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**IDENTIFICATION OF TUMOUR-ASSOCIATED CELL SURFACE ANTIGENS FOR DIA-
GNOSIS AND THERAPY**

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ABSTRACT

The present invention provides a pharmaceutical composition, comprising an agent which inhibits expression or activity of a tumor-associated antigen, said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:

- (a) a nucleic acid which comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 97, 101, 105, 109, 113, 117, 121, 125, 129, 133, 137, 141, 145, 149, 153, 157, 161, 165, 169, 173, 175, 179, 183, 187, 191, 195, 199, 203, 207, 211, 215, 219, 223, 227, 231, 235, 239, 243, 247, 251, 255, 259, 263, 267, 269, 271, 273, 275, 277, 279, 309 of the sequence listing, a part or derivative thereof,
- (b) a nucleic acid which hybridizes with the nucleic acid of (a) under stringent conditions,
- (c) a nucleic acid which is degenerate with respect to the nucleic acid of (a) or (b), and
- (d) a nucleic acid which is complementary to the nucleic acid of (a), (b) or (c).

Identification of Tumour-Associated Cell Surface Antigens for Diagnosis and Therapy

The present application is a divisional application from Australian patent application number 2012233057, which in turn is a divisional application from Australian patent application number 2011213901, which in turn is a divisional application from Australian patent application number 2004275500, the entire disclosures of which are incorporated herein by reference.

Despite interdisciplinary approaches and exhaustive use of classical therapeutic procedures, cancers are still among the leading causes of death. More recent therapeutic concepts aim at incorporating the patient's immune system into the overall therapeutic concept by using recombinant tumor vaccines and other specific measures such as antibody therapy. A prerequisite for the success of such a strategy is the recognition of tumor-specific or tumor-associated antigens or epitopes by the patient's immune system whose effector functions are to be interventionally enhanced. Tumor cells biologically differ substantially from their nonmalignant cells of origin. These differences are due to genetic alterations acquired during tumor development and result, inter alia, also in the formation of qualitatively or quantitatively altered molecular structures in the cancer cells. Tumor-associated structures of this kind which are recognized by the specific immune system of the tumor-harboring host are referred to as tumor-associated antigens. The specific recognition of tumor-associated antigens involves cellular and humoral mechanisms which are two functionally interconnected units: $CD4^+$ and $CD8^+$ T lymphocytes recognize the processed antigens presented on the molecules of the MHC (major histocompatibility complex) classes II and I, respectively, while B lymphocytes produce circulating antibody molecules which bind directly to unprocessed antigens. The potential clinical-therapeutical importance of tumor-associated antigens results from the fact that the recognition of antigens on neoplastic cells by the immune system leads to the initiation of cytotoxic effector mechanisms and, in the presence of T helper cells, can cause elimination of the cancer cells

(Pardoll, *Nat. Med.* 4:525-31, 1998). Accordingly, a central aim of tumor immunology is to molecularly define these structures. The molecular nature of these antigens has been enigmatic for a long time. Only after development of appropriate cloning techniques has it been possible to screen cDNA expression libraries of tumors systematically for tumor-associated antigens by analyzing the target structures of cytotoxic T lymphocytes (CTL) (van der Bruggen et al., *Science* 254:1643-7, 1991) or by using circulating autoantibodies (Sahin et al., *Curr. Opin. Immunol.* 9:709-16, 1997) as probes. To this end, cDNA expression libraries were prepared from fresh tumor tissue and recombinantly expressed as proteins in suitable systems. Immune effectors isolated from patients, namely CTL clones with tumor-specific lysis patterns, or circulating autoantibodies were utilized for cloning the respective antigens.

In recent years a multiplicity of antigens have been defined in various neoplasias by these approaches. The class of cancer/testis antigens (CTA) is of great interest here. CTA and genes encoding them (cancer/testis genes or CTG) are defined by their characteristic expression pattern [Tureci et al, *Mol Med Today.* 3:342-9, 1997]. They are not found in normal tissues, except testis and germ cells, but are expressed in a number of human malignomas, not tumor type-specifically but with different frequency in tumor entities of very different origins (Chen & Old, *Cancer J. Sci. Am.* 5:16-7, 1999). Serum reactivities against CTA are also not found in healthy controls but only in tumor patients. This class of antigens, in particular owing to its tissue distribution, is particularly valuable for immunotherapeutic projects and is tested in current clinical patient studies (Marchand et al., *Int. J. Cancer* 80:219-30, 1999; Knuth et al., *Cancer Chemother. Pharmacol.* 46:p46-51, 2000).

However, the probes utilized for antigen identification in the classical methods illustrated above are immunoeffectors (circulating autoantibodies or CTL clones) from patients usually having already advanced cancer. A number of data indicate that tumors can lead, for example, to tolerization and anergization of T cells and that, during the course of the disease, especially those specificities which could cause effective immune recognition are lost from the immunoeffector repertoire. Current patient studies have not yet produced any solid evidence of a real action of the previously found and utilized tumor-associated antigens. Accordingly, it cannot be ruled out that proteins evoking spontaneous immune responses are the wrong target structures.

It is an aspect of the invention to provide target structures for a diagnosis and therapy of cancers.

According to the invention, this aspect is provided by the subject matter of the claims.

According to the invention, a strategy for identifying and providing antigens expressed in association with a tumor and the nucleic acids coding therefor was pursued. This strategy is based on the evaluation of human protein and nucleic acid data bases with respect to potential cancer-specific antigens which are accessible on the cell surface. The definition of the filter criteria which are necessary for this together with a high throughput methodology for analysing all proteins, if possible, form the central part of the invention. Data mining first produces a list which is as complete as possible of all known genes which

2015201738 12 Jul 2016

- 3a -

according to the basic principle "gene to mRNA to protein" are examined for the presence of one or more transmembrane domains. This is followed by a homology search, a classification of the hits in tissue specific

groups (among others tumor tissue) and an inspection of the real existence of the mRNA. Finally, the proteins which are identified in this manner are evaluated for their aberrant activation in tumors, e.g. by expression analyses and protein chemical procedures.

Data mining is a known method of identifying tumor-associated genes. In the conventional strategies, however, transcriptoms of normal tissue libraries are usually subtracted electronically from tumor tissue libraries, with the assumption that the remaining genes are tumor-specific (Schmitt et al., *Nucleic Acids Res.* 27:4251-60, 1999; Vasmatazis et al., *Proc. Natl. Acad. Sci. USA.* 95:300-4, 1998; Scheurle et al., *Cancer Res.* 60:4037-43, 2000).

The concept of the invention, however, is based on utilizing data mining for electronically extracting all genes coding for cancer specific antigens which are accessible on the cell surfaces and then evaluating said genes for ectopic expression in tumors.

The invention thus relates in one aspect to a strategy for identifying genes differentially expressed in tumors. Said strategy combines data mining of public sequence libraries ("in silico") with subsequent evaluating laboratory-experimental ("wet bench") studies.

According to the invention, a combined strategy based on different bioinformatic scripts enabled new genes coding for cancer specific antigens which are accessible on the cell surfaces to be identified. According to the invention, these tumor-associated genes and the genetic products encoded thereby were identified and provided independently of an immunogenic action.

The tumor-associated antigens identified according to

2015201738 07 Apr 2015

the invention have an amino acid sequence encoded by a nucleic acid which is selected from the group consisting of (a) a nucleic acid which comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 97, 101, 105, 109, 113, 117, 121, 125, 129, 133, 137, 141, 145, 149, 153, 157, 161, 165, 169, 173, 175, 179, 183, 187, 191, 195, 199, 203, 207, 211, 215, 219, 223, 227, 231, 235, 239, 243, 247, 251, 255, 259, 263, 267, 269, 271, 273, 275, 277, 279, 309 of the sequence listing, a part or derivative thereof, (b) a nucleic acid which hybridizes with the nucleic acid of (a) under stringent conditions, (c) a nucleic acid which is degenerate with respect to the nucleic acid of (a) or (b), and (d) a nucleic acid which is complementary to the nucleic acid of (a), (b) or (c). In a preferred embodiment, a tumor-associated antigen identified according to the invention has an amino acid sequence encoded by a nucleic acid which is selected from the group consisting of SEQ ID NOs: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 97, 101, 105, 109, 113, 117, 121, 125, 129, 133, 137, 141, 145, 149, 153, 157, 161, 165, 169, 173, 175, 179, 183, 187, 191, 195, 199, 203, 207, 211, 215, 219, 223, 227, 231, 235, 239, 243, 247, 251, 255, 259, 263, 267, 269, 271, 273, 275, 277, 279, 309 of the sequence listing. In a further preferred embodiment, a tumor-associated antigen identified according to the invention comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 98, 102, 106, 110, 114, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 176, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220, 224, 228, 232, 236, 240, 244, 248, 252, 256, 260, 264, 268, 270, 272, 274, 276, 278, 280 to 308, 310 of the sequence listing, a part or derivative thereof.

In one aspect the present invention provides a pharmaceutical composition when used for treating a cancer disease characterized by an increased expression of a tumor-associated antigen, comprising one or more components selected from the group consisting of:

- (i) a tumor-associated antigen or a part thereof,
- (ii) a nucleic acid which codes for a tumor-associated antigen or a part thereof,
- (iii) an antibody which binds to a tumor-associated antigen or a part thereof,
- (iv) an antisense nucleic acid which hybridizes specifically with a nucleic acid coding for a tumor-associated antigen,
- (v) a host cell which expresses a tumor-associated antigen or a part thereof, and
- (vi) isolated complexes between a tumor-associated antigen or a part thereof and an HLA molecule,

wherein said part comprises at least 6 consecutive amino acids of the tumor-associated antigen, said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:

- (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
- (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).

In another aspect the present invention provides a method of diagnosing a cancer disease characterized by an increased expression of a tumor-associated antigen, which method comprises

- (i) detection of a nucleic acid which codes for the tumor-associated antigen, and/or
- (ii) detection of the tumor-associated antigen, and/or
- (iii) detection of an antibody to the tumor-associated antigen and/or
- (iv) detection of cytotoxic or T helper lymphocytes which are specific to the tumor-associated antigen or to a part thereof in a biological sample isolated from a patient, wherein the part comprises at least 6 consecutive amino acids of the tumor-associated antigen, said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
 - (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
 - (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).

In another aspect the present invention provides a method for determining regression, course or onset of a cancer disease characterized by an increased expression of a tumor-associated antigen, which method comprises monitoring a sample from a patient who has said disease or is suspected of falling ill with said disease, with respect to one or more parameters selected from the group consisting of:

- (i) the amount of nucleic acid which codes for the tumor-associated antigen,
- (ii) the amount of the tumor-associated antigen,

(iii) the amount of antibodies which bind to the tumor-associated antigen, and

(iv) the amount of cytolytic or cytokine-releasing T cells which are specific for a complex between the tumor-associated antigen or a part thereof comprising at least 6 consecutive amino acids of the tumor-associated antigen,

said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:

(a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and

(b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).

In another aspect the present invention provides a method of treating, diagnosing or monitoring a cancer disease characterized by an increased expression of a tumor-associated antigen, which method comprises administering an antibody binding to said tumor-associated antigen and coupled to a therapeutic or diagnostic agent, said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:

(a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and

(b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).

In another aspect the present invention provides a method of treating a patient having a cancer disease characterized by an increased expression of a tumor-associated antigen, which method comprises:

- (i) removing a sample containing immunoreactive cells from said patient,
- (ii) contacting said sample with a host cell expressing said tumor-associated antigen or a part thereof comprising at least 6 consecutive amino acids of the tumor-associated antigen, under conditions which favor production of cytolytic or cytokine-releasing T cells against said tumor-associated antigen or the part thereof, and
- (iii) introducing the cytolytic or cytokine-releasing T cells into the patient in an amount suitable for lysing cells expressing the tumor-associated antigen or the part thereof, said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
 - (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
 - (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).

In another aspect the present invention provides a kit when used for detecting expression of a tumor-associated antigen in tumor tissue, which kit comprises agents for detection

- (i) of the nucleic acid which codes for the tumor-associated antigen,

- (ii) of the tumor-associated antigen,
 - (iii) of antibodies which bind to the tumor-associated antigen, and/or
 - (iv) of T cells which are specific for a complex between the tumor-associated antigen or a part thereof comprising at least 6 consecutive amino acids of the tumor-associated antigen and an MHC molecule,
- said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
- (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
 - (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).

In another aspect the present invention provides a pharmaceutical composition when used for treating or preventing a cancer disease said pharmaceutical composition comprising RNA interference (RNAi) which inhibits expression or activity of the tumor antigen according to SEQ ID NO: 14 of the sequence listing.

In another aspect the present invention provides a method of treating, diagnosing or monitoring a metastasizing tumor characterized by an increased expression of at least one tumor antigen, which method comprises administering an antibody which binds to at least one tumor antigen and which is coupled to a therapeutic or diagnostic agent,

said at least one tumor antigen having a sequence encoded by a nucleic acid consisting of:

- (a) a nucleic acid comprising a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
- (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).

The present invention generally relates to the use of tumor-associated antigens identified according to the invention or of parts thereof, of nucleic acids coding therefor or of nucleic acids directed against said coding nucleic acids or of antibodies directed against the tumor-associated antigens identified according to the invention or parts thereof for therapy and diagnosis. This utilization may relate to individual but also to combinations of two or more of these antigens, functional fragments, nucleic acids, antibodies, etc., in one embodiment also in combination with other tumor-associated genes and antigens for diagnosis, therapy and progress control.

The property of the tumor-associated antigens identified according to the invention that they are localized on or at the cell surface qualifies them as suitable targets or means for therapy and diagnosis. Especially suitable for this is a part of the tumor-associated antigens identified according to the invention which corresponds to the non-transmembrane portion, in particular the extracellular portion of the antigens, or is comprised thereof. Therefore, according to the invention, a part of the tumor-associated antigens identified according to the invention which

corresponds to the non-transmembrane portion of the antigens or is comprised thereof, or a corresponding part of the nucleic acids coding for the tumor-associated antigens identified according to the invention is preferred for therapy or diagnosis. Similarly, the use of antibodies is preferred which are directed against a part of the tumor-associated antigens identified according to the invention which corresponds to the non-transmembrane portion of the antigens or is comprised thereof.

Preferred diseases for a therapy and/or diagnosis are those in which one or more of the tumor-associated

antigens identified according to the invention are selectively expressed or abnormally expressed.

