
 210 215 220

Ala Thr Leu Ser Leu Ala Val Arg Glu Asp Tyr Leu Asp Asn Ser Thr
 225 230 235 240

Glu Ala Lys Ser Tyr Arg Asp Ala Leu Tyr Lys Phe Met Val Asp Thr
 245 250 255

Ala Val Leu Leu Gly Ala Asn Ser Ser Arg Ala Glu His Asp Met Lys
 260 265 270

Ser Val Leu Arg Leu Glu Ile Lys Ile Ala Glu Ile Met Ile Pro His
 275 280 285

Glu Asn Arg Thr Ser Glu Ala Met Tyr Asn Lys Met Asn Ile Ser Glu
 290 295 300

Leu Ser Ala Met Ile Pro Gln Phe Asp Trp Leu Gly Tyr Ile Lys Lys
 305 310 315 320

Val Ile Asp Thr Arg Leu Tyr Pro His Leu Lys Asp Ile Ser Pro Ser
 325 330 335

Glu Asn Val Val Val Arg Val Pro Gln Tyr Phe Lys Asp Leu Phe Arg
 340 345 350

EX05-002patentin.txt

Ile Leu Gly Ser Glu Arg Lys Lys Thr Ile Ala Asn Tyr Leu Val Trp
 355 360 365

Arg Met Val Tyr Ser Arg Ile Pro Asn Leu Ser Arg Arg Phe Gln Tyr
 370 375 380

Arg Trp Leu Glu Phe Ser Arg Val Ile Gln Gly Thr Thr Thr Leu Leu
 385 390 395 400

Pro Gln Trp Asp Lys Cys Val Asn Phe Ile Glu Ser Ala Leu Pro Tyr
 405 410 415

Val Val Gly Lys Met Phe Val Asp Val Tyr Phe Gln Glu Asp Lys Lys
 420 425 430

Glu Met Met Glu Glu Leu Val Glu Gly Val Arg Trp Ala Phe Ile Asp
 435 440 445

Met Leu Glu Lys Glu Asn Glu Trp Met Asp Ala Gly Thr Lys Arg Lys
 450 455 460

Ala Lys Glu Lys Ala Arg Ala Val Leu Ala Lys Val Gly Tyr Pro Glu
 465 470 475 480

Phe Ile Met Asn Asp Thr His Val Asn Glu Asp Leu Lys Ala Ile Lys
 485 490 495

Phe Ser Glu Ala Asp Tyr Phe Gly Asn Val Leu Gln Thr Arg Lys Tyr
 500 505 510

Leu Ala Gln Ser Asp Phe Phe Trp Leu Arg Lys Ala Val Pro Lys Thr
 515 520 525

Glu Trp Phe Thr Asn Pro Thr Thr Val Asn Ala Phe Tyr Ser Ala Ser
 530 535 540

Thr Asn Gln Ile Arg Phe Pro Ala Gly Glu Leu Gln Lys Pro Phe Phe
 545 550 555 560

Trp Gly Thr Glu Tyr Pro Arg Ser Leu Ser Tyr Gly Ala Ile Gly Val
 565 570 575

Ile Val Gly His Glu Phe Thr His Gly Phe Asp Asn Asn Gly Arg Lys
 580 585 590

Tyr Asp Lys Asn Gly Asn Leu Asp Pro Trp Trp Ser Thr Glu Ser Glu
 595 600 605

Glu Lys Phe Lys Glu Lys Thr Lys Cys Met Ile Asn Gln Tyr Ser Asn
 610 615 620

EX05-002patentin.txt

Tyr Tyr Trp Lys Lys Ala Gly Leu Asn Val Lys Gly Lys Arg Thr Leu
625 630 635 640

Gly Glu Asn Ile Ala Asp Asn Gly Gly Leu Arg Glu Ala Phe Arg Ala
645 650 655

Tyr Arg Lys Trp Ile Asn Asp Arg Arg Gln Gly Leu Glu Glu Pro Leu
660 665 670

Leu Pro Gly Ile Thr Phe Thr Asn Asn Gln Leu Phe Phe Leu Ser Tyr
675 680 685

Ala His Val Arg Cys Asn Ser Tyr Arg Pro Glu Ala Ala Arg Glu Gln
690 695 700

Val Gln Ile Gly Ala His Ser Pro Pro Gln Phe Arg Val Asn Gly Ala
705 710 715 720

Ile Ser Asn Ser Glu Glu Phe Gln Lys Ala Phe Asn Cys Pro Pro Asn
725 730 735

Ser Thr Met Asn Arg Gly Met Asp Ser Cys Arg Leu Trp
740 745

<210> 96
<211> 656
<212> PRT
<213> Homo sapiens

<400> 96

Met Val Asn Glu Ala Arg Gly Asn Ser Ser Leu Asn Pro Cys Leu Glu
1 5 10 15

Gly Ser Ala Ser Ser Gly Ser Glu Ser Ser Lys Asp Ser Ser Arg Cys
20 25 30

Ser Thr Pro Gly Leu Asp Pro Glu Arg His Glu Arg Leu Arg Glu Lys
35 40 45

Met Arg Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe Ser Leu Glu Phe
50 55 60

Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu Ile Ser Arg Phe
65 70 75 80

Asp Arg Met Ala Ala Gly Gly Pro Leu Tyr Ile Asp Val Thr Trp His
85 90 95

Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser Ser Met Met Ile
100 105 110

Ala Ser Thr Ala Val Asn Tyr Cys Gly Leu Glu Thr Ile Leu His Met
Page 205

Page 206

EX05-002patentin.txt

385 390 395 400
 Lys Asp Tyr Tyr Leu Phe Tyr Leu Lys Ser Lys Ser Pro Lys Glu Glu
 405 410 415
 Leu Leu Lys Met Trp Gly Glu Glu Leu Thr Ser Glu Ala Ser Val Phe
 420 425 430
 Glu Val Phe Val Leu Tyr Leu Ser Gly Glu Pro Asn Arg Asn Gly His
 435 440 445
 Lys Val Thr Cys Leu Pro Trp Asn Asp Glu Pro Leu Ala Ala Glu Thr
 450 455 460
 Ser Leu Leu Lys Glu Glu Leu Leu Arg Val Asn Arg Gln Gly Ile Leu
 465 470 475 480
 Thr Ile Asn Ser Gln Pro Asn Ile Asn Gly Lys Pro Ser Ser Asp Pro
 485 490 495
 Ile Val Gly Trp Gly Pro Ser Gly Gly Tyr Val Phe Gln Lys Ala Tyr
 500 505 510
 Leu Glu Phe Phe Thr Ser Arg Glu Thr Ala Glu Ala Leu Leu Gln Val
 515 520 525
 Leu Lys Lys Tyr Glu Leu Arg Val Asn Tyr His Leu Val Asn Val Lys
 530 535 540
 Gly Glu Asn Ile Thr Asn Ala Pro Glu Leu Gln Pro Asn Ala Val Thr
 545 550 555 560
 Trp Gly Ile Phe Pro Gly Arg Glu Ile Ile Gln Pro Thr Val Val Asp
 565 570 575
 Pro Val Ser Phe Met Phe Trp Lys Asp Glu Ala Phe Ala Leu Trp Ile
 580 585 590
 Glu Gln Trp Gly Lys Leu Tyr Glu Glu Glu Ser Pro Ser Arg Thr Ile
 595 600 605
 Ile Gln Tyr Ile His Asp Asn Tyr Phe Leu Val Asn Leu Val Asp Asn
 610 615 620
 Asp Phe Pro Leu Asp Asn Cys Leu Trp Gln Val Val Glu Asp Thr Leu
 625 630 635 640
 Glu Leu Leu Asn Arg Pro Thr Gln Asn Ala Arg Glu Thr Glu Ala Pro
 645 650 655