5 The invention also relates to nucleic acids and genetic products which are expressed in association with a tumor cell and which are produced by altered splicing (splice variants) of genes or by altered translation with utilization of alternative open reading frames. Said nucleic acids comprise the sequences according to
10 SEQ ID NOs: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 97, 101, 105, 109, 113, 117, 121, 125, 129, 133, 137, 141, 145, 149, 153, 157, 161, 165, 169, 173, 175, 179, 183, 187, 191, 195, 199, 203, 207, 211, 215, 219, 223, 227,
15 231, 235, 239, 243, 247, 251, 255, 259, 263, 267, 269, 271, 273, 275, 277, 279, 309 of the sequence listing. Furthermore, the genetic products comprise all sequences according to SEQ ID NOs: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78,
20 82, 86, 90, 94, 98, 102, 106, 110, 114, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 176, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220, 224, 228, 232, 236, 240, 244, 248, 252, 256, 260, 264, 268, 270, 272, 274, 276, 278, 280 to 308, 310
25 of the sequence listing. The splice variants of the invention can be used according to the invention as targets for diagnosis and therapy of tumor diseases.

Very different mechanisms may cause splice variants to
30 be produced, for example

- utilization of variable transcription initiation sites
- utilization of additional exons
- complete or incomplete splicing out of single or
35 two or more exons,
- splice regulator sequences altered via mutation (deletion or generation of new donor/acceptor sequences),
- incomplete elimination of intron sequences.

Altered splicing of a gene results in an altered transcript sequence (splice variant). Translation of a splice variant in the region of its altered sequence results in an altered protein which may be distinctly different in the structure and function from the original protein. Tumor-associated splice variants may produce tumor-associated transcripts and tumor-associated proteins/antigens. These may be utilized as molecular markers both for detecting tumor cells and for therapeutic targeting of tumors. Detection of tumor cells, for example in blood, serum, bone marrow, sputum, bronchial lavage, bodily secretions and tissue biopsies, may be carried out according to the invention, for example, after extraction of nucleic acids by PCR amplification with splice variant-specific oligonucleotides. According to the invention, all sequence-dependent detection systems are suitable for detection. These are, apart from PCR, for example gene chip/microarray systems, Northern blot, RNase protection assays (RDA) and others. All detection systems have in common that detection is based on a specific hybridization with at least one splice variant-specific nucleic acid sequence. However, tumor cells may also be detected according to the invention by antibodies which recognize a specific epitope encoded by the splice variant. Said antibodies may be prepared by using for immunization peptides which are specific for said splice variant. Suitable for immunization are particularly the amino acids whose epitopes are distinctly different from the variant(s) of the genetic product, which is (are) preferably produced in healthy cells. Detection of the tumor cells with antibodies may be carried out here on a sample isolated from the patient or as imaging with intravenously administered antibodies.

In addition to diagnostic usability, splice variants having new or altered epitopes are attractive targets

for immunotherapy. The epitopes of the invention may be utilized for targeting therapeutically active monoclonal antibodies or T lymphocytes. In passive immunotherapy, antibodies or T lymphocytes which recognize splice variant-specific epitopes are adoptively transferred here. As in the case of other antigens, antibodies may be generated also by using standard technologies (immunization of animals, panning strategies for isolation of recombinant antibodies) with utilization of polypeptides which include these epitopes. Alternatively, it is possible to utilize for immunization nucleic acids coding for oligo- or polypeptides which contain said epitopes. Various techniques for in vitro or in vivo generation of epitope-specific T lymphocytes are known and have been described in detail (for example Kessler JH, et al. 2001, Sahin et al., 1997) and are likewise based on utilizing oligo- or polypeptides which contain the splice variant-specific epitopes or nucleic acids coding for said oligo- or polypeptides. Oligo- or polypeptides which contain the splice variant-specific epitopes or nucleic acids coding for said polypeptides may also be used for utilization as pharmaceutically active substances in active immunotherapy (vaccination, vaccine therapy).

The aberrant expression of genes in tumor cells also can be due to an altered methylation pattern of their promoters (De Smet C et al., Mol. Cell Biol. 24(11):4781-90, 2004; De Smet C et al., Mol. Cell Biol. 19(11):7327-35, 1999; De Smet C et al., Proc. Natl. Acad. Sci. U S A. 93(14):7149-53, 1996). These differences in methylation can be used as indirect markers for the condition of the respective gene changed in the tumor. Accordingly, the increase or decrease of base methylations within the promoter region can be used for diagnostic purposes.

In one aspect, the invention relates to a

pharmaceutical composition comprising an agent which recognizes the tumor-associated antigen identified according to the invention and which is preferably selective for cells which have expression or abnormal expression of a tumor-associated antigen identified according to the invention. In particular embodiments, said agent may cause induction of cell death, reduction in cell growth, damage to the cell membrane or secretion of cytokines and preferably have a tumor-inhibiting activity. In one embodiment, the agent is an antisense nucleic acid which hybridizes selectively with the nucleic acid coding for the tumor-associated antigen. In a further embodiment, the agent is an antibody which binds selectively to the tumor-associated antigen, in particular a complement-activated antibody which binds selectively to the tumor-associated antigen. In a further embodiment, the agent comprises two or more agents which each selectively recognize different tumor-associated antigens, at least one of which is a tumor-associated antigen identified according to the invention. Recognition needs not be accompanied directly with inhibition of activity or expression of the antigen. In this aspect of the invention, the antigen selectively limited to tumors preferably serves as a label for recruiting effector mechanisms to this specific location. In a preferred embodiment, the agent is a cytotoxic T lymphocyte which recognizes the antigen on an HLA molecule and lyses the cell labeled in this way. In a further embodiment, the agent is an antibody which binds selectively to the tumor-associated antigen and thus recruits natural or artificial effector mechanisms to said cell. In a further embodiment, the agent is a T helper lymphocyte which enhances effector functions of other cells specifically recognizing said antigen.

In one aspect, the invention relates to a pharmaceutical composition comprising an agent which inhibits expression or activity of a tumor-associated

antigen identified according to the invention. In a preferred embodiment, the agent is an antisense nucleic acid which hybridizes selectively with the nucleic acid coding for the tumor-associated antigen. In a further
5 embodiment, the agent is an antibody which binds selectively to the tumor-associated antigen. In a further embodiment, the agent comprises two or more agents which each selectively inhibit expression or activity of different tumor-associated antigens, at
10 least one of which is a tumor-associated antigen identified according to the invention.

The activity of a tumor-associated antigen identified according to the invention can be any activity of a
15 protein or a peptide. Thus, the therapeutic and diagnostic methods according to the invention can also aim at inhibiting or reducing this activity or testing this activity.

20 The invention furthermore relates to a pharmaceutical composition which comprises an agent which, when administered, selectively increases the amount of complexes between an HLA molecule and a peptide epitope from the tumor-associated antigen identified according
25 to the invention. In one embodiment, the agent comprises one or more components selected from the group consisting of (i) the tumor-associated antigen or a part thereof, (ii) a nucleic acid which codes for said tumor-associated antigen or a part thereof, (iii)
30 a host cell which expresses said tumor-associated antigen or a part thereof, and (iv) isolated complexes between peptide epitopes from said tumor-associated antigen and an MHC molecule. In one embodiment, the agent comprises two or more agents which each
35 selectively increase the amount of complexes between MHC molecules and peptide epitopes of different tumor-associated antigens, at least one of which is a tumor-associated antigen identified according to the invention.

2015201738 07 Apr 2015

The invention furthermore relates to a pharmaceutical composition which comprises one or more components selected from the group consisting of (i) a tumor-associated antigen identified according to the invention or a part thereof, (ii) a nucleic acid which codes for a tumor-associated antigen identified according to the invention or for a part thereof, (iii) an antibody which binds to a tumor-associated antigen identified according to the invention or to a part thereof, (iv) an antisense nucleic acid which hybridizes specifically with a nucleic acid coding for a tumor-associated antigen identified according to the invention, (v) a host cell which expresses a tumor-associated antigen identified according to the invention or a part thereof, and (vi) isolated complexes between a tumor-associated antigen identified according to the invention or a part thereof and an HLA molecule.

A nucleic acid coding for a tumor-associated antigen identified according to the invention or for a part thereof may be present in the pharmaceutical composition in an expression vector and functionally linked to a promoter.

A host cell present in a pharmaceutical composition of the invention may secrete the tumor-associated antigen or the part thereof, express it on the surface or may additionally express an HLA molecule which binds to said tumor-associated antigen or said part thereof. In one embodiment, the host cell expresses the HLA molecule endogenously. In a further embodiment, the host cell expresses the HLA molecule and/or the tumor-associated antigen or the part thereof in a recombinant manner. The host cell is preferably nonproliferative. In a preferred embodiment, the host cell is an antigen-presenting cell, in particular a dendritic cell, a monocyte or a macrophage.

2015201738 07 Apr 2015

An antibody present in a pharmaceutical composition of the invention may be a monoclonal antibody. In further embodiments, the antibody is a chimeric or humanized antibody, a fragment of a natural antibody or a synthetic antibody, all of which may be produced by combinatory techniques. The antibody may be coupled to a therapeutically or diagnostically useful agent.

10 An antisense nucleic acid present in a pharmaceutical composition of the invention may comprise a sequence of 6-50, in particular 10-30, 15-30 and 20-30, contiguous nucleotides of the nucleic acid coding for the tumor-associated antigen identified according to the invention.

In further embodiments, a tumor-associated antigen, provided by a pharmaceutical composition of the invention either directly or via expression of a nucleic acid, or a part thereof binds to MHC molecules on the surface of cells, said binding preferably causing a cytolytic response and/or inducing cytokine release.

25 A pharmaceutical composition of the invention may comprise a pharmaceutically compatible carrier and/or an adjuvant. The adjuvant may be selected from saponin, GM-CSF, CpG oligonucleotides, RNA, a cytokine or a chemokine. A pharmaceutical composition of the invention is preferably used for the treatment of a disease characterized by selective expression or abnormal expression of a tumor-associated antigen. In a preferred embodiment, the disease is cancer.

35 The invention furthermore relates to methods of treating, diagnosing or monitoring, i.e. determining the regression, progression and/or onset of, a disease characterized by expression or abnormal expression of one of more tumor-associated antigens.

In one embodiment, the methods of treatment according to the invention comprise administering a pharmaceutical composition of the invention.

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The methods of diagnosing and/or methods of monitoring according to the invention generally concern the use of means for the detection and/or the determination and/or the monitoring of the quantity of (i) a nucleic acid, which codes for the tumor-associated antigen, or a part thereof and/or (ii) the tumor-associated antigen or a part thereof and/or (iii) an antibody against the tumor-associated antigen or a part thereof and/or (iv) cytotoxic or T helper lymphocytes, which are specific for the tumor-associated antigen or a part thereof, in a biologic sample isolated from a patient.

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In one aspect, the invention relates to a method of diagnosing a disease characterized by expression or abnormal expression of a tumor-associated antigen identified according to the invention. The method comprises (i) detection of a nucleic acid which codes for the tumor-associated antigen or of a part thereof and/or (ii) detection of the tumor-associated antigen or of a part thereof, and/or (iii) detection of an antibody to the tumor-associated antigen or to a part thereof and/or (iv) detection of cytotoxic or T helper lymphocytes which are specific for the tumor-associated antigen or for a part thereof in a biological sample isolated from a patient. In particular embodiments, detection comprises (i) contacting the biological sample with an agent which binds specifically to the nucleic acid coding for the tumor-associated antigen or to the part thereof, to said tumor-associated antigen or said part thereof, to the antibody or to cytotoxic or T helper lymphocytes specific for the tumor-associated antigen or parts thereof, and (ii) detecting the formation of a complex between the agent and the nucleic acid or the part thereof, the tumor-associated

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antigen or the part thereof, the antibody or the cytotoxic or T helper lymphocytes. In one embodiment, the disease is characterized by expression or abnormal expression of two or more different tumor-associated antigens and detection comprises detection of two or more nucleic acids coding for said two or more different tumor-associated antigens or of parts thereof, detection of two or more different tumor-associated antigens or of parts thereof, detection of two or more antibodies binding to said two or more different tumor-associated antigens or to parts thereof or detection of two or more cytotoxic or T helper lymphocytes specific for said two or more different tumor-associated antigens. In a further embodiment, the biological sample isolated from the patient is compared to a comparable normal biological sample.

The methods of diagnosing according to the invention may also utilize altered methylation patterns of the promoter region of the respective tumor-associated gene product. The detection of such methylation patterns can be performed by using methods on the basis of PCR, with the aid of restriction enzymes or by sequencing. A test suitable for this can be as follows: (1) extraction of DNA from tissue samples of patients, for example using paraffin embedded material, (2) treatment of the DNA with bisulfite containing reagents (i.e. as described in Clark S.J. et al., Nucleic Acids Res. 22(15):2990-7, 1994), (3) amplification of DNA by means of PCR and (4) analysis by determining the amount of sequence specific amplification products (e.g. by means of quantitative PCR, hybridization techniques such as microarray methods).

The methods of diagnosing according to the invention can concern also the use of the tumor-associated antigens identified according to the invention as prognostic markers, in order to predict metastasis, e.g. through testing the migration behavior of cells,

and therefore a worsened course of the disease, whereby among other things planning of a more aggressive therapy is made possible.

5 In a further aspect, the invention relates to a method for determining regression, course or onset of a disease characterized by expression or abnormal expression of a tumor-associated antigen identified according to the invention, which method comprises
10 monitoring a sample from a patient who has said disease or is suspected of falling ill with said disease, with respect to one or more parameters selected from the group consisting of (i) the amount of nucleic acid which codes for the tumor-associated antigen or of a
15 part thereof, (ii) the amount of the tumor-associated antigen or a part thereof, (iii) the amount of antibodies which bind to the tumor-associated antigen or to a part thereof, and (iv) the amount of cytolytic T cells or T helper cells which are specific for a
20 complex between the tumor-associated antigen or a part thereof and an MHC molecule. The method preferably comprises determining the parameter(s) in a first sample at a first point in time and in a further sample at a second point in time and in which the course of
25 the disease is determined by comparing the two samples. In particular embodiments, the disease is characterized by expression or abnormal expression of two or more different tumor-associated antigens and monitoring comprises monitoring (i) the amount of two or more
30 nucleic acids which code for said two or more different tumor-associated antigens or of parts thereof, and/or (ii) the amount of said two or more different tumor-associated antigens or of parts thereof, and/or (iii) the amount of two or more antibodies which bind to said
35 two or more different tumor-associated antigens or to parts thereof, and/or (iv) the amount of two or more cytolytic T cells or of T helper cells which are specific for complexes between said two or more different tumor-associated antigens or of parts thereof

and MHC molecules.