EX05-002patentin.txt

<211> 403
 <212> PRT
 <213> Homo sapiens

<400> 97

Pro Gly Ala Arg Ala Leu Asp Asn Gly Leu Ala Arg Thr Pro Thr Met
 1 5 10 15

Gly Trp Leu His Trp Glu Arg Phe Met Cys Asn Leu Asp Cys Gln Glu
 20 25 30

Glu Pro Asp Ser Cys Ile Ser Glu Lys Leu Phe Met Glu Met Ala Glu
 35 40 45

Leu Met Val Ser Glu Gly Trp Lys Asp Ala Gly Tyr Glu Tyr Leu Cys
 50 55 60

Ile Asp Asp Cys Trp Met Ala Pro Gln Arg Asp Ser Glu Gly Arg Leu
 65 70 75 80

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

Tyr Val His Ser Lys Gly Leu Lys Leu Gly Ile Tyr Ala Asp Val Gly
 100 105 110

Asn Lys Thr Cys Ala Gly Phe Pro Gly Ser Phe Gly Tyr Tyr Asp Ile
 115 120 125

Asp Ala Gln Thr Phe Ala Asp Trp Gly Val Asp Leu Leu Lys Phe Asp
 130 135 140

Gly Cys Tyr Cys Asp Ser Leu Glu Asn Leu Ala Asp Gly Tyr Lys His
 145 150 155 160

Met Ser Leu Ala Leu Asn Arg Thr Gly Arg Ser Ile Val Tyr Ser Cys
 165 170 175

Glu Trp Pro Leu Tyr Met Trp Pro Phe Gln Lys Pro Asn Tyr Thr Glu
 180 185 190

Ile Arg Gln Tyr Cys Asn His Trp Arg Asn Phe Ala Asp Ile Asp Asp
 195 200 205

Ser Trp Lys Ser Ile Lys Ser Ile Leu Asp Trp Thr Ser Phe Asn Gln
 210 215 220

Glu Arg Ile Val Asp Val Ala Gly Pro Gly Gly Trp Asn Asp Pro Asp
 225 230 235 240

Met Leu Val Ile Gly Asn Phe Gly Leu Ser Trp Asn Gln Gln Val Thr
 245 250 255

EX05-002patentin.txt

Gln Met Ala Leu Trp Ala Ile Met Ala Ala Pro Leu Phe Met Ser Asn
260 265 270

Asp Leu Arg His Ile Ser Pro Gln Ala Lys Ala Leu Leu Gln Asp Lys
275 280 285

Asp Val Ile Ala Ile Asn Gln Asp Pro Leu Gly Lys Gln Gly Tyr Gln
290 295 300

Leu Arg Gln Gly Asp Asn Phe Glu Val Trp Glu Arg Pro Leu Ser Gly
305 310 315 320

Leu Ala Trp Ala Val Ala Met Ile Asn Arg Gln Glu Ile Gly Gly Pro
325 330 335

Arg Ser Tyr Thr Ile Ala Val Ala Ser Leu Gly Lys Gly Val Ala Cys
340 345 350

Asn Pro Ala Cys Phe Ile Thr Gln Leu Leu Pro Val Lys Arg Lys Leu
355 360 365

Gly Phe Tyr Glu Trp Thr Ser Arg Leu Arg Ser His Ile Asn Pro Thr
370 375 380

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

Asp Leu Leu

<210> 98
<211> 411
<212> PRT
<213> Homo sapiens

<400> 98

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

Met Leu Asp Asn Gly Leu Leu Gln Thr Pro Pro Met Gly Trp Leu Ala
20 25 30

Trp Glu Arg Phe Arg Cys Asn Ile Asn Cys Asp Glu Asp Pro Lys Asn
35 40 45

Cys Ile Ser Glu Gln Leu Phe Met Glu Met Ala Asp Arg Met Ala Gln
50 55 60

Asp Gly Trp Arg Asp Met Gly Tyr Thr Tyr Leu Asn Ile Asp Asp Cys
65 70 75 80

EX05-002patentin.txt

Trp Ile Gly Gly Arg Asp Ala Ser Gly Arg Leu Met Pro Asp Pro Lys
 85 90 95

Arg Phe Pro His Gly Ile Pro Phe Leu Ala Asp Tyr Val His Ser Leu
 100 105 110

Gly Leu Lys Leu Gly Ile Tyr Ala Asp Met Gly Asn Phe Thr Cys Met
 115 120 125

Gly Tyr Pro Gly Thr Thr Leu Asp Lys Val Val Gln Asp Ala Gln Thr
 130 135 140

Phe Ala Glu Trp Lys Val Asp Met Leu Lys Leu Asp Gly Cys Phe Ser
 145 150 155 160

Thr Pro Glu Glu Arg Ala Gln Gly Tyr Pro Lys Met Ala Ala Ala Leu
 165 170 175

Asn Ala Thr Gly Arg Pro Ile Ala Phe Ser Cys Ser Trp Pro Ala Tyr
 180 185 190

Glu Gly Gly Leu Pro Pro Arg Val Asn Tyr Ser Leu Leu Ala Asp Ile
 195 200 205

Cys Asn Leu Trp Arg Asn Tyr Asp Asp Ile Gln Asp Ser Trp Trp Ser
 210 215 220

Val Leu Ser Ile Leu Asn Trp Phe Val Glu His Gln Asp Ile Leu Gln
 225 230 235 240

Pro Val Ala Gly Pro Gly His Trp Asn Asp Pro Asp Met Leu Leu Ile
 245 250 255

Gly Asn Phe Gly Leu Ser Leu Glu Gln Ser Arg Ala Gln Met Ala Leu
 260 265 270

Trp Thr Val Leu Ala Ala Pro Leu Leu Met Ser Thr Asp Leu Arg Thr
 275 280 285

Ile Ser Ala Gln Asn Met Asp Ile Leu Gln Asn Pro Leu Met Ile Lys
 290 295 300

Ile Asn Gln Asp Pro Leu Gly Ile Gln Gly Arg Arg Ile His Lys Glu
 305 310 315 320

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

Ala Leu Val Phe Phe Ser Cys Arg Thr Asp Met Pro Tyr Arg Tyr His
 340 345 350

EX05-002patentin.txt

Ser Ser Leu Gly Gln Leu Asn Phe Thr Gly Ser Val Ile Tyr Glu Ala
 355 360 365

Gln Asp Val Tyr Ser Gly Asp Ile Ile Ser Gly Leu Arg Asp Glu Thr
 370 375 380

Asn Phe Thr Val Ile Ile Asn Pro Ser Gly Val Val Met Trp Tyr Leu
 385 390 395 400

Tyr Pro Ile Lys Asn Leu Glu Met Ser Gln Gln
 405 410

<210> 99
 <211> 779
 <212> PRT
 <213> Homo sapiens

<400> 99

Met Arg Ile Glu Glu Arg Lys Ser Gln His Leu Thr Gly Leu Thr Asp
 1 5 10 15

Glu Lys Val Lys Ala Tyr Leu Ser Leu His Pro Gln Val Leu Asp Glu
 20 25 30

Phe Val Ser Glu Ser Val Ser Ala Glu Thr Val Glu Lys Trp Leu Lys
 35 40 45

Arg Lys Asn Asn Lys Ser Glu Asp Glu Ser Ala Pro Lys Glu Val Ser
 50 55 60

Arg Tyr Gln Asp Thr Asn Met Gln Gly Val Val Tyr Glu Leu Asn Ser
 65 70 75 80

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

Tyr Glu Leu Ser Ser Ile Ile Lys Ile Ala Thr Lys Ala Asp Gly Phe
 100 105 110

Ala Leu Tyr Phe Leu Gly Glu Cys Asn Asn Ser Leu Cys Ile Phe Thr
 115 120 125

Pro Pro Gly Ile Lys Glu Gly Lys Pro Arg Leu Ile Pro Ala Gly Pro
 130 135 140

Ile Thr Gln Gly Thr Thr Val Ser Ala Tyr Val Ala Lys Ser Arg Lys
 145 150 155 160

Thr Leu Leu Val Glu Asp Ile Leu Gly Asp Glu Arg Phe Pro Arg Gly
 165 170 175

EX05-002patentin.txt

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

EX05-002patentin.txt

Leu Met Gln Phe Thr Leu Pro Val Arg Leu Cys Lys Glu Ile Glu Leu
 450 455 460

Phe His Phe Asp Ile Gly Pro Phe Glu Asn Met Trp Pro Gly Ile Phe
 465 470 475 480

Val Tyr Met Val His Arg Ser Cys Gly Thr Ser Cys Phe Glu Leu Glu
 485 490 495

Lys Leu Cys Arg Phe Ile Met Ser Val Lys Lys Asn Tyr Arg Arg Val
 500 505 510

Pro Tyr His Asn Trp Lys His Ala Val Thr Val Ala His Cys Met Tyr
 515 520 525

Ala Ile Leu Gln Asn Asn His Thr Leu Phe Thr Asp Leu Glu Arg Lys
 530 535 540

Gly Leu Leu Ile Ala Cys Leu Cys His Asp Leu Asp His Arg Gly Phe
 545 550 555 560

Ser Asn Ser Tyr Leu Gln Lys Phe Asp His Pro Leu Ala Ala Leu Tyr
 565 570 575

Ser Thr Ser Thr Met Glu Gln His His Phe Ser Gln Thr Val Ser Ile
 580 585 590

Leu Gln Leu Glu Gly His Asn Ile Phe Ser Thr Leu Ser Ser Ser Glu
 595 600 605

Tyr Glu Gln Val Leu Glu Ile Ile Arg Lys Ala Ile Ile Ala Thr Asp
 610 615 620

Leu Ala Leu Tyr Phe Gly Asn Arg Lys Gln Leu Glu Glu Met Tyr Gln
 625 630 635 640

Thr Gly Ser Leu Asn Leu Asn Asn Gln Ser His Arg Asp Arg Val Ile
 645 650 655

Gly Leu Met Met Thr Ala Cys Asp Leu Cys Ser Val Thr Lys Leu Trp
 660 665 670

Pro Val Thr Lys Leu Thr Ala Asn Asp Ile Tyr Ala Glu Phe Trp Ala
 675 680 685

Glu Gly Asp Glu Met Lys Lys Leu Gly Ile Gln Pro Ile Pro Met Met
 690 695 700

Asp Arg Asp Lys Lys Asp Glu Val Pro Gln Gly Gln Leu Gly Phe Tyr
 705 710 715 720

EX05-002patentin.txt

Asn Ala Val Ala Ile Pro Cys Tyr Thr Thr Leu Thr Gln Ile Leu Pro
 725 730 735

Pro Thr Glu Pro Leu Leu Lys Ala Cys Arg Asp Asn Leu Ser Gln Trp
 740 745 750

Glu Lys Val Ile Arg Gly Glu Glu Thr Ala Thr Trp Ile Ser Ser Pro
 755 760 765

Ser Val Ala Gln Lys Ala Ala Ala Ser Glu Asp
 770 775

<210> 100
 <211> 941
 <212> PRT
 <213> Homo sapiens

<400> 100

Met Gly Gln Ala Cys Gly His Ser Ile Leu Cys Arg Ser Gln Gln Tyr
 1 5 10 15

Pro Ala Ala Arg Pro Ala Glu Pro Arg Gly Gln Gln Val Phe Leu Lys
 20 25 30

Pro Asp Glu Pro Pro Pro Pro Pro Gln Pro Cys Ala Asp Ser Leu Gln
 35 40 45

Asp Ala Leu Leu Ser Leu Gly Ser Val Ile Asp Ile Ser Gly Leu Gln
 50 55 60

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

Val Tyr Thr Tyr Leu Leu Asp Gly Glu Ser Gln Leu Val Cys Glu Asp
 85 90 95

Pro Pro His Glu Leu Pro Gln Glu Gly Lys Val Arg Glu Ala Ile Ile
 100 105 110

Ser Gln Lys Arg Leu Gly Cys Asn Gly Leu Gly Phe Ser Asp Leu Pro
 115 120 125

Gly Lys Pro Leu Ala Arg Leu Val Ala Pro Leu Ala Pro Asp Thr Gln
 130 135 140

Val Leu Val Met Pro Leu Ala Asp Lys Glu Ala Gly Ala Val Ala Ala
 145 150 155 160

Val Ile Leu Val His Cys Gly Gln Leu Ser Asp Asn Glu Glu Trp Ser
 165 170 175

Leu Gln Ala Val Glu Lys His Thr Leu Val Ala Leu Arg Arg Val Gln
 Page 214

EX05-002patentin.txt

180

185

190

Val Leu Gln Gln Arg Gly Pro Arg Glu Ala Pro Arg Ala Val Gln Asn
 195 200 205

Pro Pro Glu Gly Thr Ala Glu Asp Gln Lys Gly Gly Ala Ala Tyr Thr
 210 215 220

Asp Arg Asp Arg Lys Ile Leu Gln Leu Cys Gly Glu Leu Tyr Asp Leu
 225 230 235 240

Asp Ala Ser Ser Leu Gln Leu Lys Val Leu Gln Tyr Leu Gln Gln Glu
 245 250 255

Thr Arg Ala Ser Arg Cys Cys Leu Leu Leu Val Ser Glu Asp Asn Leu
 260 265 270

Gln Leu Ser Cys Lys Val Ile Gly Asp Lys Val Leu Gly Glu Glu Val
 275 280 285

Ser Phe Pro Leu Thr Gly Cys Leu Gly Gln Val Val Glu Asp Lys Lys
 290 295 300

Ser Ile Gln Leu Lys Asp Leu Thr Ser Glu Asp Val Gln Gln Leu Gln
 305 310 315 320

Ser Met Leu Gly Cys Glu Leu Gln Ala Met Leu Cys Val Pro Val Ile
 325 330 335

Ser Arg Ala Thr Asp Gln Val Val Ala Leu Ala Cys Ala Phe Asn Lys
 340 345 350

Leu Glu Gly Asp Leu Phe Thr Asp Glu Asp Glu His Val Ile Gln His
 355 360 365

Cys Phe His Tyr Thr Ser Thr Val Leu Thr Ser Thr Leu Ala Phe Gln
 370 375 380

Lys Glu Gln Lys Leu Lys Cys Glu Cys Gln Ala Leu Leu Gln Val Ala
 385 390 395 400

Lys Asn Leu Phe Thr His Leu Asp Asp Val Ser Val Leu Leu Gln Glu
 405 410 415

Ile Ile Thr Glu Ala Arg Asn Leu Ser Asn Ala Glu Ile Cys Ser Val
 420 425 430

Phe Leu Leu Asp Gln Asn Glu Leu Val Ala Lys Val Phe Asp Gly Gly
 435 440 445

Val Val Asp Asp Glu Ser Tyr Glu Ile Arg Ile Pro Ala Asp Gln Gly
 Page 215

EX05-002patentin.txt

450 455 460
 Ile Ala Gly His Val Ala Thr Thr Gly Gln Ile Leu Asn Ile Pro Asp
 465 470 475 480
 Ala Tyr Ala His Pro Leu Phe Tyr Arg Gly Val Asp Asp Ser Thr Gly
 485 490 495
 Phe Arg Thr Arg Asn Ile Leu Cys Phe Pro Ile Lys Asn Glu Asn Gln
 500 505 510
 Glu Val Ile Gly Val Ala Glu Leu Val Asn Lys Ile Asn Gly Pro Trp
 515 520 525
 Phe Ser Lys Phe Asp Glu Asp Leu Ala Thr Ala Phe Ser Ile Tyr Cys
 530 535 540
 Gly Ile Ser Ile Ala His Ser Leu Leu Tyr Lys Lys Val Asn Glu Ala
 545 550 555 560
 Gln Tyr Arg Ser His Leu Ala Asn Glu Met Met Met Tyr His Met Lys
 565 570 575
 Val Ser Asp Asp Glu Tyr Thr Lys Leu Leu His Asp Gly Ile Gln Pro
 580 585 590
 Val Ala Ala Ile Asp Ser Asn Phe Ala Ser Phe Thr Tyr Thr Pro Arg
 595 600 605
 Ser Leu Pro Glu Asp Asp Thr Ser Met Ala Ile Leu Ser Met Leu Gln
 610 615 620
 Asp Met Asn Phe Ile Asn Asn Tyr Lys Ile Asp Cys Pro Thr Leu Ala
 625 630 635 640
 Arg Phe Cys Leu Met Val Lys Lys Gly Tyr Arg Asp Pro Pro Tyr His
 645 650 655
 Asn Trp Met His Ala Phe Ser Val Ser His Phe Cys Tyr Leu Leu Tyr
 660 665 670
 Lys Asn Leu Glu Leu Thr Asn Tyr Leu Glu Asp Ile Glu Ile Phe Ala
 675 680 685
 Leu Phe Ile Ser Cys Met Cys His Asp Leu Asp His Arg Gly Thr Asn
 690 695 700
 Asn Ser Phe Gln Val Ala Ser Lys Ser Val Leu Ala Ala Leu Tyr Ser
 705 710 715 720
 Ser Glu Gly Ser Val Met Glu Arg His His Phe Ala Gln Ala Ile Ala

EX05-002patentin.txt
730

725

735

Ile Leu Asn Thr His Gly Cys Asn Ile Phe Asp His Phe Ser Arg Lys
740 745 750

Asp Tyr Gln Arg Met Leu Asp Leu Met Arg Asp Ile Ile Leu Ala Thr
755 760 765

Asp Leu Ala His His Leu Arg Ile Phe Lys Asp Leu Gln Lys Met Ala
770 775 780

Glu Val Gly Tyr Asp Arg Asn Asn Lys Gln His His Arg Leu Leu Leu
785 790 795 800

Cys Leu Leu Met Thr Ser Cys Asp Leu Ser Asp Gln Thr Lys Gly Trp
805 810 815

Lys Thr Thr Arg Lys Ile Ala Glu Leu Ile Tyr Lys Glu Phe Phe Ser
820 825 830

Gln Gly Asp Leu Glu Lys Ala Met Gly Asn Arg Pro Met Glu Met Met
835 840 845

Asp Arg Glu Lys Ala Tyr Ile Pro Glu Leu Gln Ile Ser Phe Met Glu
850 855 860

His Ile Ala Met Pro Ile Tyr Lys Leu Leu Gln Asp Leu Phe Pro Lys
865 870 875 880

Ala Ala Glu Leu Tyr Glu Arg Val Ala Ser Asn Arg Glu His Trp Thr
885 890 895

Lys Val Ser His Lys Phe Thr Ile Arg Gly Leu Pro Ser Asn Asn Ser
900 905 910

Leu Asp Phe Leu Asp Glu Glu Tyr Glu Val Pro Asp Leu Asp Gly Thr
915 920 925

Arg Ala Pro Ile Asn Gly Cys Cys Ser Leu Asp Ala Glu
930 935 940

<210> 101
<211> 823
<212> PRT
<213> Homo sapiens

<400> 101

Met Val Asn Ala Trp Phe Ala Glu Arg Val His Thr Ile Pro Val Cys
1 5 10 15

Lys Glu Gly Ile Arg Gly His Thr Glu Ser Cys Ser Cys Pro Leu Gln
20 25 30

EX05-002patentin.txt

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

EX05-002patentin.txt

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

EX05-002patentin.txt

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

<210> 102

<211> 860

EX05-002patentin.txt

<212> PRT

<213> Homo sapiens

<400> 102

Met Gly Glu Val Thr Ala Glu Glu Val Glu Lys Phe Leu Asp Ser Asn
 1 5 10 15

Ile Gly Phe Ala Lys Gln Tyr Tyr Asn Leu His Tyr Arg Ala Lys Leu
 20 25 30

Ile Ser Asp Leu Leu Gly Ala Lys Glu Ala Ala Val Asp Phe Ser Asn
 35 40 45

Tyr His Ser Pro Ser Ser Met Glu Glu Ser Glu Ile Ile Phe Asp Leu
 50 55 60

Leu Arg Asp Phe Gln Glu Asn Leu Gln Thr Glu Lys Cys Ile Phe Asn
 65 70 75 80

Val Met Lys Lys Leu Cys Phe Leu Leu Gln Ala Asp Arg Met Ser Leu
 85 90 95

Phe Met Tyr Arg Thr Arg Asn Gly Ile Ala Glu Leu Ala Thr Arg Leu
 100 105 110

Phe Asn Val His Lys Asp Ala Val Leu Glu Asp Cys Leu Val Met Pro
 115 120 125

Asp Gln Glu Ile Val Phe Pro Leu Asp Met Gly Ile Val Gly His Val
 130 135 140

Ala His Ser Lys Lys Ile Ala Asn Val Pro Asn Thr Glu Glu Asp Glu
 145 150 155 160

His Phe Cys Asp Phe Val Asp Ile Leu Thr Glu Tyr Lys Thr Lys Asn
 165 170 175

Ile Leu Ala Ser Pro Ile Met Asn Gly Lys Asp Val Val Ala Ile Ile
 180 185 190

Met Ala Val Asn Lys Val Asp Gly Ser His Phe Thr Lys Arg Asp Glu
 195 200 205

Glu Ile Leu Leu Lys Tyr Leu Asn Phe Ala Asn Leu Ile Met Lys Trp
 210 215 220

Tyr His Leu Ser Tyr Leu His Asn Cys Glu Thr Arg Arg Gly Gln Ile
 225 230 235 240

Leu Leu Trp Ser Gly Ser Lys Val Phe Glu Glu Leu Thr Asp Ile Glu
 245 250 255

EX05-002patentin.txt

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

EX05-002patentin.txt

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

EX05-002patentin.txt

Gly Ile Thr Asn Asn Arg Lys Glu Trp Lys Ala Leu Ala Asp Glu Tyr
 805 810 815

Asp Ala Lys Met Lys Val Gln Glu Glu Lys Lys Gln Lys Gln Gln Ser
 820 825 830

Ala Lys Ser Ala Ala Ala Gly Asn Gln Pro Gly Gly Asn Pro Ser Pro
 835 840 845

Gly Gly Ala Thr Thr Ser Lys Ser Cys Cys Ile Gln
 850 855 860

<210> 103
 <211> 854
 <212> PRT
 <213> Homo sapiens

<400> 103

Met Ser Leu Ser Glu Glu Gln Ala Arg Ser Phe Leu Asp Gln Asn Pro
 1 5 10 15

Asp Phe Ala Arg Gln Tyr Phe Gly Lys Lys Leu Ser Pro Glu Asn Val
 20 25 30

Gly Arg Gly Cys Glu Asp Gly Cys Pro Pro Asp Cys Asp Ser Leu Arg
 35 40 45

Asp Leu Cys Gln Val Glu Glu Ser Thr Ala Leu Leu Glu Leu Val Gln
 50 55 60

Asp Met Gln Glu Ser Ile Asn Met Glu Arg Val Val Phe Lys Val Leu
 65 70 75 80

Arg Arg Leu Cys Thr Leu Leu Gln Ala Asp Arg Cys Ser Leu Phe Met
 85 90 95

Tyr Arg Gln Arg Asn Gly Val Ala Glu Leu Ala Thr Arg Leu Phe Ser
 100 105 110

Val Gln Pro Asp Ser Val Leu Glu Asp Cys Leu Val Pro Pro Asp Ser
 115 120 125

Glu Ile Val Phe Pro Leu Asp Ile Gly Val Val Gly His Val Ala Gln
 130 135 140

Thr Lys Lys Met Val Asn Val Glu Asp Val Ala Glu Cys Pro His Phe
 145 150 155 160

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

EX05-002patentin.txt

Ala Thr Pro Ile Met Asn Gly Lys Asp Val Val Ala Val Ile Met Ala
180 185 190

Val Asn Lys Leu Asn Gly Pro Phe Phe Thr Ser Glu Asp Glu Asp Val
195 200 205

Phe Leu Lys Tyr Leu Asn Phe Ala Thr Leu Tyr Leu Lys Ile Tyr His
210 215 220

Leu Ser Tyr Leu His Asn Cys Glu Thr Arg Arg Gly Gln Val Leu Leu
225 230 235 240

Trp Ser Ala Asn Lys Val Phe Glu Glu Leu Thr Asp Ile Glu Arg Gln
245 250 255

Phe His Lys Ala Phe Tyr Thr Val Arg Ala Tyr Leu Asn Cys Glu Arg
260 265 270

Tyr Ser Val Gly Leu Leu Asp Met Thr Lys Glu Lys Glu Phe Phe Asp
275 280 285

Val Trp Ser Val Leu Met Gly Glu Ser Gln Pro Tyr Ser Gly Pro Arg
290 295 300

Thr Pro Asp Gly Arg Glu Ile Val Phe Tyr Lys Val Ile Asp Tyr Ile
305 310 315 320

Leu His Gly Lys Glu Glu Ile Lys Val Ile Pro Thr Pro Ser Ala Asp
325 330 335

His Trp Ala Leu Ala Ser Gly Leu Pro Ser Tyr Val Ala Glu Ser Gly
340 345 350

Phe Ile Cys Asn Ile Met Asn Ala Ser Ala Asp Glu Met Phe Lys Phe
355 360 365

Gln Glu Gly Ala Leu Asp Asp Ser Gly Trp Leu Ile Lys Asn Val Leu
370 375 380

Ser Met Pro Ile Val Asn Lys Lys Glu Glu Ile Val Gly Val Ala Thr
385 390 395 400

Phe Tyr Asn Arg Lys Asp Gly Lys Pro Phe Asp Glu Gln Asp Glu Val
405 410 415

Leu Met Glu Ser Leu Thr Gln Phe Leu Gly Trp Ser Val Met Asn Thr
420 425 430

Asp Thr Tyr Asp Lys Met Asn Lys Leu Glu Asn Arg Lys Asp Ile Ala
435 440 445

EX05-002patentin.txt

Gln Asp Met Val Leu Tyr His Val Lys Cys Asp Arg Asp Glu Ile Gln
 450 455 460
 Leu Ile Leu Pro Thr Arg Ala Arg Leu Gly Lys Glu Pro Ala Asp Cys
 465 470 475 480
 Asp Glu Asp Glu Leu Gly Glu Ile Leu Lys Glu Glu Leu Pro Gly Pro
 485 490 495
 Thr Thr Phe Asp Ile Tyr Glu Phe His Phe Ser Asp Leu Glu Cys Thr
 500 505 510
 Glu Leu Asp Leu Val Lys Cys Gly Ile Gln Met Tyr Tyr Glu Leu Gly
 515 520 525
 Val Val Arg Lys Phe Gln Ile Pro Gln Glu Val Leu Val Arg Phe Leu
 530 535 540
 Phe Ser Ile Ser Lys Gly Tyr Arg Arg Ile Thr Tyr His Asn Trp Arg
 545 550 555 560
 His Gly Phe Asn Val Ala Gln Thr Met Phe Thr Leu Leu Met Thr Gly
 565 570 575
 Lys Leu Lys Ser Tyr Tyr Thr Asp Leu Glu Ala Phe Ala Met Val Thr
 580 585 590
 Ala Gly Leu Cys His Asp Ile Asp His Arg Gly Thr Asn Asn Leu Tyr
 595 600 605
 Gln Met Lys Ser Gln Asn Pro Leu Ala Lys Leu His Gly Ser Ser Ile
 610 615 620
 Leu Glu Arg His His Leu Glu Phe Gly Lys Phe Leu Leu Ser Glu Glu
 625 630 635 640
 Thr Leu Asn Ile Tyr Gln Asn Leu Asn Arg Arg Gln His Glu His Val
 645 650 655
 Ile His Leu Met Asp Ile Ala Ile Ile Ala Thr Asp Leu Ala Leu Tyr
 660 665 670
 Phe Lys Lys Arg Ala Met Phe Gln Lys Ile Val Asp Glu Ser Lys Asn
 675 680 685
 Tyr Gln Asp Lys Lys Ser Trp Val Glu Tyr Leu Ser Leu Glu Thr Thr
 690 695 700
 Arg Lys Glu Ile Val Met Ala Met Met Met Thr Ala Cys Asp Leu Ser
 705 710 715 720