According to the invention, detection of a nucleic acid or of a part thereof or determining or monitoring the amount of a nucleic acid or of a part thereof may be carried out using a polynucleotide probe which hybridizes specifically to said nucleic acid or said part thereof or may be carried out by selective amplification of said nucleic acid or said part thereof. In one embodiment, the polynucleotide probe comprises a sequence of 6-50, in particular 10-30, 15-30 and 20-30, contiguous nucleotides of said nucleic acid.

In certain embodiments of the methods of diagnosing of the invention, the promoter region or part thereof of a nucleic acid coding for a tumor-associated antigen identified according to the invention and being present in the form of genomic DNA is selectively amplified following treatment with a bisulfite containing reagent. The nucleic acid is preferably isolated from a sample of a patient to be examined before treatment with the bisulfite containing reagent. The oligonucleotides used in such amplification preferably have a sequence binding to the nucleic acid treated with a bisulfite containing reagent and preferably are completely complementary thereto. Preferably, the oligonucleotides are adapted to a different degree of methylation of the nucleic acid and bring about amplification products which can be differentiated.

According to the invention, detection of a tumor-associated antigen or of a part thereof or determining or monitoring the amount of a tumor-associated antigen or of a part thereof may be carried out using an antibody binding specifically to said tumor-associated antigen or said part thereof.

In certain embodiments, the tumor-associated antigen to

be detected or the part thereof is present in a complex with an MHC molecule, in particular an HLA molecule.

5 According to the invention, detection of an antibody or determining or monitoring the amount of antibodies may be carried out using a protein or peptide binding specifically to said antibody.

10 According to the invention, detection of cytolytic T cells or of T helper cells or determining or monitoring the amount of cytolytic T cells or of T helper cells which are specific for complexes between an antigen or a part thereof and MHC molecules may be carried out using a cell presenting the complex between said
15 antigen or said part thereof and an MHC molecule.

The polynucleotide probe, the antibody, the protein or peptide or the cell, which is used for detection or determining or monitoring, is preferably labeled in a
20 detectable manner. In particular embodiments, the detectable marker is a radioactive marker or an enzymic marker. T lymphocytes may additionally be detected by detecting their proliferation, their cytokine production, and their cytotoxic activity triggered by
25 specific stimulation with the complex of MHC and tumor-associated antigen or parts thereof. T lymphocytes may also be detected via a recombinant MHC molecule or else a complex of two or more MHC molecules which are loaded with the particular immunogenic fragment of one or more
30 of the tumor-associated antigens and which can identify the specific T lymphocytes by contacting the specific T cell receptor.

35 In a further aspect, the invention relates to a method of treating, diagnosing or monitoring a disease characterized by expression or abnormal expression of a tumor-associated antigen identified according to the invention, which method comprises administering an antibody which binds to said tumor-associated antigen

or to a part thereof and which is coupled to a therapeutic or diagnostic agent. The antibody may be a monoclonal antibody. In further embodiments, the antibody is a chimeric or humanized antibody or a
5 fragment of a natural antibody.

The invention also relates to a method of treating a patient having a disease characterized by expression or abnormal expression of a tumor-associated antigen
10 identified according to the invention, which method comprises (i) removing a sample containing immunoreactive cells from said patient, (ii) contacting said sample with a host cell expressing said tumor-associated antigen or a part thereof, under conditions
15 which favor production of cytolytic T cells against said tumor-associated antigen or a part thereof, and (iii) introducing the cytolytic T cells into the patient in an amount suitable for lysing cells expressing the tumor-associated antigen or a part
20 thereof. The invention likewise relates to cloning the T cell receptor of cytolytic T cells against the tumor-associated antigen. Said receptor may be transferred to other T cells which thus receive the desired specificity and, as under (iii), may be introduced into
25 the patient.

In one embodiment, the host cell endogenously expresses an HLA molecule. In a further embodiment, the host cell recombinantly expresses an HLA molecule and/or the
30 tumor-associated antigen or the part thereof. The host cell is preferably nonproliferative. In a preferred embodiment, the host cell is an antigen-presenting cell, in particular a dendritic cell, a monocyte or a macrophage.

35

In a further aspect, the invention relates to a method of treating a patient having a disease characterized by expression or abnormal expression of a tumor-associated antigen, which method comprises (i) identifying a

2015201738 07 Apr 2015

nucleic acid which codes for a tumor-associated antigen identified according to the invention and which is expressed by cells associated with said disease, (ii) transfecting a host cell with said nucleic acid or a part thereof, (iii) culturing the transfected host cell for expression of said nucleic acid (this is not obligatory when a high rate of transfection is obtained), and (iv) introducing the host cells or an extract thereof into the patient in an amount suitable for increasing the immune response to the patient's cells associated with the disease. The method may further comprise identifying an MHC molecule presenting the tumor-associated antigen or a part thereof, with the host cell expressing the identified MHC molecule and presenting said tumor-associated antigen or a part thereof. The immune response may comprise a B cell response or a T cell response. Furthermore, a T cell response may comprise production of cytolytic T cells and/or T helper cells which are specific for the host cells presenting the tumor-associated antigen or a part thereof or specific for cells of the patient which express said tumor-associated antigen or a part thereof.

25 The invention also relates to a method of treating a disease characterized by expression or abnormal expression of a tumor-associated antigen identified according to the invention, which method comprises (i) identifying cells from the patient which express abnormal amounts of the tumor-associated antigen, (ii) isolating a sample of said cells, (iii) culturing said cells, and (iv) introducing said cells into the patient in an amount suitable for triggering an immune response to the cells.

35 Preferably, the host cells used according to the invention are nonproliferative or are rendered nonproliferative. A disease characterized by expression or abnormal expression of a tumor-associated antigen is

in particular cancer.

The present invention furthermore relates to a nucleic acid selected from the group consisting of (a) a nucleic acid which comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 97, 101, 105, 109, 113, 117, 121, 125, 129, 133, 137, 141, 145, 149, 153, 157, 161, 165, 169, 173, 175, 179, 183, 187, 191, 195, 199, 203, 207, 211, 215, 219, 223, 227, 231, 235, 239, 243, 247, 251, 255, 259, 263, 267, 269, 271, 273, 275, 277, 279, 309 of the sequence listing, a part or derivative thereof, (b) a nucleic acid which hybridizes with the nucleic acid of (a) under stringent conditions, (c) a nucleic acid which is degenerate with respect to the nucleic acid of (a) or (b), and (d) a nucleic acid which is complementary to the nucleic acid of (a), (b) or (c). The invention furthermore relates to a nucleic acid, which codes for a protein or polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 98, 102, 106, 110, 114, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 176, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220, 224, 228, 232, 236, 240, 244, 248, 252, 256, 260, 264, 268, 270, 272, 274, 276, 278, 280 to 308, 310 of the sequence listing, a part or derivative thereof.

In a further aspect, the invention relates to promoter sequences of nucleic acids of the invention. These sequences may be functionally linked to another gene, preferably in an expression vector, and thus ensure selective expression of said gene in appropriate cells.

In a further aspect, the invention relates to a recombinant nucleic acid molecule, in particular DNA or RNA molecule, which comprises a nucleic acid of the

invention.

The invention also relates to host cells which contain a nucleic acid of the invention or a recombinant nucleic acid molecule comprising a nucleic acid of the invention.

The host cell may also comprise a nucleic acid coding for a HLA molecule. In one embodiment, the host cell endogenously expresses the HLA molecule. In a further embodiment, the host cell recombinantly expresses the HLA molecule and/or the nucleic acid of the invention or a part thereof. Preferably, the host cell is nonproliferative. In a preferred embodiment, the host cell is an antigen-presenting cell, in particular a dendritic cell, a monocyte or a macrophage.

In a further embodiment, the invention relates to oligonucleotides which hybridize with a nucleic acid identified according to the invention and which may be used as genetic probes or as "antisense" molecules. Nucleic acid molecules in the form of oligonucleotide primers or competent samples, which hybridize with a nucleic acid identified according to the invention or parts thereof, may be used for finding nucleic acids which are homologous to said nucleic acid identified according to the invention. PCR amplification, Southern and Northern hybridization may be employed for finding homologous nucleic acids. Hybridization may be carried out under low stringency, more preferably under medium stringency and most preferably under high stringency conditions. The term "stringent conditions" according to the invention refers to conditions which allow specific hybridization between polynucleotides.

In a further aspect, the invention relates to a protein or polypeptide which is encoded by a nucleic acid selected from the group consisting of (a) a nucleic acid which comprises a nucleic acid sequence selected

2015201738 07 Apr 2015

from the group consisting of SEQ ID NOs: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 97, 101, 105, 109, 113, 117, 121, 125, 129, 133, 137, 141, 145, 149, 153, 157, 161, 165, 169, 173, 175, 179, 183, 187, 191, 195, 199, 203, 207, 211, 215, 219, 223, 227, 231, 235, 239, 243, 247, 251, 255, 259, 263, 267, 269, 271, 273, 275, 277, 279, 309 of the sequence listing, a part or derivative thereof, (b) a nucleic acid which hybridizes with the nucleic acid of (a) under stringent conditions, (c) a nucleic acid which is degenerate with respect to the nucleic acid of (a) or (b), and (d) a nucleic acid which is complementary to the nucleic acid of (a), (b) or (c). In a preferred embodiment, the invention relates to a protein or polypeptide which comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 98, 102, 106, 110, 114, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 176, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220, 224, 228, 232, 236, 240, 244, 248, 252, 256, 260, 264, 268, 270, 272, 274, 276, 278, 280 to 308, 310 of the sequence listing, a part or derivative thereof.

In a further aspect, the invention relates to an immunogenic fragment of a tumor-associated antigen identified according to the invention. Said fragment preferably binds to a human HLA receptor or to a human antibody. A fragment of the invention preferably comprises a sequence of at least 6, in particular at least 8, at least 10, at least 12, at least 15, at least 20, at least 30 or at least 50, amino acids.

In a further aspect, the invention relates to an agent which binds to a tumor-associated antigen identified according to the invention or to a part thereof. In a preferred embodiment, the agent is an antibody. In further embodiments, the antibody is a chimeric, a

humanized antibody or an antibody produced by combinatory techniques or is a fragment of an antibody. Furthermore, the invention relates to an antibody which binds selectively to a complex of (i) a tumor-associated antigen identified according to the invention or a part thereof and (ii) an MHC molecule to which said tumor-associated antigen identified according to the invention or said part thereof binds, with said antibody not binding to (i) or (ii) alone. An antibody of the invention may be a monoclonal antibody. In further embodiments, the antibody is a chimeric or humanized antibody or a fragment of a natural antibody.

The invention furthermore relates to a conjugate between an agent of the invention which binds to a tumor-associated antigen identified according to the invention or to a part thereof or an antibody of the invention and a therapeutic or diagnostic agent. In one embodiment, the therapeutic or diagnostic agent is a toxin.

In a further aspect, the invention relates to a kit for detecting expression or abnormal expression of a tumor-associated antigen identified according to the invention, which kit comprises agents for detection (i) of the nucleic acid which codes for the tumor-associated antigen or of a part thereof, (ii) of the tumor-associated antigen or of a part thereof, (iii) of antibodies which bind to the tumor-associated antigen or to a part thereof, and/or (iv) of T cells which are specific for a complex between the tumor-associated antigen or a part thereof and an MHC molecule. In one embodiment, the agents for detection of the nucleic acid or the part thereof are nucleic acid molecules for selective amplification of said nucleic acid, which comprise, in particular a sequence of 6-50, in particular 10-30, 15-30 and 20-30, contiguous nucleotides of said nucleic acid.

Detailed description of the invention

According to the invention, genes are described which are expressed in tumor cells selectively or aberrantly and which are tumor-associated antigens.

According to the invention, these genes or their derivatives are preferred target structures for therapeutic approaches. Conceptionally, said therapeutic approaches may aim at inhibiting the activity of the selectively expressed tumor-associated genetic product. This is useful, if said aberrant selective expression is functionally important in tumor pathogenecity and if its ligation is accompanied by selective damage of the corresponding cells. Other therapeutic concepts contemplate tumor-associated antigens as labels which recruit effector mechanisms having cell-damaging potential selectively to tumor cells. Here, the function of the target molecule itself and its role in tumor development are totally irrelevant.

"Derivative" of a nucleic acid means according to the invention that single or multiple nucleotide substitutions, deletions and/or additions are present in said nucleic acid. Furthermore, the term "derivative" also comprises chemical derivatization of a nucleic acid on a base, on a sugar or on a phosphate of a nucleotide. The term "derivative" also comprises nucleic acids which contain nucleotides and nucleotide analogs not occurring naturally.

According to the invention, a nucleic acid is preferably deoxyribonucleic acid (DNA) or ribonucleic acid (RNA). Nucleic acids comprise according to the invention genomic DNA, cDNA, mRNA, recombinantly produced and chemically synthesized molecules. According to the invention, a nucleic acid may be present as a single-stranded or double-stranded and

2015201738 07 Apr 2015

linear or covalently circularly closed molecule.

The nucleic acids described according to the invention have preferably been isolated. The term "isolated nucleic acid" means according to the invention that the
5 nucleic acid was (i) amplified *in vitro*, for example by polymerase chain reaction (PCR), (ii) recombinantly produced by cloning, (iii) purified, for example by cleavage and gel-electrophoretic fractionation, or (iv)
10 synthesized, for example by chemical synthesis. An isolated nucleic acid is a nucleic acid which is available for manipulation by recombinant DNA techniques.

15 A nucleic acid is "complementary" to another nucleic acid if the two sequences are capable of hybridizing and forming a stable duplex with one another, with hybridization preferably being carried out under conditions which allow specific hybridization between
20 polynucleotides (stringent conditions). Stringent conditions are described, for example, in Molecular Cloning: A Laboratory Manual, J. Sambrook et al., Editors, 2nd Edition, Cold Spring Harbor Laboratory press, Cold Spring Harbor, New York, 1989 or Current
25 Protocols in Molecular Biology, F.M. Ausubel et al., Editors, John Wiley & Sons, Inc., New York and refer, for example, to hybridization at 65°C in hybridization buffer (3.5 x SSC, 0.02% Ficoll, 0.02%
polyvinylpyrrolidone, 0.02% bovine serum albumin,
30 2.5 mM NaH₂PO₄ (pH 7), 0.5% SDS, 2 mM EDTA). SSC is 0.15 M sodium chloride/0.15 M sodium citrate, pH 7. After hybridization, the membrane to which the DNA has been transferred is washed, for example, in 2 x SSC at room temperature and then in 0.1-0.5 x SSC/0.1 x SDS at
35 temperatures of up to 68°C.