EX05-002patentin.txt

Ala Ile Thr Lys Pro Trp Glu Val Gln Ser Lys Val Ala Leu Leu Val
 725 730 735

Ala Ala Glu Phe Trp Glu Gln Gly Asp Leu Glu Arg Thr Val Leu Asp
 740 745 750

Gln Gln Pro Ile Pro Met Met Asp Arg Asn Lys Ala Ala Glu Leu Pro
 755 760 765

Lys Leu Gln Val Gly Phe Ile Asp Phe Val Cys Thr Phe Val Tyr Lys
 770 775 780

Glu Phe Ser Arg Phe His Glu Glu Ile Leu Pro Met Phe Asp Arg Leu
 785 790 795 800

Gln Asn Asn Arg Lys Glu Trp Lys Ala Leu Ala Asp Glu Tyr Glu Ala
 805 810 815

Lys Val Lys Ala Leu Glu Glu Lys Glu Glu Glu Glu Arg Val Ala Ala
 820 825 830

Lys Lys Val Gly Thr Glu Ile Cys Asn Gly Gly Pro Ala Pro Lys Ser
 835 840 845

Ser Thr Cys Cys Ile Leu
 850

<210> 104
 <211> 858
 <212> PRT
 <213> Homo sapiens

<400> 104

Met Gly Glu Ile Asn Gln Val Ala Val Glu Lys Tyr Leu Glu Glu Asn
 1 5 10 15

Pro Gln Phe Ala Lys Glu Tyr Phe Asp Arg Lys Leu Arg Val Glu Val
 20 25 30

Leu Gly Glu Ile Phe Lys Asn Ser Gln Val Pro Val Gln Ser Ser Met
 35 40 45

Ser Phe Ser Glu Leu Thr Gln Val Glu Glu Ser Ala Leu Cys Leu Glu
 50 55 60

Leu Leu Trp Thr Val Gln Glu Glu Gly Gly Thr Pro Glu Gln Gly Val
 65 70 75 80

His Arg Ala Leu Gln Arg Leu Ala His Leu Leu Gln Ala Asp Arg Cys
 85 90 95

Ser Met Phe Leu Cys Arg Ser Arg Asn Gly Ile Pro Glu Val Ala Ser
 Page 227

EX05-002patentin.txt

100

105

110

Arg Leu Leu Val Val Thr Pro Thr Ser Lys Phe Glu Asp Asn Leu Val
 115 120 125

Gly Pro Asp Lys Glu Val Val Phe Pro Leu Asp Ile Gly Ile Val Gly
 130 135 140

Trp Ala Ala His Thr Lys Lys Thr His Asn Val Pro Asp Val Lys Lys
 145 150 155 160

Asn Ser His Phe Ser Asp Phe Met Asp Lys Gln Thr Gly Tyr Val Thr
 165 170 175

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

Val Ile Met Ala Val Asn Lys Val Asn Ala Ser Glu Phe Ser Lys Gln
 195 200 205

Asp Glu Glu Val Phe Ser Lys Tyr Leu Asn Phe Val Ser Ile Ile Leu
 210 215 220

Arg Leu His His Thr Ser Tyr Met Tyr Asn Ile Glu Ser Arg Arg Ser
 225 230 235 240

Gln Ile Leu Met Trp Ser Ala Asn Lys Val Phe Glu Glu Leu Thr Asp
 245 250 255

Val Glu Arg Gln Phe His Lys Ala Leu Tyr Thr Val Arg Ser Tyr Leu
 260 265 270

Asn Cys Glu Arg Tyr Ser Ile Gly Leu Leu Asp Met Thr Lys Glu Lys
 275 280 285

Glu Phe Tyr Asp Glu Trp Pro Ile Lys Leu Gly Glu Val Glu Pro Tyr
 290 295 300

Lys Gly Pro Lys Thr Pro Asp Gly Arg Glu Val Asn Phe Tyr Lys Ile
 305 310 315 320

Ile Asp Tyr Ile Leu His Gly Lys Glu Glu Ile Lys Val Ile Pro Thr
 325 330 335

Pro Pro Ala Asp His Trp Thr Leu Ile Ser Gly Leu Pro Thr Tyr Val
 340 345 350

Ala Glu Asn Gly Phe Ile Cys Asn Met Met Asn Ala Pro Ala Asp Glu
 355 360 365

Tyr Phe Thr Phe Pro Lys Gly Pro Val Asp Glu Thr Gly Trp Val Ile
 Page 228

EX05-002patentin.txt

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

EX05-002patentin.txt
650

645

655

Gln Phe Glu Thr Val Ile His Leu Phe Glu Val Ala Ile Ile Ala Thr
660 665 670

Asp Leu Ala Leu Tyr Phe Lys Lys Arg Thr Met Phe Gln Lys Ile Val
675 680 685

Asp Ala Cys Glu Gln Met Gln Thr Glu Glu Glu Ala Ile Lys Tyr Val
690 700

Thr Val Asp Pro Thr Lys Lys Glu Ile Ile Met Ala Met Met Met Thr
705 710 715 720

Ala Cys Asp Leu Ser Ala Ile Thr Lys Pro Trp Glu Val Gln Ser Gln
725 730 735

Val Ala Leu Met Val Ala Asn Glu Phe Trp Glu Gln Gly Asp Leu Glu
740 745 750

Arg Thr Val Leu Gln Gln Gln Pro Ile Pro Met Met Asp Arg Asn Lys
755 760 765

Arg Asp Glu Leu Pro Lys Leu Gln Val Gly Phe Ile Asp Phe Val Cys
770 775 780

Thr Phe Val Tyr Lys Glu Phe Ser Arg Phe His Lys Glu Ile Thr Pro
785 790 795 800

Met Leu Ser Gly Leu Gln Asn Asn Arg Val Glu Trp Lys Ser Leu Ala
805 810 815

Asp Glu Tyr Asp Ala Lys Met Lys Val Ile Glu Glu Glu Ala Lys Lys
820 825 830

Gln Glu Gly Gly Ala Glu Lys Ala Ala Glu Asp Ser Gly Gly Gly Asp
835 840 845

Asp Lys Lys Ser Lys Thr Cys Leu Met Leu
850 855

<210> 105
<211> 1377
<212> PRT
<213> Homo sapiens

<400> 105

Met Asp Ala Leu Asn Arg Asn Gln Ile Gly Pro Gly Cys Gln Thr Gln
1 5 10 15

Thr Met Val Gln Lys Gly Pro Leu Asp Leu Ile Glu Thr Gly Lys Gly
20 25 30

EX05-002patentin.txt

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

EX05-002patentin.txt

Gly Ala Arg Ser Glu Ser Pro Arg Leu Ser Arg Lys Gly Gly His Glu
305 310 315 320

Arg Pro Pro Ser Pro Gly Leu Arg Gly Leu Leu Thr Asp Ser Pro Ala
325 330 335

Ala Thr Val Leu Ala Glu Ala Arg Arg Ala Thr Glu Ser Pro Arg Leu
340 345 350

Gly Gly Gln Leu Pro Val Val Ala Ile Ser Leu Ser Glu Tyr Pro Ala
355 360 365

Ser Gly Ala Leu Ser Gln Pro Thr Ser Ile Pro Gly Ser Pro Lys Phe
370 375 380

Gln Pro Pro Val Pro Ala Pro Arg Asn Lys Ile Gly Thr Leu Gln Asp
385 390 395 400

Arg Pro Pro Ser Pro Phe Arg Glu Pro Pro Gly Ser Glu Arg Val Leu
405 410 415

Thr Thr Ser Pro Ser Arg Gln Leu Val Gly Arg Thr Phe Ser Asp Gly
420 425 430

Leu Ala Thr Arg Thr Leu Gln Pro Pro Glu Ser Pro Arg Leu Gly Arg
435 440 445

Arg Gly Leu Asp Ser Met Arg Glu Leu Pro Pro Leu Ser Pro Ser Leu
450 455 460

Ser Arg Arg Ala Leu Ser Pro Leu Pro Thr Arg Thr Thr Pro Asp Pro
465 470 475 480

Lys Leu Asn Arg Glu Val Ala Glu Ser Pro Arg Pro Arg Arg Trp Ala
485 490 495

Ala His Gly Ala Ser Pro Glu Asp Phe Ser Leu Thr Leu Gly Ala Arg
500 505 510

Gly Arg Arg Thr Arg Ser Pro Ser Pro Thr Leu Gly Glu Ser Leu Ala
515 520 525

Pro His Lys Gly Ser Phe Ser Gly Arg Leu Ser Pro Ala Tyr Ser Leu
530 535 540

Gly Ser Leu Thr Gly Ala Ser Pro Cys Gln Ser Pro Cys Val Gln Arg
545 550 555 560

Lys Leu Ser Ser Gly Asp Leu Arg Val Pro Val Thr Arg Glu Arg Lys
565 570 575

EX05-002patentin.txt

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

EX05-002patentin.txt

Ala Ile Leu Asp Ser Gln Ala Gly Gln Ile Arg Ala Gln Ala Val Gln
 850 855 860
 Glu Ser Glu Arg Leu Ala Arg Asp Lys Asn Ala Ser Leu Gln Leu Leu
 865 870 875 880
 Gln Lys Glu Lys Glu Lys Leu Thr Val Leu Glu Arg Arg Tyr His Ser
 885 890 895
 Leu Thr Gly Gly Arg Pro Phe Pro Lys Thr Thr Ser Thr Leu Lys Glu
 900 905 910
 Met Glu Lys Leu Leu Leu Pro Ala Val Asp Leu Glu Gln Trp Tyr Gln
 915 920 925
 Glu Leu Met Ala Gly Leu Gly Thr Gly Pro Ala Ala Ala Ser Pro His
 930 935 940
 Ser Ser Pro Pro Pro Leu Pro Ala Lys Ala Ser Arg Gln Leu Gln Val
 945 950 955 960
 Tyr Arg Ser Lys Met Asp Gly Glu Ala Thr Ser Pro Leu Pro Arg Thr
 965 970 975
 Arg Ser Gly Pro Leu Pro Ser Ser Ser Gly Ser Ser Ser Ser Ser Ser
 980 985 990
 Gln Leu Ser Val Ala Thr Leu Gly Arg Ser Pro Ser Pro Lys Ser Ala
 995 1000 1005
 Leu Leu Thr Gln Asn Gly Thr Gly Ser Leu Pro Arg Asn Leu Ala
 1010 1015 1020
 Ala Thr Leu Gln Asp Ile Glu Thr Lys Arg Gln Leu Ala Leu Gln
 1025 1030 1035
 Gln Lys Gly Gln Gln Val Ile Glu Glu Gln Arg Arg Arg Leu Ala
 1040 1045 1050
 Glu Leu Lys Gln Lys Ala Ala Ala Glu Ala Gln Cys Gln Trp Asp
 1055 1060 1065
 Ala Leu His Gly Ala Ala Pro Phe Pro Ala Gly Pro Ser Gly Phe
 1070 1075 1080
 Pro Pro Leu Met His His Ser Ile Leu His His Leu Pro Ala Gly
 1085 1090 1095
 Arg Glu Arg Gly Glu Glu Gly Glu His Ala Tyr Asp Thr Leu Ser
 1100 1105 1110