According to the invention, complementary nucleic acids have at least 40%, in particular at least 50%, at least 60%, at least 70%, at least 80%, at least 90% and

preferably at least 95%, at least 98% or at least 99%, identical nucleotides.

5 Nucleic acids coding for tumor-associated antigens may, according to the invention, be present alone or in combination with other nucleic acids, in particular heterologous nucleic acids. In preferred embodiments, a nucleic acid is functionally linked to expression control sequences or regulatory sequences which may be
10 homologous or heterologous with respect to said nucleic acid. A coding sequence and a regulatory sequence are "functionally" linked to one another, if they are covalently linked to one another in such a way that expression or transcription of said coding sequence is
15 under the control or under the influence of said regulatory sequence. If the coding sequence is to be translated into a functional protein, then, with a regulatory sequence functionally linked to said coding sequence, induction of said regulatory sequence results
20 in transcription of said coding sequence, without causing a frame shift in the coding sequence or said coding sequence not being capable of being translated into the desired protein or peptide.

25 The term "expression control sequence" or "regulatory sequence" comprises according to the invention promoters, enhancers and other control elements which regulate expression of a gene. In particular embodiments of the invention, the expression control
30 sequences can be regulated. The exact structure of regulatory sequences may vary as a function of the species or cell type, but generally comprises 5'untranscribed and 5'untranslated sequences which are involved in initiation of transcription and
35 translation, respectively, such as TATA box, capping sequence, CAAT sequence, and the like. More specifically, 5'untranscribed regulatory sequences comprise a promoter region which includes a promoter sequence for transcriptional control of the

functionally linked gene. Regulatory sequences may also comprise enhancer sequences or upstream activator sequences.

5 Thus, on the one hand, the tumor-associated antigens illustrated herein may be combined with any expression control sequences and promoters. On the other hand, however, the promoters of the tumor-associated genetic products illustrated herein may, according to the
10 invention, be combined with any other genes. This allows the selective activity of these promoters to be utilized.

According to the invention, a nucleic acid may
15 furthermore be present in combination with another nucleic acid which codes for a polypeptide controlling secretion of the protein or polypeptide encoded by said nucleic acid from a host cell. According to the invention, a nucleic acid may also be present in
20 combination with another nucleic acid which codes for a polypeptide causing the encoded protein or polypeptide to be anchored on the cell membrane of the host cell or compartmentalized into particular organelles of said cell.

25 In a preferred embodiment, a recombinant DNA molecule is according to the invention a vector, where appropriate with a promoter, which controls expression of a nucleic acid, for example a nucleic acid coding
30 for a tumor-associated antigen of the invention. The term "vector" is used here in its most general meaning and comprises any intermediary vehicle for a nucleic acid which enables said nucleic acid, for example, to be introduced into prokaryotic and/or eukaryotic cells
35 and, where appropriate, to be integrated into a genome. Vectors of this kind are preferably replicated and/or expressed in the cells. An intermediary vehicle may be adapted, for example, to the use in electroporation, in bombardment with microprojectiles, in liposomal

administration, in the transfer with the aid of agrobacteria or in insertion via DNA or RNA viruses. Vectors comprise plasmids, phagemids, bacteriophages or viral genomes.

5

The nucleic acids coding for a tumor-associated antigen identified according to the invention may be used for transfection of host cells. Nucleic acids here mean both recombinant DNA and RNA. Recombinant RNA may be prepared by in-vitro transcription of a DNA template. Furthermore, it may be modified by stabilizing sequences, capping and polyadenylation prior to application. According to the invention, the term "host cell" relates to any cell which can be transformed or transfected with an exogenous nucleic acid. The term "host cells" comprises according to the invention prokaryotic (e.g. *E. coli*) or eukaryotic cells (e.g. dendritic cells, B cells, CHO cells, COS cells, K562 cells, yeast cells and insect cells). Particular preference is given to mammalian cells such as cells from humans, mice, hamsters, pigs, goats, primates. The cells may be derived from a multiplicity of tissue types and comprise primary cells and cell lines. Specific examples comprise keratinocytes, peripheral blood leukocytes, stem cells of the bone marrow and embryonic stem cells. In further embodiments, the host cell is an antigen-presenting cell, in particular a dendritic cell, monocyte or a macrophage. A nucleic acid may be present in the host cell in the form of a single copy or of two or more copies and, in one embodiment, is expressed in the host cell.

According to the invention, the term "expression" is used in its most general meaning and comprises the production of RNA or of RNA and protein. It also comprises partial expression of nucleic acids. Furthermore, expression may be carried out transiently or stably. Preferred expression systems in mammalian cells comprise pcDNA3.1 and pRc/CMV (Invitrogen,

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Carlsbad, CA), which contain a selective marker such as a gene imparting resistance to G418 (and thus enabling stably transfected cell lines to be selected) and the enhancer-promoter sequences of cytomegalovirus (CMV).

5

In those cases of the invention in which an HLA molecule presents a tumor-associated antigen or a part thereof; an expression vector may also comprise a nucleic acid sequence coding for said HLA molecule. The
10 nucleic acid sequence coding for the HLA molecule may be present on the same expression vector as the nucleic acid coding for the tumor-associated antigen or the part thereof, or both nucleic acids may be present on different expression vectors. In the latter case, the
15 two expression vectors may be cotransfected into a cell. If a host cell expresses neither the tumor-associated antigen or the part thereof nor the HLA molecule, both nucleic acids coding therefor are transfected into the cell either on the same expression
20 vector or on different expression vectors. If the cell already expresses the HLA molecule, only the nucleic acid sequence coding for the tumor-associated antigen or the part thereof can be transfected into the cell.

25 The invention also comprises kits for amplification of a nucleic acid coding for a tumor-associated antigen. Such kits comprise, for example, a pair of amplification primers which hybridize to the nucleic acid coding for the tumor-associated antigen. The
30 primers preferably comprise a sequence of 6-50, in particular 10-30, 15-30 and 20-30 contiguous nucleotides of the nucleic acid and are nonoverlapping, in order to avoid the formation of primer dimers. One of the primers will hybridize to one strand of the
35 nucleic acid coding for the tumor-associated antigen, and the other primer will hybridize to the complementary strand in an arrangement which allows amplification of the nucleic acid coding for the tumor-associated antigen.

2015201738 07 Apr 2015

2015201738 07 Apr 2015

"Antisense" molecules or "antisense" nucleic acids may be used for regulating, in particular reducing, expression of a nucleic acid. The term "antisense molecule" or "antisense nucleic acid" refers according to the invention to an oligonucleotide which is an oligoribonucleotide, oligodeoxyribonucleotide, modified oligoribonucleotide or modified oligodeoxyribonucleotide and which hybridizes under physiological conditions to DNA comprising a particular gene or to mRNA of said gene, thereby inhibiting transcription of said gene and/or translation of said mRNA. According to the invention, the "antisense molecule" also comprises a construct which contains a nucleic acid or a part thereof in reverse orientation with respect to its natural promoter. An antisense transcript of a nucleic acid or of a part thereof may form a duplex with the naturally occurring mRNA specifying the enzyme and thus prevent accumulation of or translation of the mRNA into the active enzyme. Another possibility is the use of ribozymes for inactivating a nucleic acid. Antisense oligonucleotides preferred according to the invention have a sequence of 6-50, in particular 10-30, 15-30 and 20-30, contiguous nucleotides of the target nucleic acid and preferably are fully complementary to the target nucleic acid or to a part thereof.

In preferred embodiments, the antisense oligonucleotide hybridizes with an N-terminal or 5' upstream site such as a translation initiation site, transcription initiation site or promoter site. In further embodiments, the antisense oligonucleotide hybridizes with a 3'untranslated region or mRNA splicing site.

In one embodiment, an oligonucleotide of the invention consists of ribonucleotides, deoxyribonucleotides or a combination thereof, with the 5' end of one nucleotide and the 3' end of another nucleotide being linked to

one another by a phosphodiester bond. These oligonucleotides may be synthesized in the conventional manner or produced recombinantly.

5 In preferred embodiments, an oligonucleotide of the invention is a "modified" oligonucleotide. Here, the oligonucleotide may be modified in very different ways, without impairing its ability to bind its target, in order to increase, for example, its stability or
10 therapeutic efficacy. According to the invention, the term "modified oligonucleotide" means an oligonucleotide in which (i) at least two of its nucleotides are linked to one another by a synthetic internucleoside bond (i.e. an internucleoside bond
15 which is not a phosphodiester bond) and/or (ii) a chemical group which is usually not found in nucleic acids is covalently linked to the oligonucleotide. Preferred synthetic internucleoside bonds are phosphorothioates, alkyl phosphonates,
20 phosphorodithioates, phosphate esters, alkyl phosphonothioates, phosphoramidates, carbamates, carbonates, phosphate triesters, acetamides, carboxymethyl esters and peptides.

25 The term "modified oligonucleotide" also comprises oligonucleotides having a covalently modified base and/or sugar. "Modified oligonucleotides" comprise, for example, oligonucleotides with sugar residues which are covalently bound to low molecular weight organic groups
30 other than a hydroxyl group at the 3' position and a phosphate group at the 5' position. Modified oligonucleotides may comprise, for example, a 2'-O-alkylated ribose residue or another sugar instead of ribose, such as arabinose.

35

Preferably, the proteins and polypeptides described according to the invention have been isolated. The terms "isolated protein" or "isolated polypeptide" mean that the protein or polypeptide has been separated from

its natural environment. An isolated protein or polypeptide may be in an essentially purified state. The term "essentially purified" means that the protein or polypeptide is essentially free of other substances with which it is associated in nature or *in vivo*.

Such proteins and polypeptides may be used, for example, in producing antibodies and in an immunological or diagnostic assay or as therapeutics. Proteins and polypeptides described according to the invention may be isolated from biological samples such as tissue or cell homogenates and may also be expressed recombinantly in a multiplicity of pro- or eukaryotic expression systems.

For the purposes of the present invention, "derivatives" of a protein or polypeptide or of an amino acid sequence comprise amino acid insertion variants, amino acid deletion variants and/or amino acid substitution variants.

Amino acid insertion variants comprise amino- and/or carboxy-terminal fusions and also insertions of single or two or more amino acids in a particular amino acid sequence. In the case of amino acid sequence variants having an insertion, one or more amino acid residues are inserted into a particular site in an amino acid sequence, although random insertion with appropriate screening of the resulting product is also possible. Amino acid deletion variants are characterized by the removal of one or more amino acids from the sequence. Amino acid substitution variants are characterized by at least one residue in the sequence being removed and another residue being inserted in its place. Preference is given to the modifications being in positions in the amino acid sequence which are not conserved between homologous proteins or polypeptides. Preference is given to replacing amino acids with other ones having similar properties such as hydrophobicity,

hydrophilicity, electronegativity, volume of the side chain and the like (conservative substitution). Conservative substitutions, for example, relate to the exchange of one amino acid with another amino acid listed below in the same group as the amino acid to be substituted:

1. small aliphatic, nonpolar or slightly polar residues: Ala, Ser, Thr (Pro, Gly)
2. negatively charged residues and their amides: Asn, Asp, Glu, Gln
3. positively charged residues: His, Arg, Lys
4. large aliphatic, nonpolar residues: Met, Leu, Ile, Val (Cys)
5. large aromatic residues: Phe, Tyr, Trp.

Owing to their particular part in protein architecture, three residues are shown in brackets. Gly is the only residue without a side chain and thus imparts flexibility to the chain. Pro has an unusual geometry which greatly restricts the chain. Cys can form a disulfide bridge.

The amino acid variants described above may be readily prepared with the aid of known peptide synthesis techniques such as, for example, by solid phase synthesis (Merrifield, 1964) and similar methods or by recombinant DNA manipulation. Techniques for introducing substitution mutations at predetermined sites into DNA which has a known or partially known sequence are well known and comprise M13 mutagenesis, for example. The manipulation of DNA sequences for preparing proteins having substitutions, insertions or deletions, is described in detail in Sambrook et al. (1989), for example.

According to the invention, "derivatives" of proteins or polypeptides also comprise single or multiple substitutions, deletions and/or additions of any

molecules associated with the enzyme, such as carbohydrates, lipids and/or proteins or polypeptides. The term "derivative" also extends to all functional chemical equivalents of said proteins or polypeptides.

5

According to the invention, a part or fragment of a tumor-associated antigen has a functional property of the polypeptide from which it has been derived. Such functional properties comprise the interaction with antibodies, the interaction with other polypeptides or proteins, the selective binding of nucleic acids and an enzymatic activity. A particular property is the ability to form a complex with HLA and, where appropriate, generate an immune response. This immune response may be based on stimulating cytotoxic or T helper cells. A part or fragment of a tumor-associated antigen of the invention preferably comprises a sequence of at least 6, in particular at least 8, at least 10, at least 12, at least 15, at least 20, at least 30 or at least 50, consecutive amino acids of the tumor-associated antigen. A part or fragment of a tumor-associated antigen is preferably a part of the tumor-associated antigen which corresponds to the non-membrane portion, in particular the extracellular portion of the antigen or is comprised thereof.

A part or a fragment of a nucleic acid coding for a tumor-associated antigen relates according to the invention to the part of the nucleic acid, which codes at least for the tumor-associated antigen and/or for a part or a fragment of said tumor-associated antigen, as defined above. Preferably, a part or fragment of a nucleic acid coding for a tumor-associated antigen is that part which corresponds to the open reading frame, in particular as indicated in the sequence listing.

The isolation and identification of genes coding for tumor-associated antigens also make possible the

2015201738 07 Apr 2015

diagnosis of a disease characterized by expression of one or more tumor-associated antigens. These methods comprise determining one or more nucleic acids which code for a tumor-associated antigen and/or determining the encoded tumor-associated antigens and/or peptides derived therefrom. The nucleic acids may be determined in the conventional manner, including by polymerase chain reaction or hybridization with a labeled probe. Tumor-associated antigens or peptides derived therefrom may be determined by screening patient antisera with respect to recognizing the antigen and/or the peptides. They may also be determined by screening T cells of the patient for specificities for the corresponding tumor-associated antigen.

The present invention also enables proteins binding to tumor-associated antigens described herein to be isolated, including antibodies and cellular binding partners of said tumor-associated antigens.

According to the invention, particular embodiments ought to involve providing "dominant negative" polypeptides derived from tumor-associated antigens. A dominant negative polypeptide is an inactive protein variant which, by way of interacting with the cellular machinery, displaces an active protein from its interaction with the cellular machinery or which competes with the active protein, thereby reducing the effect of said active protein. For example, a dominant negative receptor which binds to a ligand but does not generate any signal as response to binding to the ligand can reduce the biological effect of said ligand. Similarly, a dominant negative catalytically inactive kinase which usually interacts with target proteins but does not phosphorylate said target proteins may reduce phosphorylation of said target proteins as response to a cellular signal. Similarly, a dominant negative transcription factor which binds to a promoter site in the control region of a gene but does not increase

transcription of said gene may reduce the effect of a normal transcription factor by occupying promoter binding sites, without increasing transcription.