EX05-002patentin.txt

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

EX05-002patentin.txt

Ala Glu Gly Tyr Thr Gln Phe Met Asn
1370 1375

<210> 106
<211> 589
<212> PRT
<213> Homo sapiens

<400> 106

Met Ala Pro Ser Ala Cys Cys Cys Ser Pro Ala Ala Leu Gln Arg Arg
1 5 10 15

Leu Pro Ile Leu Ala Trp Leu Pro Ser Tyr Ser Leu Gln Trp Leu Lys
20 25 30

Met Asp Phe Val Ala Gly Leu Ser Val Gly Leu Thr Ala Ile Pro Gln
35 40 45

Ala Leu Ala Tyr Ala Glu Val Ala Gly Leu Pro Pro Gln Tyr Gly Leu
50 55 60

Tyr Ser Ala Phe Met Gly Cys Phe Val Tyr Phe Phe Leu Gly Thr Ser
65 70 75 80

Arg Asp Val Thr Leu Gly Pro Thr Ala Ile Met Ser Leu Leu Val Ser
85 90 95

Phe Tyr Thr Phe His Glu Pro Ala Tyr Ala Val Leu Leu Ala Phe Leu
100 105 110

Ser Gly Cys Ile Gln Leu Ala Met Gly Val Leu Arg Leu Gly Phe Leu
115 120 125

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

Ala Val Thr Ile Gly Phe Gly Gln Ile Lys Asn Leu Leu Gly Leu Gln
145 150 155 160

Asn Ile Pro Arg Pro Phe Phe Leu Gln Val Tyr His Thr Phe Leu Arg
165 170 175

Ile Ala Glu Thr Arg Val Gly Asp Ala Val Leu Gly Leu Val Cys Met
180 185 190

Leu Leu Leu Leu Val Leu Lys Leu Met Arg Asp His Val Pro Pro Val
195 200 205

His Pro Glu Met Pro Pro Gly Val Arg Leu Ser Arg Gly Leu Val Trp
210 215 220

EX05-002patentin.txt

Ala Ala Thr Thr Ala Arg Asn Ala Leu Val Val Ser Phe Ala Ala Leu
 225 230 235 240
 Val Ala Tyr Ser Phe Glu Val Thr Gly Tyr Gln Pro Phe Ile Leu Thr
 245 250 255
 Gly Glu Thr Ala Glu Gly Leu Pro Pro Val Arg Ile Pro Pro Phe Ser
 260 265 270
 Val Thr Thr Ala Asn Gly Thr Ile Ser Phe Thr Glu Met Val Gln Asp
 275 280 285
 Met Gly Ala Gly Leu Ala Val Val Pro Leu Met Gly Leu Leu Glu Ser
 290 295 300
 Ile Ala Val Ala Lys Ala Phe Ala Ser Gln Asn Asn Tyr Arg Ile Asp
 305 310 315 320
 Ala Asn Gln Glu Leu Leu Ala Ile Gly Leu Thr Asn Met Leu Gly Ser
 325 330 335
 Leu Val Ser Ser Tyr Pro Val Thr Gly Ser Phe Gly Arg Thr Ala Val
 340 345 350
 Asn Ala Gln Ser Gly Val Cys Thr Pro Ala Gly Gly Leu Val Thr Gly
 355 360 365
 Val Leu Val Leu Leu Ser Leu Asp Tyr Leu Thr Ser Leu Phe Tyr Tyr
 370 375 380
 Ile Pro Lys Ser Ala Leu Ala Ala Val Ile Ile Met Ala Val Ala Pro
 385 390 395 400
 Leu Phe Asp Thr Lys Ile Phe Arg Thr Leu Trp Arg Val Lys Arg Leu
 405 410 415
 Asp Leu Leu Pro Leu Cys Val Thr Phe Leu Leu Cys Phe Trp Glu Val
 420 425 430
 Gln Tyr Gly Ile Leu Ala Gly Ala Leu Val Ser Leu Leu Met Leu Leu
 435 440 445
 His Ser Ala Ala Arg Pro Glu Thr Lys Val Ser Glu Gly Pro Val Leu
 450 455 460
 Val Leu Gln Pro Ala Ser Gly Leu Ser Phe Pro Ala Met Glu Ala Leu
 465 470 475 480
 Arg Glu Glu Ile Leu Ser Arg Ala Leu Glu Val Ser Pro Pro Arg Cys
 485 490 495

EX05-002patentin.txt

Leu Val Leu Glu Cys Thr His Val Cys Ser Ile Asp Tyr Thr Val Val
500 505 510

Leu Gly Leu Gly Glu Leu Leu Gln Asp Phe Gln Lys Gln Gly Val Ala
515 520 525

Leu Ala Phe Val Gly Leu Gln Val Pro Val Leu Arg Val Leu Leu Ser
530 535 540

Ala Asp Leu Lys Gly Phe Gln Tyr Phe Ser Thr Leu Glu Glu Ala Glu
545 550 555 560

Lys His Leu Arg Gln Lys Pro Gly Thr Gln Pro Tyr Asn Ile Arg Glu
565 570 575

Asp Ser Ile Leu Asp Gln Lys Val Ala Leu Leu Lys Ala
580 585

<210> 107
<211> 973
<212> PRT
<213> Homo sapiens

<400> 107

Met Tyr Asn Met Arg Arg Leu Ser Leu Ser Pro Thr Phe Ser Met Gly
1 5 10 15

Phe His Leu Leu Val Thr Val Ser Leu Leu Phe Ser His Val Asp His
20 25 30

Val Ile Ala Glu Thr Glu Met Glu Gly Glu Gly Asn Glu Thr Gly Glu
35 40 45

Cys Thr Gly Ser Tyr Tyr Cys Lys Lys Gly Val Ile Leu Pro Ile Trp
50 55 60

Glu Pro Gln Asp Pro Ser Phe Gly Asp Lys Ile Ala Arg Ala Thr Val
65 70 75 80

Tyr Phe Val Ala Met Val Tyr Met Phe Leu Gly Val Ser Ile Ile Ala
85 90 95

Asp Arg Phe Met Ser Ser Ile Glu Val Ile Thr Ser Gln Glu Lys Glu
100 105 110

Ile Thr Ile Lys Lys Pro Asn Gly Glu Thr Thr Lys Thr Thr Val Arg
115 120 125

Ile Trp Asn Glu Thr Val Ser Asn Leu Thr Leu Met Ala Leu Gly Ser
130 135 140

EX05-002patentin.txt

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

EX05-002patentin.txt

Gln Cys Leu Glu Asn Cys Gly Thr Val Ala Leu Thr Ile Ile Arg Arg
 420 425 430

Gly Gly Asp Leu Thr Asn Thr Val Phe Val Asp Phe Arg Thr Glu Asp
 435 440 445

Gly Thr Ala Asn Ala Gly Ser Asp Tyr Glu Phe Thr Glu Gly Thr Val
 450 455 460

Val Phe Lys Pro Gly Asp Thr Gln Lys Glu Ile Arg Val Gly Ile Ile
 465 470 475 480

Asp Asp Asp Ile Phe Glu Glu Asp Glu Asn Phe Leu Val His Leu Ser
 485 490 495

Asn Val Lys Val Ser Ser Glu Ala Ser Glu Asp Gly Ile Leu Glu Ala
 500 505 510

Asn His Val Ser Thr Leu Ala Cys Leu Gly Ser Pro Ser Thr Ala Thr
 515 520 525

Val Thr Ile Phe Asp Asp Asp His Ala Gly Ile Phe Thr Phe Glu Glu
 530 535 540

Pro Val Thr His Val Ser Glu Ser Ile Gly Ile Met Glu Val Lys Val
 545 550 555 560

Leu Arg Thr Ser Gly Ala Arg Gly Asn Val Ile Val Pro Tyr Lys Thr
 565 570 575

Ile Glu Gly Thr Ala Arg Gly Gly Gly Glu Asp Phe Glu Asp Thr Cys
 580 585 590

Gly Glu Leu Glu Phe Gln Asn Asp Glu Ile Val Lys Thr Ile Ser Val
 595 600 605

Lys Val Ile Asp Asp Glu Glu Tyr Glu Lys Asn Lys Thr Phe Phe Leu
 610 615 620

Glu Ile Gly Glu Pro Arg Leu Val Glu Met Ser Glu Lys Lys Ala Leu
 625 630 635 640

Leu Leu Asn Glu Leu Gly Gly Phe Thr Ile Thr Gly Lys Tyr Leu Phe
 645 650 655

Gly Gln Pro Val Phe Arg Lys Val His Ala Arg Glu His Pro Ile Leu
 660 665 670

Ser Thr Val Ile Thr Ile Ala Asp Glu Tyr Asp Asp Lys Gln Pro Leu
 675 680 685

EX05-002patentin.txt

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

His Leu Arg Val Phe Phe Val Thr Ala Ser Trp Ser Ile Phe Ala Tyr
Page 242

EX05-002patentin.txt

225	230	235	240
Val Trp Leu Tyr	Leu Ile Leu Ala Val	Phe Ser Pro Gly Val	Val Gln
	245	250	255
Val Trp Glu	Ala Leu Leu Thr Leu	Val Phe Phe Pro Val	Cys Val Val
	260	265	270
Phe Ala Trp	Met Ala Asp Lys Arg	Leu Leu Phe Tyr	Lys Tyr Val Tyr
	275	280	285
Lys Arg Tyr	Arg Thr Asp Pro Arg	Ser Gly Ile Ile	Ile Gly Ala Glu
	290	295	300
Gly Asp Pro	Pro Lys Ser Ile Glu Leu	Asp Gly Thr Phe Val	Gly Ala
305	310	315	320
Glu Ala Pro	Gly Glu Leu Gly Gly Leu	Gly Pro Gly Pro Ala	Glu Ala
	325	330	335
Arg Glu Leu	Asp Ala Ser Arg Arg	Glu Val Ile Gln Ile	Leu Lys Asp
	340	345	350
Leu Lys Gln	Lys His Pro Asp Lys	Asp Leu Glu Gln	Leu Val Gly Ile
	355	360	365
Ala Asn Tyr	Tyr Ala Leu Leu His Gln	Gln Lys Ser Arg Ala	Phe Tyr
	370	375	380
Arg Ile Gln	Ala Thr Arg Leu Met Thr	Gly Ala Gly Asn Val	Leu Arg
385	390	395	400
Arg His Ala	Ala Asp Ala Ser Arg Arg	Ala Ala Pro Ala Glu	Gly Ala
	405	410	415
Gly Glu Asp	Glu Asp Asp Gly Ala Ser	Arg Ile Phe Phe Glu	Pro Ser
	420	425	430
Leu Tyr His	Cys Leu Glu Asn Cys	Gly Ser Val Leu	Leu Ser Val Thr
	435	440	445
Cys Gln Gly	Gly Glu Gly Asn Ser Thr	Phe Tyr Val Asp Tyr	Arg Thr
	450	455	460
Glu Asp Gly	Ser Ala Lys Ala Gly Ser	Asp Tyr Glu Tyr Ser	Glu Gly
465	470	475	480
Thr Leu Val	Phe Lys Pro Gly Glu Thr	Gln Lys Glu Leu Arg	Ile Gly
	485	490	495
Ile Ile Asp	Asp Asp Ile Phe Glu Glu	Asp Glu His Phe Phe	Val Arg