- 5 The result of expression of a dominant negative polypeptide in a cell is a reduction in the function of active proteins. The skilled worker may prepare dominant negative variants of a protein, for example, by conventional mutagenesis methods and by evaluating
10 the dominant negative effect of the variant polypeptide.

- The invention also comprises substances such as polypeptides which bind to tumor-associated antigens.
15 Such binding substances may be used, for example, in screening assays for detecting tumor-associated antigens and complexes of tumor-associated antigens with their binding partners and in a purification of said tumor-associated antigens and of complexes thereof
20 with their binding partners. Such substances may also be used for inhibiting the activity of tumor-associated antigens, for example by binding to such antigens.

- The invention therefore comprises binding substances
25 such as, for example, antibodies or antibody fragments, which are capable of selectively binding to tumor-associated antigens. Antibodies comprise polyclonal and monoclonal antibodies which are produced in the conventional manner.

- 30 It is known that only a small part of an antibody molecule, the paratope, is involved in binding of the antibody to its epitope (cf. Clark, W.R. (1986), *The Experimental Foundations of Modern Immunology*, Wiley &
35 Sons, Inc., New York; Roitt, I. (1991), *Essential Immunology*, 7th Edition, Blackwell Scientific Publications, Oxford). The pFc' and Fc regions are, for example, effectors of the complement cascade but are not involved in antigen binding. An antibody from which

the pFc' region has been enzymatically removed or which has been produced without the pFc' region, referred to as F(ab')₂ fragment, carries both antigen binding sites of a complete antibody. Similarly, an antibody from which the Fc region has been enzymatically removed or which has been produced without said Fc region, referred to Fab fragment, carries one antigen binding site of an intact antibody molecule. Furthermore, Fab fragments consist of a covalently bound light chain of an antibody and part of the heavy chain of said antibody, referred to as Fd. The Fd fragments are the main determinants of antibody specificity (a single Fd fragment can be associated with up to ten different light chains, without altering the specificity of the antibody) and Fd fragments, when isolated, retain the ability to bind to an epitope.

Located within the antigen-binding part of an antibody are complementary-determining regions (CDRs) which interact directly with the antigen epitope and framework regions (FRs) which maintain the tertiary structure of the paratope. Both the Fd fragment of the heavy chain and the light chain of IgG immunoglobulins contain four framework regions (FR1 to FR4) which are separated in each case by three complementary-determining regions (CDR1 to CDR3). The CDRs and, in particular, the CDR3 regions and, still more particularly, the CDR3 region of the heavy chain are responsible to a large extent for antibody specificity.

Non-CDR regions of a mammalian antibody are known to be able to be replaced by similar regions of antibodies with the same or a different specificity, with the specificity for the epitope of the original antibody being retained. This made possible the development of "humanized" antibodies in which nonhuman CDRs are covalently linked to human FR and/or Fc/pFc' regions to produce a functional antibody.

2015201738 07 Apr 2015

WO 92/04381 for example, describes production and use of humanized murine RSV antibodies in which at least part of the murine FR regions have been replaced with FR regions of a human origin. Antibodies of this kind, including fragments of intact antibodies with antigen-binding capability, are often referred to as "chimeric" antibodies.

The invention also provides $F(ab')_2$, Fab, Fv, and Fd fragments of antibodies, chimeric antibodies, in which the Fc and/or FR and/or CDR1 and/or CDR2 and/or light chain-CDR3 regions have been replaced with homologous human or nonhuman sequences, chimeric $F(ab')_2$ -fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain-CDR3 regions have been replaced with homologous human or nonhuman sequences, chimeric Fab-fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain-CDR3 regions have been replaced with homologous human or nonhuman sequences, and chimeric Fd-fragment antibodies in which the FR and/or CDR1 and/or CDR2 regions have been replaced with homologous human or nonhuman sequences. The invention also comprises "single-chain" antibodies.

Preferably, an antibody used according to the invention is directed against one of the sequences according to SEQ ID NOs: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 98, 102, 106, 110, 114, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 176, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220, 224, 228, 232, 236, 240, 244, 248, 252, 256, 260, 264, 268, 270, 272, 274, 276, 278, 280 to 308, 310 of the sequence listing, a part or derivative thereof, in particular a sequence according to SEQ ID Nos: 281 to 308 of the sequence listing and/or may be obtained by immunization using these peptides.

The invention also comprises polypeptides which bind

specifically to tumor-associated antigens. Polypeptide binding substances of this kind may be provided, for example, by degenerate peptide libraries which may be prepared simply in solution in an immobilized form or
5 as phage-display libraries. It is likewise possible to prepare combinatorial libraries of peptides with one or more amino acids. Libraries of peptoids and nonpeptidic synthetic residues may also be prepared.

10 Phage display may be particularly effective in identifying binding peptides of the invention. In this connection, for example, a phage library is prepared (using, for example, the M13, fd or lambda phages) which presents inserts of from 4 to about 80 amino acid
15 residues in length. Phages are then selected which carry inserts which bind to the tumor-associated antigen. This process may be repeated via two or more cycles of a reselection of phages binding to the tumor-associated antigen. Repeated rounds result in a
20 concentration of phages carrying particular sequences. An analysis of DNA sequences may be carried out in order to identify the sequences of the expressed polypeptides. The smallest linear portion of the sequence binding to the tumor-associated antigen may be
25 determined. The "two-hybrid system" of yeast may also be used for identifying polypeptides which bind to a tumor-associated antigen. Tumor-associated antigens described according to the invention or fragments thereof may be used for screening peptide libraries,
30 including phage-display libraries, in order to identify and select peptide binding partners of the tumor-associated antigens. Such molecules may be used, for example, for screening assays, purification protocols, for interference with the function of the tumor-associated antigen and for other purposes known to the
35 skilled worker.

The antibodies described above and other binding molecules may be used, for example, for identifying

tissue which expresses a tumor-associated antigen. Antibodies may also be coupled to specific diagnostic substances for displaying cells and tissues expressing tumor-associated antigens. They may also be coupled to therapeutically useful substances. Diagnostic substances comprise, in a nonlimiting manner, barium sulfate, iocetamic acid, iopanoic acid, calcium ipodate, sodium diatrizoate, meglumine diatrizoate, metrizamide, sodium tyropanoate and radio diagnostic, including positron emitters such as fluorine-18 and carbon-11, gamma emitters such as iodine-123, technetium-99m, iodine-131 and indium-111, nuclides for nuclear magnetic resonance, such as fluorine and gadolinium. According to the invention, the term "therapeutically useful substance" means any therapeutic molecule which, as desired, is selectively guided to a cell which expresses one or more tumor-associated antigens, including anticancer agents, radioactive iodine-labeled compounds, toxins, cytostatic or cytolytic drugs, etc. Anticancer agents comprise, for example, aminoglutethimide, azathioprine, bleomycin sulfate, busulfan, carmustine, chlorambucil, cisplatin, cyclophosphamide, cyclosporine, cytarabidine, dacarbazine, dactinomycin, daunorubin, doxorubicin, taxol, etoposide, fluorouracil, interferon- α , lomustine, mercaptopurine, methotrexate, mitotane, procarbazine HCl, thioguanine, vinblastine sulfate and vincristine sulfate. Other anticancer agents are described, for example, in Goodman and Gilman, "The Pharmacological Basis of Therapeutics", 8th Edition, 1990, McGraw-Hill, Inc., in particular Chapter 52 (Antineoplastic Agents (Paul Calabresi and Bruce A. Chabner). Toxins may be proteins such as pokeweed antiviral protein, cholera toxin, pertussis toxin, ricin, gelonin, abrin, diphtheria exotoxin or *Pseudomonas* exotoxin. Toxin residues may also be high energy-emitting radionuclides such as cobalt-60.

The term "patient" means according to the invention a

human being, a nonhuman primate or another animal, in particular a mammal such as a cow, horse, pig, sheep, goat, dog, cat or a rodent such as a mouse and rat. In a particularly preferred embodiment, the patient is a human being.

According to the invention, the term "disease" refers to any pathological state in which tumor-associated antigens are expressed or abnormally expressed. "Abnormal expression" means according to the invention that expression is altered, preferably increased, compared to the state in a healthy individual. An increase in expression refers to an increase by at least 10%, in particular at least 20%, at least 50% or at least 100%. In one embodiment, the tumor-associated antigen is expressed only in tissue of a diseased individual, while expression in a healthy individual is repressed. One example of such a disease is cancer, in particular seminomas, melanomas, teratomas, gliomas, colon cancer, rectal cancer, kidney cancer, breast cancer, prostate cancer, cancer of the uterus, ovarian cancer, endometrial cancer, cancer of the esophagus, blood cancer, liver cancer, pancreatic cancer, skin cancer, brain cancer and lung cancer, lymphomas, and neuroblastomas. Examples for this are lung tumor, breast tumor, prostate tumor, colon tumor, renal cell carcinoma, cervical carcinoma, colon carcinoma and mamma carcinoma or metastases of the above cancer types or tumors.

According to the invention, a biological sample may be a tissue sample and/or a cellular sample and may be obtained in the conventional manner such as by tissue biopsy, including punch biopsy, and by taking blood, bronchial aspirate, urine, feces or other body fluids, for use in the various methods described herein.

According to the invention, the term "immunoreactive cell" means a cell which can mature into an immune cell

2015201738 07 Apr 2015

(such as B cell, T helper cell, or cytolytic T cell) with suitable stimulation. Immunoreactive cells comprise CD34⁺ hematopoietic stem cells, immature and mature T cells and immature and mature B cells. If production of cytolytic or T helper cells recognizing a tumor-associated antigen is desired, the immunoreactive cell is contacted with a cell expressing a tumor-associated antigen under conditions which favor production, differentiation and/or selection of cytolytic T cells and of T helper cells. The differentiation of T cell precursors into a cytolytic T cell, when exposed to an antigen, is similar to clonal selection of the immune system.

Some therapeutic methods are based on a reaction of the immune system of a patient, which results in a lysis of antigen-presenting cells such as cancer cells which present one or more tumor-associated antigens. In this connection, for example autologous cytotoxic T lymphocytes specific for a complex of a tumor-associated antigen and an MHC molecule are administered to a patient having a cellular abnormality. The production of such cytotoxic T lymphocytes *in vitro* is known. An example of a method of differentiating T cells can be found in WO-A-96/33265. Generally, a sample containing cells such as blood cells is taken from the patient and the cells are contacted with a cell which presents the complex and which can cause propagation of cytotoxic T lymphocytes (e.g. dendritic cells). The target cell may be a transfected cell such as a COS cell. These transfected cells present the desired complex on their surface and, when contacted with cytotoxic T lymphocytes, stimulate propagation of the latter. The clonally expanded autologous cytotoxic T lymphocytes are then administered to the patient.

In another method of selecting antigen-specific cytotoxic T lymphocytes, fluorogenic tetramers of MHC class I molecule/peptide complexes are used for

detecting specific clones of cytotoxic T lymphocytes (Altman et al., *Science* 274:94-96, 1996; Dunbar et al., *Curr. Biol.* 8:413-416, 1998). Soluble MHC class I molecules are folded *in vitro* in the presence of β_2 microglobulin and a peptide antigen binding to said class I molecule. The MHC/peptide complexes are purified and then labeled with biotin. Tetramers are formed by mixing the biotinylated peptide-MHC complexes with labeled avidin (e.g. phycoerythrin) in a molar ratio of 4:1. Tetramers are then contacted with cytotoxic T lymphocytes such as peripheral blood or lymph nodes. The tetramers bind to cytotoxic T lymphocytes which recognize the peptide antigen/MHC class I complex. Cells which are bound to the tetramers may be sorted by fluorescence-controlled cell sorting to isolate reactive cytotoxic T lymphocytes. The isolated cytotoxic T lymphocytes may then be propagated *in vitro*.

20 In a therapeutic method referred to as adoptive transfer (Greenberg, *J. Immunol.* 136(5):1917, 1986; Riddel et al., *Science* 257:238, 1992; Lynch et al., *Eur. J. Immunol.* 21:1403-1410, 1991; Kast et al., *Cell* 59:603-614, 1989), cells presenting the desired complex (e.g. dendritic cells) are combined with cytotoxic T lymphocytes of the patient to be treated, resulting in a propagation of specific cytotoxic T lymphocytes. The propagated cytotoxic T lymphocytes are then administered to a patient having a cellular anomaly characterized by particular abnormal cells presenting the specific complex. The cytotoxic T lymphocytes then lyse the abnormal cells, thereby achieving a desired therapeutic effect.

35 Often, of the T cell repertoire of a patient, only T cells with low affinity for a specific complex of this kind can be propagated, since those with high affinity have been extinguished due to development of tolerance. An alternative here may be a transfer of the T cell

receptor itself. For this too, cells presenting the desired complex (e.g. dendritic cells) are combined with cytotoxic T lymphocytes of healthy individuals. This results in propagation of specific cytotoxic T lymphocytes with high affinity if the donor had no previous contact with the specific complex. The high affinity T cell receptor of these propagated specific T lymphocytes is cloned and can be transduced via gene transfer, for example using retroviral vectors, into T cells of other patients, as desired. Adoptive transfer is then carried out using these genetically altered T lymphocytes (Stanislowski et al., Nat Immunol. 2:962-70, 2001; Kessels et al., Nat Immunol. 2:957-61, 2001).

The therapeutic aspects above start out from the fact that at least some of the abnormal cells of the patient present a complex of a tumor-associated antigen and an HLA molecule. Such cells may be identified in a manner known per se. As soon as cells presenting the complex have been identified, they may be combined with a sample from the patient, which contains cytotoxic T lymphocytes. If the cytotoxic T lymphocytes lyse the cells presenting the complex, it can be assumed that a tumor-associated antigen is presented.

Adoptive transfer is not the only form of therapy which can be applied according to the invention. Cytotoxic T lymphocytes may also be generated *in vivo* in a manner known per se. One method uses nonproliferative cells expressing the complex. The cells used here will be those which usually express the complex, such as irradiated tumor cells or cells transfected with one or both genes necessary for presentation of the complex (i.e. the antigenic peptide and the presenting HLA molecule). Various cell types may be used. Furthermore, it is possible to use vectors which carry one or both of the genes of interest. Particular preference is given to viral or bacterial vectors. For example, nucleic acids coding for a tumor-associated antigen or

for a part thereof may be functionally linked to promoter and enhancer sequences which control expression of said tumor-associated antigen or a fragment thereof in particular tissues or cell types.