EX05-002patentin.txt

500

505

510

Leu Leu Asn Leu Arg Val Gly Asp Ala Gln Gly Met Phe Glu Pro Asp
 515 520 525

Gly Gly Gly Arg Pro Lys Gly Arg Leu Val Ala Pro Leu Leu Ala Thr
 530 535 540

Val Thr Ile Leu Asp Asp Asp His Ala Gly Ile Phe Ser Phe Gln Asp
 545 550 555 560

Arg Leu Leu His Val Ser Glu Cys Met Gly Thr Val Asp Val Arg Val
 565 570 575

Val Arg Ser Ser Gly Ala Arg Gly Thr Val Arg Leu Pro Tyr Arg Thr
 580 585 590

Val Asp Gly Thr Ala Arg Gly Gly Gly Val His Tyr Glu Asp Ala Cys
 595 600 605

Gly Glu Leu Glu Phe Gly Asp Asp Glu Thr Met Lys Thr Leu Gln Val
 610 615 620

Lys Ile Val Asp Asp Glu Glu Tyr Glu Lys Lys Asp Asn Phe Phe Ile
 625 630 635 640

Glu Leu Gly Gln Pro Gln Trp Leu Lys Arg Gly Ile Ser Ala Leu Leu
 645 650 655

Leu Asn Gln Gly Asp Gly Asp Arg Lys Leu Thr Ala Glu Glu Glu Glu
 660 665 670

Ala Arg Arg Ile Ala Glu Met Gly Lys Pro Val Leu Gly Glu Asn Cys
 675 680 685

Arg Leu Glu Val Ile Ile Glu Glu Ser Tyr Asp Phe Lys Asn Thr Val
 690 695 700

Asp Lys Leu Ile Lys Lys Thr Asn Leu Ala Leu Val Ile Gly Thr His
 705 710 715 720

Ser Trp Arg Glu Gln Phe Leu Glu Ala Ile Thr Val Ser Ala Gly Asp
 725 730 735

Glu Glu Glu Glu Glu Asp Gly Ser Arg Glu Glu Arg Leu Pro Ser Cys
 740 745 750

Phe Asp Tyr Val Met His Phe Leu Thr Val Phe Trp Lys Val Leu Phe
 755 760 765

Ala Cys Val Pro Pro Thr Glu Tyr Cys His Gly Trp Ala Cys Phe Gly
 Page 244

EX05-002patentin.txt

770

775

780

Val Ser Ile Leu Val Ile Gly Leu Leu Thr Ala Leu Ile Gly Asp Leu
785 790 795 800

Ala Ser His Phe Gly Cys Thr Val Gly Leu Lys Asp Ser Val Asn Ala
805 810 815

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

Lys Val Ala Ala Leu Gln Asp Gln Cys Ala Asp Ala Ser Ile Gly Asn
835 840 845

Val Thr Gly Ser Asn Ala Val Asn Val Phe Leu Gly Leu Gly Val Ala
850 855 860

Trp Ser Val Ala Ala Val Tyr Trp Ala Val Gln Gly Arg Pro Phe Glu
865 870 875 880

Val Arg Thr Gly Thr Leu Ala Phe Ser Val Thr Leu Phe Thr Val Phe
885 890 895

Ala Phe Val Gly Ile Ala Val Leu Leu Tyr Arg Arg Arg Pro His Ile
900 905 910

Gly Gly Glu Leu Gly Gly Pro Arg Gly Pro Lys Leu Ala Thr Thr Ala
915 920 925

Leu Phe Leu Gly Leu Trp Leu Leu Tyr Ile Leu Phe Ala Ser Leu Glu
930 935 940

Ala Tyr Cys His Ile Arg Gly Phe
945 950

<210> 109
<211> 924
<212> PRT
<213> Homo sapiens

<400> 109

Met Ala Trp Leu Arg Leu Gln Pro Leu Thr Ser Ala Phe Leu His Phe
1 5 10 15

Gly Leu Val Thr Phe Val Leu Phe Leu Asn Gly Leu Arg Ala Glu Ala
20 25 30

Gly Gly Ser Gly Asp Val Pro Ser Thr Gly Gln Asn Asn Glu Ser Cys
35 40 45

Ser Gly Ser Ser Asp Cys Lys Glu Gly Val Ile Leu Pro Ile Trp Tyr
50 55 60

EX05-002patentin.txt

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

EX05-002patentin.txt

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

EX05-002patentin.txt

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

EX05-002patentin.txt

Arg Pro His Leu Gly Gly Glu Leu Gly Gly Pro Arg Gly Cys Lys Leu
885 890 895

Ala Thr Thr Trp Leu Phe Val Ser Leu Trp Leu Leu Tyr Ile Leu Phe
900 905 910

Ala Thr Leu Glu Ala Tyr Cys Tyr Ile Lys Gly Phe
915 920

<210> 110
<211> 444
<212> PRT
<213> Homo sapiens

<400> 110

Met Ile Glu Asp Asn Lys Glu Asn Lys Asp His Ser Leu Glu Arg Gly
1 5 10 15

Arg Ala Ser Leu Ile Phe Ser Leu Lys Asn Glu Val Gly Gly Leu Ile
20 25 30

Lys Ala Leu Lys Ile Phe Gln Glu Lys His Val Asn Leu Leu His Ile
35 40 45

Glu Ser Arg Lys Ser Lys Arg Arg Asn Ser Glu Phe Glu Ile Phe Val
50 55 60

Asp Cys Asp Ile Asn Arg Glu Gln Leu Asn Asp Ile Phe His Leu Leu
65 70 75 80

Lys Ser His Thr Asn Val Leu Ser Val Asn Leu Pro Asp Asn Phe Thr
85 90 95

Leu Lys Glu Asp Gly Met Glu Thr Val Pro Trp Phe Pro Lys Lys Ile
100 105 110

Ser Asp Leu Asp His Cys Ala Asn Arg Val Leu Met Tyr Gly Ser Glu
115 120 125

Leu Asp Ala Asp His Pro Gly Phe Lys Asp Asn Val Tyr Arg Lys Arg
130 135 140

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

Ile Pro Lys Val Glu Phe Thr Glu Glu Glu Ile Lys Thr Trp Gly Thr
165 170 175

Val Phe Gln Glu Leu Asn Lys Leu Tyr Pro Thr His Ala Cys Arg Glu
180 185 190

EX05-002patentin.txt

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

<210> 111
 <211> 490
 <212> PRT

EX05-002patentin.txt

<213> Homo sapiens

<400> 111

Met Gln Pro Ala Met Met Met Phe Ser Ser Lys Tyr Trp Ala Arg Arg
 1 5 10 15

Gly Phe Ser Leu Asp Ser Ala Val Pro Glu Glu His Gln Leu Leu Gly
 20 25 30

Ser Ser Thr Leu Asn Lys Pro Asn Ser Gly Lys Asn Asp Asp Lys Gly
 35 40 45

Asn Lys Gly Ser Ser Lys Arg Glu Ala Ala Thr Glu Ser Gly Lys Thr
 50 55 60

Ala Val Val Phe Ser Leu Lys Asn Glu Val Gly Gly Leu Val Lys Ala
 65 70 75 80

Leu Arg Leu Phe Gln Glu Lys Arg Val Asn Met Val His Ile Glu Ser
 85 90 95

Arg Lys Ser Arg Arg Arg Ser Ser Glu Val Glu Ile Phe Val Asp Cys
 100 105 110

Glu Cys Gly Lys Thr Glu Phe Asn Glu Leu Ile Gln Leu Leu Lys Phe
 115 120 125

Gln Thr Thr Ile Val Thr Leu Asn Pro Pro Glu Asn Ile Trp Thr Glu
 130 135 140

Glu Glu Glu Leu Glu Asp Val Pro Trp Phe Pro Arg Lys Ile Ser Glu
 145 150 155 160

Leu Asp Lys Cys Ser His Arg Val Leu Met Tyr Gly Ser Glu Leu Asp
 165 170 175

Ala Asp His Pro Gly Phe Lys Asp Asn Val Tyr Arg Gln Arg Arg Lys
 180 185 190

Tyr Phe Val Asp Val Ala Met Gly Tyr Lys Tyr Gly Gln Pro Ile Pro
 195 200 205

Arg Val Glu Tyr Thr Glu Glu Glu Thr Lys Thr Trp Gly Val Val Phe
 210 215 220

Arg Glu Leu Ser Lys Leu Tyr Pro Thr His Ala Cys Arg Glu Tyr Leu
 225 230 235 240

Lys Asn Phe Pro Leu Leu Thr Lys Tyr Cys Gly Tyr Arg Glu Asp Asn
 245 250 255

EX05-002patentin.txt

Val Pro Gln Leu Glu Asp Val Ser Met Phe Leu Lys Glu Arg Ser Gly
 260 265 270

Phe Thr Val Arg Pro Val Ala Gly Tyr Leu Ser Pro Arg Asp Phe Leu
 275 280 285

Ala Gly Leu Ala Tyr Arg Val Phe His Cys Thr Gln Tyr Ile Arg His
 290 295 300

Gly Ser Asp Pro Leu Tyr Thr Pro Glu Pro Asp Thr Cys His Glu Leu
 305 310 315 320

Leu Gly His Val Pro Leu Leu Ala Asp Pro Lys Phe Ala Gln Phe Ser
 325 330 335

Gln Glu Ile Gly Leu Ala Ser Leu Gly Ala Ser Asp Glu Asp Val Gln
 340 345 350

Lys Leu Ala Thr Cys Tyr Phe Phe Thr Ile Glu Phe Gly Leu Cys Lys
 355 360 365

Gln Glu Gly Gln Leu Arg Ala Tyr Gly Ala Gly Leu Leu Ser Ser Ile
 370 375 380

Gly Glu Leu Lys His Ala Leu Ser Asp Lys Ala Cys Val Lys Ala Phe
 385 390 395 400

Asp Pro Lys Thr Thr Cys Leu Gln Glu Cys Leu Ile Thr Thr Phe Gln
 405 410 415

Glu Ala Tyr Phe Val Ser Glu Ser Phe Glu Glu Ala Lys Glu Lys Met
 420 425 430

Arg Asp Phe Ala Lys Ser Ile Thr Arg Pro Phe Ser Val Tyr Phe Asn
 435 440 445

Pro Tyr Thr Gln Ser Ile Glu Ile Leu Lys Asp Thr Arg Ser Ile Glu
 450 455 460

Asn Val Val Gln Asp Leu Arg Ser Asp Leu Asn Thr Val Cys Asp Ala
 465 470 475 480

Leu Asn Lys Met Asn Gln Tyr Leu Gly Ile
 485 490

<210> 112

<211> 457

<212> PRT

<213> Homo sapiens

<400> 112

Met Asp Arg Ser Leu Arg Asn Val Leu Val Val Ser Phe Gly Phe Leu
 Page 252

Page 253

EX05-002patentin.txt

275

280

285

Ile Gln Phe Val Gly Tyr Val Met Ile Cys Phe Ser Ala Thr Asp Ala
 290 295 300

Leu Cys Ser Val Leu Tyr Gly Lys Val Ser Gln Tyr Thr Gly Arg Ala
 305 310 315 320

Val Leu Tyr Val Leu Gly Ala Val Thr His Val Ser Cys Met Ile Ala
 325 330 335

Leu Leu Leu Trp Arg Pro Arg Ala Asp His Leu Ala Val Phe Phe Val
 340 345 350

Phe Ser Gly Leu Trp Gly Val Ala Asp Ala Val Trp Gln Thr Gln Asn
 355 360 365

Asn Ala Leu Tyr Gly Val Leu Phe Glu Lys Ser Lys Glu Ala Ala Phe
 370 375 380

Ala Asn Tyr Arg Leu Trp Glu Ala Leu Gly Phe Val Ile Ala Phe Gly
 385 390 395 400

Tyr Ser Met Phe Leu Cys Val His Val Lys Leu Tyr Ile Leu Leu Gly
 405 410 415

Val Leu Ser Leu Thr Met Val Ala Tyr Gly Leu Val Glu Cys Val Glu
 420 425 430

Ser Lys Asn Pro Ile Arg Pro His Ala Pro Gly Gln Val Asn Gln Ala
 435 440 445

Glu Asp Glu Glu Ile Gln Thr Lys Met
 450 455

<210> 113
 <211> 597
 <212> PRT
 <213> Homo sapiens

<400> 113

Met Glu Ala Glu Pro Pro Leu Tyr Pro Met Ala Gly Ala Ala Gly Pro
 1 5 10 15

Gln Gly Asp Glu Asp Leu Leu Gly Val Pro Asp Gly Pro Glu Ala Pro
 20 25 30

Leu Asp Glu Leu Val Gly Ala Tyr Pro Asn Tyr Asn Glu Glu Glu Glu
 35 40 45

Glu Arg Arg Tyr Tyr Arg Arg Lys Arg Leu Gly Val Leu Lys Asn Val
 50 55 60

EX05-002patentin.txt

Leu Ala Ala Ser Ala Gly Gly Met Leu Thr Tyr Gly Val Tyr Leu Gly
65 70 75 80

Leu Leu Gln Met Gln Leu Ile Leu His Tyr Asp Glu Thr Tyr Arg Glu
85 90 95

Val Lys Tyr Gly Asn Met Gly Leu Pro Asp Ile Asp Ser Lys Met Leu
100 105 110

Met Gly Ile Asn Val Thr Pro Ile Ala Ala Leu Leu Tyr Thr Pro Val
115 120 125

Leu Ile Arg Phe Phe Gly Thr Lys Trp Met Met Phe Leu Ala Val Gly
130 135 140

Ile Tyr Ala Leu Phe Val Ser Thr Asn Tyr Trp Glu Arg Tyr Tyr Thr
145 150 155 160

Leu Val Pro Ser Ala Val Ala Leu Gly Met Ala Ile Val Pro Leu Trp
165 170 175

Ala Ser Met Gly Asn Tyr Ile Thr Arg Met Ala Gln Lys Tyr His Glu
180 185 190

Tyr Ser His Tyr Lys Glu Gln Asp Gly Gln Gly Met Lys Gln Arg Pro
195 200 205

Pro Arg Gly Ser His Ala Pro Tyr Leu Leu Val Phe Gln Ala Ile Phe
210 215 220

Tyr Ser Phe Phe His Leu Ser Phe Ala Cys Ala Gln Leu Pro Met Ile
225 230 235 240

Tyr Phe Leu Asn His Tyr Leu Tyr Asp Leu Asn His Thr Leu Tyr Asn
245 250 255

Val Gln Ser Cys Gly Thr Asn Ser His Gly Ile Leu Ser Gly Phe Asn
260 265 270

Lys Thr Val Leu Arg Thr Leu Pro Arg Ser Gly Asn Leu Ile Val Val
275 280 285

Glu Ser Val Leu Met Ala Val Ala Phe Leu Ala Met Leu Leu Val Leu
290 295 300

Gly Leu Cys Gly Ala Ala Tyr Arg Pro Thr Glu Glu Ile Asp Leu Arg
305 310 315 320

Ser Val Gly Trp Gly Asn Ile Phe Gln Leu Pro Phe Lys His Val Arg
325 330 335

EX05-002patentin.txt

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

EX05-002patentin.txt

<210> 114
 <211> 414
 <212> PRT
 <213> Homo sapiens

<400> 114

Met Ser Lys Lys Ile Ser Gly Gly Ser Val Val Glu Met Gln Gly Asp
 1 5 10 15

Glu Met Thr Arg Ile Ile Trp Glu Leu Ile Lys Glu Lys Leu Ile Phe
 20 25 30

Pro Tyr Val Glu Leu Asp Leu His Ser Tyr Asp Leu Gly Ile Glu Asn
 35 40 45

Arg Asp Ala Thr Asn Asp Gln Val Thr Lys Asp Ala Ala Glu Ala Ile
 50 55 60

Lys Lys His Asn Val Gly Val Lys Cys Ala Thr Ile Thr Pro Asp Glu
 65 70 75 80

Lys Arg Val Glu Glu Phe Lys Leu Lys Gln Met Trp Lys Ser Pro Asn
 85 90 95

Gly Thr Ile Arg Asn Ile Leu Gly Gly Thr Val Phe Arg Glu Ala Ile
 100 105 110

Ile Cys Lys Asn Ile Pro Arg Leu Val Ser Gly Trp Val Lys Pro Ile
 115 120 125

Ile Ile Gly Arg His Ala Tyr Gly Asp Gln Tyr Arg Ala Thr Asp Phe
 130 135 140

Val Val Pro Gly Pro Gly Lys Val Glu Ile Thr Tyr Thr Pro Ser Asp
 145 150 155 160

Gly Thr Gln Lys Val Thr Tyr Leu Val His Asn Phe Glu Glu Gly Gly
 165 170 175

Gly Val Ala Met Gly Met Tyr Asn Gln Asp Lys Ser Ile Glu Asp Phe
 180 185 190

Ala His Ser Ser Phe Gln Met Ala Leu Ser Lys Gly Trp Pro Leu Tyr
 195 200 205

Leu Ser Thr Lys Asn Thr Ile Leu Lys Lys Tyr Asp Gly Arg Phe Lys
 210 215 220

Asp Ile Phe Gln Glu Ile Tyr Asp Lys Gln Tyr Lys Ser Gln Phe Glu
 225 230 235 240

EX05-002patentin.txt

Ala Gln Lys Ile Trp Tyr Glu His Arg Leu Ile Asp Asp Met Val Ala
 245 250 255

Gln Ala Met Lys Ser Glu Gly Gly Phe Ile Trp Ala Cys Lys Asn Tyr
 260 265 270

Asp Gly Asp Val Gln Ser Asp Ser Val Ala Gln Gly Tyr Gly Ser Leu
 275 280 285

Gly Met Met Thr Ser Val Leu Val Cys Pro Asp Gly Lys Thr Val Glu
 290 295 300

Ala Glu Ala Ala His Gly Thr Val Thr Arg His Tyr Arg Met Tyr Gln
 305 310 315 320

Lys Gly Gln Glu Thr Ser Thr Asn Pro Ile Ala Ser Ile Phe Ala Trp
 325 330 335

Thr Arg Gly Leu Ala His Arg Ala Lys Leu Asp Asn Asn Lys Glu Leu
 340 345 350

Ala Phe Phe Ala Asn Ala Leu Glu Glu Val Ser Ile Glu Thr Ile Glu
 355 360 365

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

Asn Val Gln Arg Ser Asp Tyr Leu Asn Thr Phe Glu Phe Met Asp Lys
 385 390 395 400

Leu Gly Glu Asn Leu Lys Ile Lys Leu Ala Gln Ala Lys Leu
 405 410

<210> 115
 <211> 452
 <212> PRT
 <213> Homo sapiens

<400> 115

Met Ala Gly Tyr Leu Arg Val Val Arg Ser Leu Cys Arg Ala Ser Gly
 1 5 10 15

Ser Arg Pro Ala Trp Ala Pro Ala Ala Leu Thr Ala Pro Thr Ser Gln
 20 25 30

Glu Gln Pro Arg Arg His Tyr Ala Asp Lys Arg Ile Lys Val Ala Lys
 35 40 45

Pro Val Val Glu Met Asp Gly Asp Glu Met Thr Arg Ile Ile Trp Gln
 50 55 60

EX05-002patentin.txt

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

EX05-002patentin.txt

Pro Asp Gly Lys Thr Ile Glu Ala Glu Ala Ala His Gly Thr Val Thr
 340 345 350

Arg His Tyr Arg Glu His Gln Lys Gly Arg Pro Thr Ser Thr Asn Pro
 355 360 365

Ile Ala Ser Ile Phe Ala Trp Thr Arg Gly Leu Glu His Arg Gly Lys
 370 375 380

Leu Asp Gly Asn Gln Asp Leu Ile Arg Phe Ala Gln Met Leu Glu Lys
 385 390 400

Val Cys Val Glu Thr Val Glu Ser Gly Ala Met Thr Lys Asp Leu Ala
 405 410 415

Gly Cys Ile His Gly Leu Ser Asn Val Lys Leu Asn Glu His Phe Leu
 420 425 430

Asn Thr Thr Asp Phe Leu Asp Thr Ile Lys Ser Asn Leu Asp Arg Ala
 435 440 445

Leu Gly Arg Gln
 450

<210> 116
 <211> 505
 <212> PRT
 <213> Homo sapiens

<400> 116

Met Ala Glu Ser Ala Gly Ala Ser Ser Phe Phe Pro Leu Val Val Leu
 1 5 10 15

Leu Leu Ala Gly Ser Gly Gly Ser Gly Pro Arg Gly Val Gln Ala Leu
 20 25 30

Leu Cys Ala Cys Thr Ser Cys Leu Gln Ala Asn Tyr Thr Cys Glu Thr
 35 40 45

Asp Gly Ala Cys Met Val Ser Ile Phe Asn Leu Asp Gly Met Glu His
 50 55 60

His Val Arg Thr Cys Ile Pro Lys Val Glu Leu Val Pro Ala Gly Lys
 65 70 75 80

Pro Phe Tyr Cys Leu Ser Ser Glu Asp Leu Arg Asn Thr His Cys Cys
 85 90 95

Tyr Thr Asp Tyr Cys Asn Arg Ile Asp Leu Arg Val Pro Ser Gly His
 100 105 110

Leu Lys Glu Pro Glu His Pro Ser Met Trp Gly Pro Val Glu Leu Val
 Page 260

Page 261

<210>	117
<211>	493
<212>	PRT
<213>	Homo sapiens
<400>	117

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

EX05-002patentin.txt

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

EX05-002patentin.txt

Ile Ala Arg Arg Cys Ser Val Gly Gly Ile Val Glu Glu Tyr Gln Leu
 405 410 415

Pro Tyr Tyr Asp Met Val Pro Ser Asp Pro Ser Ile Glu Glu Met Arg
 420 425 430

Lys Val Val Cys Asp Gln Lys Phe Arg Pro Ser Ile Pro Asn Gln Trp
 435 440 445

Gln Ser Cys Glu Ala Leu Arg Val Met Gly Arg Ile Met Arg Glu Cys
 450 455 460

Trp Tyr Ala Asn Gly Ala Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys
 465 470 475 480

Thr Ile Ser Gln Leu Cys Val Lys Glu Asp Cys Lys Ala
 485 490

<210> 118
 <211> 503
 <212> PRT
 <213> Homo sapiens

<400> 118

Met Glu Ala Ala Val Ala Ala Pro Arg Pro Arg Leu Leu Leu Leu Val
 1 5 10 15

Leu Ala Ala Ala Ala Ala Ala Ala Ala Ala Leu Leu Pro Gly Ala Thr
 20 25 30

Ala Leu Gln Cys Phe Cys His Leu Cys Thr Lys Asp Asn Phe Thr Cys
 35 40 45

Val Thr Asp Gly Leu Cys Phe Val Ser Val Thr Glu Thr Thr Asp Lys
 50 55 60

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

Asp Arg Pro Phe Val Cys Ala Pro Ser Ser Lys Thr Gly Ser Val Thr
 85 90 95

Thr Thr Tyr Cys Cys Asn Gln Asp His Cys Asn Lys Ile Glu Leu Pro
 100 105 110

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

Val Ile Ala Gly Pro Val Cys Phe Val Cys Ile Ser Leu Met Leu Met
 130 135 140

EX05-002patentin.txt

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

EX05-002patentin.txt

Ile Gly Gly Ile His Glu Asp Tyr Gln Leu Pro Tyr Tyr Asp Leu Val
 420 425 430

Pro Ser Asp Pro Ser Val Glu Glu Met Arg Lys Val Val Cys Glu Gln
 435 440 445

Lys Leu Arg Pro Asn Ile Pro Asn Arg Trp Gln Ser Cys Glu Ala Leu
 450 455 460

Arg Val Met Ala Lys Ile Met Arg Glu Cys Trp Tyr Ala Asn Gly Ala
 465 470 475 480

Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Ser Gln Leu Ser
 485 490 495