5 The nucleic acid may be incorporated into an expression vector. Expression vectors may be nonmodified extrachromosomal nucleic acids, plasmids or viral genomes into which exogenous nucleic acids may be inserted. Nucleic acids coding for a tumor-associated
10 antigen may also be inserted into a retroviral genome, thereby enabling the nucleic acid to be integrated into the genome of the target tissue or target cell. In these systems, a microorganism such as vaccinia virus, pox virus, Herpes simplex virus, retrovirus or
15 adenovirus carries the gene of interest and de facto "infects" host cells. Another preferred form is the introduction of the tumor-associated antigen in the form of recombinant RNA which may be introduced into cells by liposomal transfer or by electroporation, for
20 example. The resulting cells present the complex of interest and are recognized by autologous cytotoxic T lymphocytes which then propagate.

A similar effect can be achieved by combining the
25 tumor-associated antigen or a fragment thereof with an adjuvant in order to make incorporation into antigen-presenting cells *in vivo* possible. The tumor-associated antigen or a fragment thereof may be represented as protein, as DNA (e.g. within a vector) or as RNA. The
30 tumor-associated antigen is processed to produce a peptide partner for the HLA molecule, while a fragment thereof may be presented without the need for further processing. The latter is the case in particular, if these can bind to HLA molecules. Preference is given to
35 administration forms in which the complete antigen is processed *in vivo* by a dendritic cell, since this may also produce T helper cell responses which are needed for an effective immune response (Ossendorp et al., *Immunol Lett.* 74:75-9, 2000; Ossendorp et al., *J. Exp.*

Med. 187:693-702, 1998). In general, it is possible to administer an effective amount of the tumor-associated antigen to a patient by intradermal injection, for example. However, injection may also be carried out intranodally into a lymph node (Maloy et al., *Proc Natl Acad Sci USA* 98:3299-303, 2001). It may also be carried out in combination with reagents which facilitate uptake into dendritic cells. Preferred tumor-associated antigens comprise those which react with allogenic cancer antisera or with T cells of many cancer patients. Of particular interest, however, are those against which no spontaneous immune responses pre-exist. Evidently, it is possible to induce against these immune responses which can lyse tumors (Keogh et al., *J. Immunol.* 167:787-96, 2001; Appella et al., *Biomed Pept Proteins Nucleic Acids* 1:177-84, 1995; Wentworth et al., *Mol Immunol.* 32:603-12, 1995).

The pharmaceutical compositions described according to the invention may also be used as vaccines for immunization. According to the invention, the terms "immunization" or "vaccination" mean an increase in or activation of an immune response to an antigen. It is possible to use animal models for testing an immunizing effect on cancer by using a tumor-associated antigen or a nucleic acid coding therefor. For example, human cancer cells may be introduced into a mouse to generate a tumor, and one or more nucleic acids coding for tumor-associated antigens may be administered. The effect on the cancer cells (for example reduction in tumor size) may be measured as a measure for the effectiveness of an immunization by the nucleic acid.

As part of the composition for an immunization, one or more tumor-associated antigens or stimulating fragments thereof are administered together with one or more adjuvants for inducing an immune response or for increasing an immune response. An adjuvant is a substance which is incorporated into the antigen or

administered together with the latter and which enhances the immune response. Adjuvants may enhance the immune response by providing an antigen reservoir (extracellularly or in macrophages), activating
5 macrophages and stimulating particular lymphocytes. Adjuvants are known and comprise in a nonlimiting way monophosphoryl lipid A (MPL, SmithKline Beecham), saponin such as QS21 (SmithKline Beecham), DQS21 (SmithKline Beecham; WO 96/33739), QS7, QS17, QS18 and
10 QS-L1 (So et al., Mol. Cells 7:178-186, 1997), incomplete Freund's adjuvant, complete Freund's adjuvant, vitamin E, montanide, alum, CpG oligonucleotides (cf. Krieg et al., Nature 374:546-9, 1995) and various water-in-oil emulsions prepared from
15 biologically degradable oils such as squalene and/or tocopherol. Preferably, the peptides are administered in a mixture with DQS21/MPL. The ratio of DQS21 to MPL is typically about 1:10 to 10:1, preferably about 1:5 to 5:1 and in particular about 1:1. For administration
20 to humans, a vaccine formulation typically contains DQS21 and MPL in a range from about 1 µg to about 100 µg.

Other substances which stimulate an immune response of
25 the patient may also be administered. It is possible, for example, to use cytokines in a vaccination, owing to their regulatory properties on lymphocytes. Such cytokines comprise, for example, interleukin-12 (IL-12) which was shown to increase the protective actions of
30 vaccines (cf. Science 268:1432-1434, 1995), GM-CSF and IL-18.

There are a number of compounds which enhance an immune response and which therefore may be used in a
35 vaccination. Said compounds comprise costimulating molecules provided in the form of proteins or nucleic acids. Examples of such costimulating molecules are B7-1 and B7-2 (CD80 and CD86, respectively) which are expressed on dendritic cells (DC) and interact with the

CD28 molecule expressed on the T cells. This interaction provides a costimulation (signal 2) for an antigen/MHC/TCR-stimulated (signal 1) T cell, thereby enhancing propagation of said T cell and the effector function. B7 also interacts with CTLA4 (CD152) on T cells, and studies involving CTLA4 and B7 ligands demonstrate that B7-CTLA4 interaction can enhance antitumor immunity and CTL propagation (Zheng, P. et al., *Proc. Natl. Acad. Sci. USA* 95(11):6284-6289 (1998)).

B7 is typically not expressed on tumor cells so that these are no effective antigen-presenting cells (APCs) for T cells. Induction of B7 expression would enable tumor cells to stimulate more effectively propagation of cytotoxic T lymphocytes and an effector function. Costimulation by a combination of B7/IL-6/IL-12 revealed induction of IFN-gamma and Th1-cytokine profile in a T cell population, resulting in further enhanced T cell activity (Gajewski et al., *J. Immunol.* 154:5637-5648 (1995)).

A complete activation of cytotoxic T lymphocytes and a complete effector function require an involvement of T helper cells via interaction between the CD40 ligand on said T helper cells and the CD40 molecule expressed by dendritic cells (Ridge et al., *Nature* 393:474 (1998), Bennett et al., *Nature* 393:478 (1998), Schönberger et al., *Nature* 393:480 (1998)). The mechanism of this costimulating signal probably relates to the increase in B7 production and associated IL-6/IL-12 production by said dendritic cells (antigen-presenting cells). CD40-CD40L interaction thus complements the interaction of signal 1 (antigen/MHC-TCR) and signal 2 (B7-CD28).

The use of anti-CD40 antibodies for stimulating dendritic cells would be expected to directly enhance a response to tumor antigens which are usually outside

2015201738 07 Apr 2015

the range of an inflammatory response or which are presented by nonprofessional antigen-presenting cells (tumor cells). In these situations, T helper and B7-costimulating signals are not provided. This mechanism could be used in connection with therapies based on antigen-pulsed dendritic cells or in situations in which T helper epitopes have not been defined in known TRA precursors.

10 The invention also provides for administration of nucleic acids, polypeptides or peptides. Polypeptides and peptides may be administered in a manner known per se. In one embodiment, nucleic acids are administered by ex vivo methods, i.e. by removing cells from a patient, genetic modification of said cells in order to incorporate a tumor-associated antigen and reintroduction of the altered cells into the patient. This generally comprises introducing a functional copy of a gene into the cells of a patient *in vitro* and reintroducing the genetically altered cells into the patient. The functional copy of the gene is under the functional control of regulatory elements which allow the gene to be expressed in the genetically altered cells. Transfection and transduction methods are known to the skilled worker. The invention also provides for administering nucleic acids *in vivo* by using vectors such as viruses and target-controlled liposomes.

30 In a preferred embodiment, a viral vector for administering a nucleic acid coding for a tumor-associated antigen is selected from the group consisting of adenoviruses, adeno-associated viruses, pox viruses, including vaccinia virus and attenuated pox viruses, Semliki Forest virus, retroviruses, Sindbis virus and Ty virus-like particles. Particular preference is given to adenoviruses and retroviruses. The retroviruses are typically replication-deficient (i.e. they are incapable of generating infectious particles).

Various methods may be used in order to introduce according to the invention nucleic acids into cells *in vitro* or *in vivo*. Methods of this kind comprise

5 transfection of nucleic acid CaPO_4 precipitates, transfection of nucleic acids associated with DEAE, transfection or infection with the above viruses carrying the nucleic acids of interest, liposome-mediated transfection, and the like. In particular

10 embodiments, preference is given to directing the nucleic acid to particular cells. In such embodiments, a carrier used for administering a nucleic acid to a cell (e.g. a retrovirus or a liposome) may have a bound target control molecule. For example, a molecule such

15 as an antibody specific for a surface membrane protein on the target cell or a ligand for a receptor on the target cell may be incorporated into or attached to the nucleic acid carrier. Preferred antibodies comprise antibodies which bind selectively a tumor-associated

20 antigen. If administration of a nucleic acid via liposomes is desired, proteins binding to a surface membrane protein associated with endocytosis may be incorporated into the liposome formulation in order to make target control and/or uptake possible. Such

25 proteins comprise capsid proteins or fragments thereof which are specific for a particular cell type, antibodies to proteins which are internalized, proteins addressing an intracellular site, and the like.

30 The therapeutic compositions of the invention may be administered in pharmaceutically compatible preparations. Such preparations may usually contain pharmaceutically compatible concentrations of salts, buffer substances, preservatives, carriers,

35 supplementing immunity-enhancing substances such as adjuvants (e.g. CpG oligonucleotides) and cytokines and, where appropriate, other therapeutically active compounds.

The therapeutically active compounds of the invention may be administered via any conventional route, including by injection or infusion. The administration may be carried out, for example, orally, intravenously, intraperitoneally, intramuscularly, subcutaneously or transdermally. Preferably, antibodies are therapeutically administered by way of a lung aerosol. Antisense nucleic acids are preferably administered by slow intravenous administration.

The compositions of the invention are administered in effective amounts. An "effective amount" refers to the amount which achieves a desired reaction or a desired effect alone or together with further doses. In the case of treatment of a particular disease or of a particular condition characterized by expression of one or more tumor-associated antigens, the desired reaction relates to inhibition of the course of the disease. This comprises slowing down the progress of the disease and, in particular, interrupting the progress of the disease. The desired reaction in a treatment of a disease or of a condition may also be delay of the onset or a prevention of the onset of said disease or said condition.

An effective amount of a composition of the invention will depend on the condition to be treated, the severeness of the disease, the individual parameters of the patient, including age, physiological condition, size and weight, the duration of treatment, the type of an accompanying therapy (if present), the specific route of administration and similar factors.

The pharmaceutical compositions of the invention are preferably sterile and contain an effective amount of the therapeutically active substance to generate the desired reaction or the desired effect.

The doses administered of the compositions of the

invention may depend on various parameters such as the type of administration, the condition of the patient, the desired period of administration, etc. In the case that a reaction in a patient is insufficient with an initial dose, higher doses (or effectively higher doses achieved by a different, more localized route of administration) may be used.

Generally, doses of the tumor-associated antigen of from 1 ng to 1 mg, preferably from 10 ng to 100 μ g, are formulated and administered for a treatment or for generating or increasing an immune response. If the administration of nucleic acids (DNA and RNA) coding for tumor-associated antigens is desired, doses of from 1 ng to 0.1 mg are formulated and administered.

The pharmaceutical compositions of the invention are generally administered in pharmaceutically compatible amounts and in pharmaceutically compatible compositions. The term "pharmaceutically compatible" refers to a nontoxic material which does not interact with the action of the active component of the pharmaceutical composition. Preparations of this kind may usually contain salts, buffer substances, preservatives, carriers and, where appropriate, other therapeutically active compounds. When used in medicine, the salts should be pharmaceutically compatible. However, salts which are not pharmaceutically compatible may be used for preparing pharmaceutically compatible salts and are included in the invention. Pharmacologically and pharmaceutically compatible salts of this kind comprise in a nonlimiting way those prepared from the following acids: hydrochloric, hydrobromic, sulfuric, nitric, phosphoric, maleic, acetic, salicylic, citric, formic, malonic, succinic acids, and the like. Pharmaceutically compatible salts may also be prepared as alkali metal salts or alkaline earth metal salts, such as sodium salts, potassium salts or calcium salts.

A pharmaceutical composition of the invention may comprise a pharmaceutically compatible carrier. According to the invention, the term "pharmaceutically compatible carrier" refers to one or more compatible solid or liquid fillers, diluents or encapsulating substances, which are suitable for administration to humans. The term "carrier" refers to an organic or inorganic component, of a natural or synthetic nature, in which the active component is combined in order to facilitate application. The components of the pharmaceutical composition of the invention are usually such that no interaction occurs which substantially impairs the desired pharmaceutical efficacy.

The pharmaceutical compositions of the invention may contain suitable buffer substances such as acetic acid in a salt, citric acid in a salt, boric acid in a salt and phosphoric acid in a salt.

The pharmaceutical compositions may, where appropriate, also contain suitable preservatives such as benzalkonium chloride, chlorobutanol, paraben and thimerosal.

The pharmaceutical compositions are usually provided in a uniform dosage form and may be prepared in a manner known per se. Pharmaceutical compositions of the invention may be in the form of capsules, tablets, lozenges, solutions, suspensions, syrups, elixir or in the form of an emulsion, for example.

Compositions suitable for parenteral administration usually comprise a sterile aqueous or nonaqueous preparation of the active compound, which is preferably isotonic to the blood of the recipient. Examples of compatible carriers and solvents are Ringer solution and isotonic sodium chloride solution. In addition,

usually sterile, fixed oils are used as solution or suspension medium.

The present invention is described in detail by the figures and examples below, which are used only for illustration purposes and are not meant to be limiting. Owing to the description and the examples, further embodiments which are likewise included in the invention are accessible to the skilled worker.

Figures:

Fig. 1: qPCR analysis of SEQ ID NO: 1 in melanomas

Quantitative expression analysis of SEQ ID NO: 1 in healthy skin tissue, in testis and in melanomas. Logarithmic representation of relative expression (-fold activation).

Fig. 2: Conventional RT-PCR analysis of SEQ ID NO: 1 in melanomas

RT-PCR expression analysis of SEQ ID NO: 1 in melanomas (n = 14) and melanoma cell lines (n = 4) in comparison with healthy skin (n = 4) and with testis (n = 3).

Fig. 3: qPCR analysis of SEQ ID NO: 5 in healthy tissue and in tumor samples

Quantitative expression analysis of SEQ ID NO: 5 in normal tissues (left-hand side) and in various tumors (pools consisting of in each case 3-5 individual samples, right-hand side). **A** Logarithmic representation of relative expression (-fold activation). **B** Image after gel-electrophoretic fractionation of the amplified fragments.

Fig. 4: Detailed analysis of SEQ ID NO: 5-specific expression

A Quantitative expression analysis of SEQ ID NO: 5 in various ENT, renal and uterine tumors in comparison with expression in the corresponding normal tissues.

Logarithmic representation. **B** Image after gel-electrophoretic fractionation of the amplified fragments.

5 **Fig. 5: Northern blot analysis with a SEQ ID NO: 5-specific sequence**

Hybridization of a DIG-labeled DNA probe, prepared by PCR amplification using the primers according to SEQ ID NO: 7 and 8, with testis-specific RNA. Lane 1: 10 2 µg of testis-specific RNA; lane 2: 1 µg of testis-specific RNA.

Fig. 6: qPCR analysis of LOC203413

Quantitative expression analysis of LOC203413 in 15 healthy tissues (left) and in tumor samples (pools consisting of in each case 3-5 individual samples, right). **A** Logarithmic representation of expression (-fold activation). **B** Result after gel-electrophoretic fractionation.

20

Fig. 7: Detailed analysis of LOC203413-specific expression in gastric carcinomas

Quantitative expression analysis of LOC203413 in various gastric tumor samples (n = 10) in comparison 25 with expression in healthy stomach (n = 6). **A** Linear representation of relative expression. **B** Image after gel-electrophoretic fractionation of the amplicons.

Fig. 8: qPCR analysis of LOC90625-specific expression

30 Quantitative expression analysis of LOC90625 in normal tissues (left) and tumor tissues (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation).

35

Fig. 9: Detailed analysis of LOC90652-specific expression in various types of tumors

Quantitative expression analysis of LOC90625 in samples of carcinomas of the esophagus (n = 8), pancreas

(n = 5) and prostate (n = 10) in comparison with the respective healthy tissue (n = 3/4); logarithmic representation of relative expression (-fold activation).

5 **Fig. 10: qRT-PCR analysis of FAM26A in various types of tumors**

Quantitative RT-PCR expression analysis of FAM26A in carcinomas of the **A** ovary, **B** stomach, esophagus, pancreas and liver, in comparison with the respective healthy tissue. Linear representation of relative expression (-fold activation).

10 **Fig. 11: Characterization of FAM26A-specific antibodies**

Western blot analysis of the antisera generated by immunization with a peptide of SEQ ID NO: 291 (**A**) and SEQ ID NO: 292 (**B**). Extracts of CHO cells were analyzed after transfection with in each case epitope-specific (A 1, 3; B 2, 4) or in each case epitope-unspecific (A 2, 4; B 1, 3) plasmids. The arrow indicates the specific fragments.

15 **Fig. 12: Analysis of the FAM26A protein in tumors**

Detection of FAM26A in cervical, ovarian and pancreatic tumors by means of FAM26A-specific antibodies (SEQ ID NO: 292).

20 **Fig. 13: Analysis of the FAM26A protein in cell lines**

Analysis of the FAM26A protein in cell lines with the aid of SEQ ID NO: 291-specific antibodies. **A** Western blot analysis with preimmune serum as specificity control (lanes 1-5) and FAM26A-specific antibodies. **B** Immunofluorescence analysis of SW480 cells.

25 **Fig. 14: Immunohistochemical detection of FAM26A in testis**

Immunohistochemical analysis of the FAM26A protein in healthy testis with the aid of SEQ ID NO: 292-specific antiserum in different dilutions (**A-C**).

Fig. 15: Immunohistochemical analysis of FAM26A in tumors

Immunohistochemical analysis of the FAM26A protein in carcinoma samples (40-fold magnification, 1:300 dilution) with the aid of the SEQ ID NO: 292-specific antiserum. **A** Ovarian papillary cystadenocarcinoma. **B** Plate epithelial carcinoma of the cervix.

Fig. 16: qRT-PCR analysis of SEMA5B-specific expression

Quantitative expression analysis of SEMA5B in normal tissues (left) and tumor samples (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation).

Fig. 17: Detailed analysis of SEMA5B-specific expression in renal cell carcinoma samples

Quantitative expression analysis of SEMA5B in **A** renal cell carcinoma samples (n = 12) in comparison with healthy renal tissue (N = 3) and in **B** mammary carcinomas (N = 12) in comparison with healthy breast tissue (N = 3); logarithmic representation of relative expression (-fold activation).

Fig. 18: qRT-PCR analysis of GJB5-specific expression

Quantitative expression analysis of GJB5 in healthy tissue samples (left) and carcinomas (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation).

Fig. 19: Detailed analysis of GJB5-specific expression in various types of tumors

Quantitative expression analysis of GJB5 in **A** colon carcinoma samples (n = 12), **B** esophageal tumors (n = 8), **C** gastric carcinomas (n = 10) and **D** pancreatic tumors (n = 5) in comparison with in each case healthy tissue samples; logarithmic (A, C) or linear (B, D) representation of relative expression (-fold

activation).

Fig. 20: qRT-PCR analysis of KLK5-specific expression

Quantitative expression analysis of KLK5 in healthy tissue samples (left) and tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation).

Fig. 21: Detailed analysis of KLK5-specific expression in various types of tumors

Quantitative expression analysis of KLK5 in esophageal tumors (n = 8), in ENT carcinomas (n = 5) and in cervical tumors (n = 4) in comparison with the respective healthy tissue samples; logarithmic representation of relative expression (-fold activation).

Fig. 22: qRT-PCR analysis of LOC352765-specific expression

Quantitative expression analysis of LOC352765 in healthy tissue samples (left) and tumors (pools consisting of in each case 3-5 individual samples; right). Logarithmic representation of relative expression (-fold activation).

Fig. 23: Detailed analysis of LOC352765-specific expression in various types of tumors

Quantitative expression analysis of LOC352765 in colon carcinomas (n = 8), in mammary carcinomas (n = 5) and in ENT tumors (n = 4) in comparison with respective healthy tissue samples; logarithmic representation of relative expression (-fold activation).

Fig. 24: qRT-PCR analysis of SVCT1-specific expression

Quantitative expression analysis of SVCT1 in healthy tissue samples (left) and tumors (pools consisting of in each case 3-5 individual samples; right). Logarithmic representation of relative expression

(-fold activation).

Fig. 25: Detailed analysis of SVCT1-specific expression in various types of tumors

Quantitative expression analysis of SVCT1 in **A** kidney carcinomas (n = 8), **B** esophageal tumors (n = 5) and ENT tumors (n = 4) in comparison with in each case healthy tissue samples; logarithmic representation of relative expression (-fold activation).

Fig. 26: qRT-PCR analysis of LOC199953-specific expression in renal cell carcinomas and in ENT tumors

Quantitative expression analysis of LOC199953 in renal cell carcinomas (n = 12) and ENT tumors (n = 5) in comparison with healthy kidney- and skin-specific tissue samples; linear representation of relative expression (-fold activation).

Fig. 27: qRT-PCR analysis of TMEM31-specific expression

Quantitative expression analysis of TMEM31 in healthy tissue samples (left) and tumors (pools consisting of in each case 3-5 individual samples; right). Logarithmic representation of relative expression (-fold activation).

Fig. 28: Detailed analysis of TMEM31-specific expression in various types of tumors

Quantitative expression analysis of TMEM31 in **A** gastric carcinomas (n = 10) and **B** mammary carcinomas (n = 12) in comparison with in each case healthy tissue samples; logarithmic representation of relative expression (-fold activation).

Fig. 29: qRT-PCR analysis of FLJ25132-specific expression in ovarian tumors and in prostate carcinomas

Quantitative expression analysis of FLJ25132 in ovarian tumors (n = 8) and in prostate carcinomas (n = 10) in comparison with in each case healthy tissue samples; linear representation of relative expression (-fold

activation).

Fig. 30: qRT-PCR analysis of SEQ ID NO: 57-specific expression

5 Quantitative expression analysis of SEQ ID NO: 57 in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation).

10

Fig. 31: Detailed analysis of SEQ ID NO: 57-specific expression in various types of tumors

15 Quantitative expression analysis of SEQ ID NO: 57 in **A** esophageal tumors (n = 8), **B** liver carcinomas (n = 8), **C** kidney carcinomas and **D** cervical and ENT tumors in comparison with in each case healthy tissue samples; linear (A, C, D) or logarithmic (B) representation of relative expression (-fold activation).

20 **Fig. 32: qRT-PCR analysis of LOC119395-specific expression**

Quantitative expression analysis of LOC119395 in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation).

25

Fig. 33: Detailed analysis of LOC119395-specific expression in various types of tumors

30 Quantitative expression analysis of LOC119395 in **A** breast tumors (n = 12), **B** esophageal carcinomas (n = 8) and **C** colon and gastric carcinomas, in comparison with in each case healthy tissue samples; logarithmic representation of relative expression (-fold activation).

35

Fig. 34: qRT-PCR analysis of LOC121838-specific expression

A Quantitative analysis of LOC121838-specific expres-

sion in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation). **B** Detailed analysis of LOC121838-specific RNA in ovarian tissues, logarithmic representation.

Fig. 35: qRT-PCR analysis of LOC221103-specific expression

Quantitative expression analysis of LOC221103-RNA in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation).

Fig. 36: Detailed qRT-PCR analysis of LOC221103-specific expression in liver samples

Quantitative expression analysis of LOC221103-RNA in liver tumors (n = 8) and in a healthy liver sample. Linear representation of relative expression (-fold activation).

Fig. 37: qRT-PCR analysis of LOC338579-specific expression

Quantitative expression analysis of LOC338579-specific RNA in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Logarithmic representation of relative expression (-fold activation).

Fig. 38: qRT-PCR analysis of LOC90342-specific expression

Quantitative expression analysis of LOC90342-specific RNA in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Logarithmic representation of relative expression (-fold activation).

Fig. 39: qRT-PCR analysis of LRFN1-specific expression

Quantitative expression analysis of LRFN1-specific RNA in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Logarithmic representation of relative expression (-fold activation).

Fig. 40: qRT-PCR analysis of LOC285916-specific expression

A Quantitative analysis of LOC285916-specific expression in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation). **B** Detailed analysis of LOC285916-specific RNA in kidney tissues and in ENT tumors, logarithmic representation.

Fig. 41: qRT-PCR analysis of MGC71744-specific expression

A Quantitative analysis of MGC71744-specific expression in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation). **B** Detailed analysis of MGC71744-specific RNA in various kidney tissues, logarithmic representation.

Fig. 42: qRT-PCR analysis of LOC342982-specific expression

Quantitative expression analysis of LOC342982-specific RNA in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Logarithmic representation of relative expression (-fold activation).

Fig. 43: qRT-PCR analysis of LOC343169-specific expression

A Quantitative analysis of LOC343169-specific expression in healthy tissue samples (left) and in tumors

(pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation). **B** Detailed analysis of LOC343169-specific RNA in various ovarian tissues, logarithmic representation.

Fig. 44: qRT-PCR analysis of LOC340204-specific expression

A Quantitative analysis of LOC340204-specific expression in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation). **B** Gel image of selected tissue samples after gel-electrophoretic fractionation.

Fig. 45: qRT-PCR analysis of LOC340067-specific expression

Quantitative expression analysis of LOC340067-specific RNA in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Logarithmic representation of relative expression (-fold activation).

Fig. 46: qRT-PCR analysis of LOC342780-specific expression

Quantitative expression analysis of LOC342780-specific RNA in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Logarithmic representation of relative expression (-fold activation).

Fig. 47: qRT-PCR analysis of LOC339511-specific expression

A Quantitative analysis of LOC339511-specific expression in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation). **B** Detailed analysis of LOC339511-specific RNA in various liver-specific

tissues; linear representation.

Fig. 48: qRT-PCR analysis of C14orf37-specific expression

Quantitative expression analysis of C14orf37 in healthy tissue samples (left) and in tumors (pools consisting of in each case 3-5 individual samples; right). Linear representation of relative expression (-fold activation).

Fig. 49: qRT-PCR analysis of ATP1A4-specific expression

A Quantitative expression analysis of ATP1A4 in healthy tissue samples and in tumors (pools consisting of in each case 3-5 individual samples). Logarithmic representation of relative expression (-fold activation). **B** Detailed analysis of ATP1A4-specific RNA in various breast-specific tissues; logarithmic representation.

Where the terms "comprise", "comprises", "comprised" or "comprising" are used in this specification (including the claims) they are to be interpreted as specifying the presence of the stated features, integers, steps or components, but not precluding the presence of one or more other features, integers, steps or components, or group thereof.

The discussion of documents, acts, materials, devices, articles and the like is included in this specification solely for the purpose of providing a context for the present invention. It is not suggested or represented that any or all of these matters formed part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this application.

Examples:**Materials and methods**

- 5 The terms "*in silico*" and "electronic" refer solely to the utilization of methods based on databases, which may also be used to simulate laboratory experimental processes.
- 10 Unless expressly defined otherwise, all other terms and expressions are used so as to be understood by the skilled worker. The techniques and methods mentioned are carried out in a manner known per se and are described, for example, in Sambrook et al., *Molecular Cloning: A*
- 15 *Laboratory Manual*, 2nd edition (1989), Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. All methods including the use of kits and reagents are carried out according to the manufacturers' information.

20 **Example 1:**

Data mining-based strategy for identifying tumor-associated antigens

- According to the invention, public human protein and
- 25 nucleic acid databases were screened with regard to cancer-specific antigens accessible on the cell surface. The definition of the screening criteria required therefor, together with high throughput methods for analyzing, if possible, all proteins,
- 30 formed the central component of this strategy.

- The starting point consisted of the potential genes, predicted mainly by the human genome project, which have been deposited as solely exemplary protein (XP) or
- 35 mRNA (XM) entries in the RefSeq database (Pruitt et al., *Trends Genet.* Jan; 16(1):44-47, 2000) of the National Center for Biotechnology Information (NCBI). In another approach, the validated protein entries (NP) and, respectively, the corresponding mRNAs (NM) of the

same database were also analyzed in the same manner. Following the fundamental principle of (hypothetical) gene $\rightarrow$ mRNA $\rightarrow$ protein, the proteins were first studied for the presence of transmembrane domains by combining a plurality of prediction programs for protein analysis. A total of 19 544 entries of the human XP fraction of the RefSeq database were analyzed, with 2025 hypothetical proteins satisfying said screening criteria. The human NP fraction provided a total of 19 110 entries with a proportion of 4634 filtered proteins.