Gln Gln Glu Gly Ile Lys Met
 500

<210> 119
 <211> 1009
 <212> PRT
 <213> Homo sapiens

<400> 119

Met Gly Gln Leu Cys Trp Leu Pro Leu Leu Ala Pro Leu Leu Leu Leu
 1 5 10 15

Arg Pro Pro Gly Val Gln Ser Ala Gly Pro Ile Arg Ala Phe Val Val
 20 25 30

Pro His Ser His Met Asp Val Gly Trp Val Tyr Thr Val Gln Glu Ser
 35 40 45

Met Arg Ala Tyr Ala Ala Asn Val Tyr Thr Ser Val Val Glu Glu Leu
 50 55 60

Ala Arg Gly Gln Gln Arg Arg Phe Ile Ala Val Glu Gln Glu Phe Phe
 65 70 75 80

Arg Leu Trp Trp Asp Gly Val Ala Ser Asp Gln Gln Lys Tyr Gln Val
 85 90 95

Arg Gln Leu Leu Glu Glu Gly Arg Leu Glu Phe Val Ile Gly Gly Gln
 100 105 110

Val Met His Asp Glu Ala Val Thr His Leu Asp Asp Gln Ile Leu Gln
 115 120 125

Leu Thr Glu Gly His Gly Phe Leu Tyr Glu Thr Phe Gly Ile Arg Pro
 130 135 140

EX05-002patentin.txt

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

EX05-002patentin.txt

Val Gln His His Asp Ala Ile Thr Gly Thr Glu Ser Pro Lys Val Arg
 420 425 430
 Asp Met Tyr Ala Thr His Leu Ala Ser Gly Met Leu Gly Met Arg Lys
 435 440 445
 Leu Met Ala Ser Ile Val Leu Asp Glu Leu Gln Pro Gln Ala Pro Met
 450 455 460
 Ala Ala Ser Ser Asp Ala Gly Pro Ala Gly His Phe Ala Ser Val Tyr
 465 470 475 480
 Asn Pro Leu Ala Trp Thr Val Thr Thr Ile Val Thr Leu Thr Val Gly
 485 490 495
 Phe Pro Gly Val Arg Val Thr Asp Glu Ala Gly His Pro Val Pro Ser
 500 505 510
 Gln Ile Gln Asn Ser Thr Glu Thr Pro Ser Ala Tyr Asp Leu Leu Ile
 515 520 525
 Leu Thr Thr Ile Pro Gly Leu Ser Tyr Arg His Tyr Asn Ile Arg Pro
 530 535 540
 Thr Ala Gly Ala Gln Glu Gly Thr Gln Glu Pro Ala Ala Thr Val Ala
 545 550 555 560
 Ser Thr Leu Gln Phe Gly Arg Arg Leu Arg Arg Arg Thr Ser His Ala
 565 570 575
 Gly Arg Tyr Leu Val Pro Val Ala Asn Asp Cys Tyr Ile Val Leu Leu
 580 585 590
 Asp Gln Asp Thr Asn Leu Met His Ser Ile Trp Glu Arg Gln Ser Asn
 595 600 605
 Arg Thr Val Arg Val Thr Gln Glu Phe Leu Glu Tyr His Val Asn Gly
 610 615 620
 Asp Val Lys Gln Gly Pro Ile Ser Asp Asn Tyr Leu Phe Thr Pro Gly
 625 630 635 640
 Lys Ala Ala Val Pro Ala Trp Glu Ala Val Glu Met Glu Ile Val Ala
 645 650 655
 Gly Gln Leu Val Thr Glu Ile Arg Gln Tyr Phe Tyr Arg Asn Met Thr
 660 665 670
 Ala Gln Asn Tyr Thr Tyr Ala Ile Arg Ser Arg Leu Thr His Val Pro
 675 680 685

EX05-002patentin.txt

Gln Gly His Asp Gly Glu Leu Leu Cys His Arg Ile Glu Gln Glu Tyr
 690 695 700

Gln Ala Gly Pro Leu Glu Leu Asn Arg Glu Ala Val Leu Arg Thr Ser
 705 710 715 720

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

Gln Met Gln Arg Arg Pro Tyr Val Ser Tyr Val Asn Asn Ser Ile Ala
 740 745 750

Arg Asn Tyr Tyr Pro Met Val Gln Ser Ala Phe Met Glu Asp Gly Lys
 755 760 765

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

Gly Asn Gly Gln Val Glu Val Met Leu His Arg Arg Leu Trp Asn Asn
 785 790 795 800

Phe Asp Trp Asp Leu Gly Tyr Asn Leu Thr Leu Asn Asp Thr Ser Val
 805 810 815

Val His Pro Val Leu Trp Leu Leu Leu Gly Ser Trp Ser Leu Thr Thr
 820 825 830

Ala Leu Arg Gln Arg Ser Ala Leu Ala Leu Gln His Arg Pro Val Val
 835 840 845

Leu Phe Gly Asp Leu Ala Gly Thr Ala Pro Lys Leu Pro Gly Pro Gln
 850 855 860

Gln Gln Glu Ala Val Thr Leu Pro Pro Asn Leu His Leu Gln Ile Leu
 865 870 875 880

Ser Ile Pro Gly Trp Arg Tyr Ser Ser Asn His Thr Glu His Ser Gln
 885 890 895

Asn Leu Arg Lys Gly His Arg Gly Glu Ala Gln Ala Asp Leu Arg Arg
 900 905 910

Val Leu Leu Arg Leu Tyr His Leu Tyr Glu Val Gly Glu Asp Pro Val
 915 920 925

Leu Ser Gln Pro Val Thr Val Asn Leu Glu Ala Val Leu Gln Ala Leu
 930 935 940

Gly Ser Val Val Ala Val Glu Glu Arg Ser Leu Thr Gly Thr Trp Asp
 945 950 955 960

Leu Ser Met Leu His Arg Trp Ser Trp Arg Thr Gly Pro Gly Arg His
965 970 975

Arg Gly Asp Thr Thr Ser Pro Ser Arg Pro Pro Gly Gly Pro Ile Ile
980 985 990

Thr Val His Pro Lys Glu Ile Arg Thr Phe Phe Ile His Phe Gln Gln
995 1000 1005

<210>	120
<211>	655
<212>	PRT
<213>	Homo sapiens
<400>	120

Met Val Thr Thr Leu Gly Pro Lys Met Ala Ala Glu Trp Gly Gly Gly
1 5 10 15Val Gly Tyr Ser Gly Ser Gly Pro Gly Arg Ser Arg Trp Arg Trp Ser
20 25 30

Gly Ser Val Trp Val Arg Ser Val Leu Leu Leu Leu Gly Gly Leu Arg
35 40 45

Ala Ser Ala Thr Ser Thr Pro Val Ser Leu Gly Ser Ser Pro Pro Cys
50 55 60

Arg His His Val Pro Ser Asp Thr Glu Val Ile Asn Lys Val His Leu
65 70 75 80

Lys Ala Asn His Val Val Lys Arg Asp Val Asp Glu His Leu Arg Ile
85 90 95

Lys Thr Val Tyr Asp Lys Ser Val Glu Glu Leu Leu Pro Glu Lys Lys
100 105 110

Asn Leu Val Lys Asn Lys Leu Phe Pro Gln Ala Ile Ser Tyr Leu Glu
115 120 125

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

Gln Cys Ala Thr Asn Gln Tyr Leu Arg Lys Glu Asn Asp Pro His Arg
145 150 155 160

Tyr Cys Thr Gly Glu Cys Ala Ala His Thr Lys Cys Gly Pro Val Ile
165 170 175

Val Pro Glu Glu His Leu Gln Gln Cys Arg Val Tyr Arg Gly Gly Lys
Page 270

EX05-002patentin.txt

180

185

190

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

Ala Asp Phe Val Leu Tyr Val Gly Ala Leu Ala Thr Glu Arg Cys Ser
 210 215 220

His Glu Asn Ile Ile Ser Tyr Ala Ala Tyr Cys Gln Gln Glu Ala Asn
 225 230 235 240

Met Asp Arg Pro Ile Ala Gly Tyr Ala Asn Leu Cys Pro Asn Met Ile
 245 250 255

Ser Thr Gln Pro Gln Glu Phe Val Gly Met Leu Ser Thr Val Lys His
 260 265 270

Glu Val Ile His Ala Leu Gly Phe Ser Ala Gly Leu Phe Ala Phe Tyr
 275 280 285

His Asp Lys Asp Gly Asn Pro Leu Thr Ser Arg Phe Ala Asp Gly Leu
 290 295 300

Pro Pro Phe Asn Tyr Ser Leu Gly Leu Tyr Gln Trp Ser Asp Lys Val
 305 310 315 320

Val Arg Lys Val Glu Arg Leu Trp Asp Val Arg Asp Asn Lys Ile Val
 325 330 335

Arg His Thr Val Tyr Leu Leu Val Thr Pro Arg Val Val Glu Glu Ala
 340 345 350

Arg Lys His Phe Asp Cys Pro Val Leu Glu Gly Met Glu Leu Glu Asn
 355 360 365

Gln Gly Gly Val Gly Thr Glu Leu Asn His Trp Glu Lys Arg Leu Leu
 370 375 380

Glu Asn Glu Ala Met Thr Gly Ser His Thr Gln Asn Arg Val Leu Ser
 385 390 395 400

Arg Ile Thr Leu Ala Leu Met Glu Asp Thr Gly Arg Gln Met Leu Ser
 405 410 415

Pro Tyr Cys Asp Thr Leu Arg Ser Asn Pro Leu Gln Leu Thr Cys Arg
 420 425 430

Gln Asp Gln Arg Ala Val Ala Val Cys Asn Leu Gln Lys Phe Pro Lys
 435 440 445

Pro Leu Pro Gln Glu Tyr Gln Tyr Phe Asp Glu Leu Ser Gly Ile Pro
 Page 271

EX05-002patentin.txt
460

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/02638

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 33/53; G01N 33/566

US CL : 435/7.1; 436/501

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/7.1; 436/501

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ROOPMATHY RAJAH et al., Insulin-like Growth Factor Binding Protein-3 Mediates Tumor Necrosis Factor-alpha-induced Apoptosis: Role of Bcl-2 Phosphorylation. Cell Growth & Differentiation, Volume 13, April 2002, pages 163-171, see entire document.	1-6, 8-9, 11-13 and 16-22
Y	GRIMBERG et al., IGFBP-3 mediates p53-induced apoptosis during serum starvation. International Journal of Oncology, Volume 21, No.2, pages 327-335, August 2002, see abstract.	7
Y	BENBASSAT et al., Interleukin-1alpha (IL-1alpha) and tumor necrosis factoralpha (TNFalpha) regulate insulin-like growth factor binding protein-1 (IGFBP-1) levels and mRNA abundance in vivo and in vitro. Hormone and Metabolic Research, Volume 31, Number 2-3, pages 209-215, February - March 1999.	14, 15, and 23-24
A	YEH et al., Characterization and Cloning of a 58/53-kDa Substrate of the Insulin Receptor Tyrosine Kinase. Volume 271, Number 6, pages 2921-2928, February 9, 1996, see entire document.	1-24

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"B" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

02 May 2005 (02.05.2005)

Date of mailing of the international search report

17 MAY 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Lisa V. Daniels-Cook

Telephone No. (571) 272-1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/02638

Continuation of B. FIELDS SEARCHED Item 3:
EAST AND WEST PATENT DATABASE
PALM INVENTOR
STN-biosis, caplus, embase, medline, cancerlit, japio