The corresponding mRNA of each of these 2025 and 4634 proteins, respectively, was then subjected to a homology search in the EST database (Boguski et al., *Nat. Genet.* 4(4):332-333, 1993) of the NCBI with the aid of the BLAST algorithm (Altschul et al., *Nucleic Acids Res.* 25:3389-3402, 1997). The screening criteria in this search were set to stringent. A total of 1270 hypothetical mRNAs scored at least one hit in the EST database, with the number of hits exceeding 1000 in some cases.

Subsequently, the tissue-specific origin of the underlying cDNA library as well as the name of the library were determined for each of these valid hits. The tissues resulting therefrom were divided into 4 different groups ranging from dispensable organs (group 3) to absolutely essential organs (group 0). Another group, group 4, consisted of any samples obtained from cancer tissue. The distribution of hits to the five groups was recorded in a table which was sorted according to the best ratio of the sum of groups 3 and 4 to the sum of groups 0-2. Those mRNAs whose EST hits originated exclusively from cancer tissue reached a top position, followed by those which can additionally be found also in tissues of dispensable organs of group 3.

Since the transcripts determined in the first approach and the corresponding proteins are firstly hypothetical constructs, further screening criteria were used with the intention to prove the real existence of the mRNAs and consequently also of the proteins. For this purpose, each mRNA was compared to the predicted gene locus. Only those transcripts which have at least one splicing process, i.e. which spread over at least 2 exons, were used for more detailed analyses.

Sequential application of all the filters mentioned led to the tumor-associated antigens of the invention which can be considered extracellularly accessible, owing to a predicted transmembrane domain and the topology related thereto. The expression profile derived from the EST data indicates, in all cases, cancer-specific expression which may at most extend only to dispensable organs.

Example 2:

Strategy of validating the tumor-associated antigens identified by *in silico* analysis

In order to utilize the targets for immunotherapeutic purposes (antibody therapy by means of monoclonal antibodies, vaccination, T-cell receptor-mediated therapeutic approaches; cf. EP-B-0 879 282) or other targeted approaches (small compounds, siRNA etc.) in cancer therapy as well as for diagnostic problems, the validation of the targets identified according to the invention is of central importance. In this connection, validation is carried out by expression analysis at both RNA and protein levels.

1. Examination of RNA expression

The identified tumor antigens are first validated with the aid of RNA which is obtained from various tissues or from tissue-specific cell lines. Since the differential expression pattern of healthy tissue in

comparison with tumor tissue is of decisive importance for the subsequent therapeutic application, the target genes are preferably characterized with the aid of these tissue samples.

5 Total RNA is isolated from native tissue samples or from tumor cell lines by standard methods of molecular biology. Said isolation may be carried out, for example, with the aid of the RNeasy Maxi kit (Qiagen, 10 Cat. No. 75162) according to the manufacturer's instructions. This isolation method is based on the use of chaotropic reagent guanidinium isothiocyanate. Alternatively, acidic phenol can be used for isolation (Chomczynski & Sacchi, Anal. Biochem. 162: 156-159, 15 1987). After the tissue has been worked up by means of guanidinium isothiocyanate, RNA is extracted with acidic phenol, subsequently precipitated with isopropanol and taken up in DEPC-treated water.

20 2-4 µg of the RNA isolated in this way are subsequently transcribed into cDNA, for example by means of Superscript II (Invitrogen) according to the manufacturer's protocol. cDNA synthesis is primed with the aid of random hexamers (e.g. Roche Diagnostics) 25 according to standard protocols of the relevant manufacturer. For quality control, the cDNAs are amplified over 30 cycles, using primers specific for the p53 gene which is expressed only lowly. Only p53-positive cDNA samples will be used for the subsequent 30 reaction steps.

The targets are analyzed in detail by carrying out an expression analysis by means of PCR or quantitative PCR (qPCR) on the basis of a cDNA archive which has been 35 isolated from various normal and tumor tissues and from tumor cell lines. For this purpose, 0.5 µl of cDNA of the above reaction mixture is amplified by a DNA polymerase (e.g. 1 U of HotStarTaq DNA polymerase, Qiagen) according to the protocols of the particular

manufacturer (total volume of the reaction mixture:
25-50 µl). Aside from said polymerase, the amplifica-
tion mixture comprises 0.3 mM dNTPs, reaction buffer
(final concentration 1 x, depending on the manufacturer
of the DNA polymerase) and in each case 0.3 mM gene-
specific forward and reverse primers.

The specific primers of the target gene are, as far as
possible, selected in such a way that they are located
in two different exons so that genomic contaminations
do not lead to false-positive results. In a non-
quantitative end point PCR, the cDNA is typically
incubated at 95°C for 15 minutes in order to denature
the DNA and to activate the Hot-Start enzyme.
Subsequently the DNA is amplified over 35 cycles (1 min
at 95°C, 1 min at the primer-specific hybridization
temperature (approx. 55-65°C), 1 min at 72°C to
elongate the amplicons). Subsequently, 10 µl of the PCR
mixture are applied to agarose gels and fractionated in
the electric field. The DNA is made visible in the gels
by staining with ethidium bromide and the PCR result is
documented by way of a photograph.

As an alternative to conventional PCR, expression of a
target gene may also be analyzed by quantitative real
time PCR. Meanwhile various analytical systems are
available for this analysis, of which the best known
ones are the ABI PRISM sequence detection system
(TaqMan, Applied Biosystems), the iCycler (Biorad) and
the Light cycler (Roche Diagnostics). As described
above, a specific PCR mixture is subjected to a run in
the real time instruments. By adding a DNA-
intercalating dye (e.g. ethidium bromide, CybrGreen),
the newly synthesized DNA is made visible by specific
light excitation (according to the dye manufacturers'
information). A multiplicity of points measured during
amplification enables the entire process to be
monitored and the nucleic acid concentration of the
target gene to be determined quantitatively. The PCR

mixture is normalized by measuring a housekeeping gene (e.g. 18S RNA, β -actin). Alternative strategies via fluorescently labeled DNA probes likewise allow quantitative determination of the target gene of a specific tissue sample (see TaqMan applications from Applied Biosystems).

2. Cloning

The complete target gene which is required for further characterization of the tumor antigen is cloned according to common molecular-biological methods (e.g. in "Current Protocols in Molecular Biology", John Wiley & Sons Ltd., Wiley InterScience). In order to clone the target gene or to analyze its sequence, said gene is first amplified by a DNA polymerase having a proof reading function (e.g. pfu, Roche Diagnostics). The amplicon is then ligated by standard methods into a cloning vector. Positive clones are identified by sequence analysis and subsequently characterized with the aid of prediction programs and known algorithms.

3. Prediction of the protein

Many of the genes found according to the invention (in particular those from the RefSeq XM domain) are newly discovered genes which require cloning of the full-length gene, determination of the open reading frame and deduction and analysis of the protein sequence. In order to clone the full-length sequence, we used common protocols for the rapid amplification of cDNA ends and the screening of cDNA expression libraries with gene-specific probes (*Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd edition (1989), Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.*).

After assembling the fragments found in this way, potential open reading frames (ORF) were predicted using common prediction programs. Since the position of

the PolyA tail and of polyadenylation motifs predetermines the orientation of the potential gene product, only the 3 reading frames of that particular orientation remain out of a possible 6 reading frames.

5 The former often yield only one sufficiently large open reading frame which may code for a protein, while the other reading frames have too many stop codons and would not code for any realistic protein. In the case of alternative open reading frames, identification of

10 the authentic ORF is assisted by taking into account the Kozak criteria for optimal transcription initiation and by analyzing the deduced protein sequences which may arise. Said ORF is further verified by generating immune sera against proteins deduced from the potential

15 ORFs and analyzing said immune sera for recognition of a real protein in tissues and cell lines.

4. Production of antibodies

20 The tumor-associated antigens identified according to the invention are characterized, for example, by using antibodies. The invention further comprises the diagnostic or therapeutic use of antibodies. Antibodies may recognize proteins in the native and/or denatured

25 state (Anderson et al., *J. Immunol.* 143: 1899-1904, 1989; Gardsvoll, *J. Immunol. Methods* 234: 107-116, 2000; Kayyem et al., *Eur. J. Biochem.* 208: 1-8, 1992; Spiller et al., *J. Immunol. Methods* 224: 51-60, 1999).

30 Antisera comprising specific antibodies which specifically bind to the target protein may be prepared by various standard methods; cf., for example, "Monoclonal Antibodies: A Practical Approach" by Phillip Shepherd, Christopher Dean ISBN 0-19-963722-9,

35 "Antibodies: A Laboratory Manual" by Ed Harlow, David Lane ISBN: 0879693142 and "Using Antibodies: A Laboratory Manual: Portable Protocol NO" by Edward Harlow, David Lane, Ed Harlow ISBN: 0879695447. It is also possible here to generate affine and

specific antibodies which recognize complex membrane proteins in their native form (Azorsa et al., *J. Immunol. Methods* 229: 35-48, 1999; Anderson et al., *J. Immunol.* 143: 1899-1904, 1989; Gardsvoll, *J. Immunol. Methods.* 234: 107-116, 2000). This is especially important in the preparation of antibodies which are intended to be used therapeutically but also for many diagnostic applications. For this purpose, both the complete protein and extracellular partial sequences may be used for immunization.

Immunization and production of polyclonal antibodies
A species (e.g. rabbits, mice) is immunized by a first injection of the desired target protein. The immune response of the animal to the immunogen can be enhanced by a second or third immunization within a defined period of time (approx. 2-4 weeks after the previous immunization). Blood is taken from said animals and immune sera obtained, again after various defined time intervals (1st bleeding after 4 weeks, then every 2-3 weeks, up to 5 takings). The immune sera taken in this way comprise polyclonal antibodies which may be used to detect and characterize the target protein in Western blotting, by flow cytometry, immunofluorescence or immunohistochemistry.

The animals are usually immunized by any of four well-established methods, with other methods also in existence. The immunization may be carried out using peptides specific for the target protein, using the complete protein, using extracellular partial sequences of a protein which can be identified experimentally or via prediction programs. Since the prediction programs do not always work perfectly, it is also possible to employ two domains separated from one another by a transmembrane domain. In this case, one of the two domains has to be extracellular, which may then be proved experimentally (see below).

- (1) In the first case, peptides (length: 8-12 amino acids) are synthesized by *in vitro* methods (possibly carried out by a commercial service), and said peptides are used for immunization. Normally 3 immunizations are carried out (e.g. with a concentration of 5-100 µg/immunization). The immunization may also be carried out by commercial service providers.
- (2) Alternatively, immunization may be carried out using recombinant proteins. For this purpose, the cloned DNA of the target gene is cloned into an expression vector and the target protein is synthesized, for example, cell-free *in vitro*, in bacteria (e.g. *E. coli*), in yeast (e.g. *S. pombe*), in insect cells or in mammalian cells, according to the conditions of the particular manufacturer (e.g. Roche Diagnostics, Invitrogen, Clontech, Qiagen). It is also possible to synthesize the target protein with the aid of viral expression systems (e.g. baculovirus, vacciniavirus, adenovirus). After it has been synthesized in one of said systems, the target protein is purified, normally by employing chromatographic methods. In this context, it is also possible to use for immunization proteins which have a molecular anchor as an aid for purification (e.g. His tag, Qiagen; FLAG tag, Roche Diagnostics; GST fusion proteins). A multiplicity of protocols can be found, for example, in "Current Protocols in Molecular Biology", John Wiley & Sons Ltd., Wiley InterScience. After the target protein has been purified, an immunization is carried out as described above.

- 5 (3) If a cell line is available which synthesizes the desired protein endogenously, it is also possible to use this cell line directly for preparing the specific antiserum. In this case, immunization is carried out by 1-3 injections with in each case approx. $1-5 \times 10^7$ cells.
- 10 (4) The immunization may also be carried out by injecting DNA (DNA immunization). For this purpose, the target gene is first cloned into an expression vector so that the target sequence is under the control of a strong eukaryotic promoter (e.g. CMV promoter).
- 15 Subsequently, DNA (e.g. 1-10 μ g per injection) is transferred as immunogen using a gene gun into capillary regions with a strong blood flow in an organism (e.g. mouse, rabbit). The transferred DNA is taken up by the animal's
- 20 cells, the target gene is expressed, and the animal finally develops an immune response to the target protein (Jung et al., *Mol. Cells* 12: 41-49, 2001; Kasinrerk et al., *Hybrid Hybridomics* 21: 287-293, 2002).

25

Production of monoclonal antibodies

Monoclonal antibodies are traditionally produced with the aid of the hybridoma technology (technical details: see "Monoclonal Antibodies: A Practical Approach" by Philip Shepherd, Christopher Dean ISBN 0-19-963722-9; "Antibodies: A Laboratory Manual" by Ed Harlow, David Lane ISBN: 0879693142, "Using Antibodies: A Laboratory Manual: Portable Protocol NO" by Edward Harlow, David Lane, Ed Harlow ISBN: 0879695447).

30

35 A new method which is also used is the "SLAM" technology. Here, B cells are isolated from whole blood and the cells are made monoclonal. Subsequently the supernatant of the isolated B cell is analyzed for its antibody specificity. In contrast to the hybridoma

technology, the variable region of the antibody gene is then amplified by single-cell PCR and cloned into a suitable vector. In this manner production of monoclonal antibodies is accelerated (de Wildt et al., J. Immunol. Methods 207:61-67, 1997).

5. Validation of the targets by protein-chemical methods using antibodies

The antibodies which can be produced as described above can be used to make a number of important statements about the target protein. Specifically the following analyses of validating the target protein are useful:

Specificity of the antibody

Assays based on cell culture with subsequent Western blotting are most suitable for demonstrating the fact that an antibody binds specifically only to the desired target protein (various variations are described, for example, in "Current Protocols in Proteinchemistry", John Wiley & Sons Ltd., Wiley InterScience). For the demonstration, cells are transfected with a cDNA for the target protein, which is under the control of a strong eukaryotic promoter (e.g. cytomegalovirus promoter; CMV). A wide variety of methods (e.g. electroporation, liposome-based transfection, calcium phosphate precipitation) are well established for transfecting cell lines with DNA (e.g. Lemoine et al., *Methods Mol. Biol.* 75: 441-7, 1997). As an alternative, it is also possible to use cell lines which express the target gene endogenously (detection via target gene-specific RT-PCR). As a control, in the ideal case, homologous genes are cotransfected in the experiment, in order to be able to demonstrate in the following Western blot the specificity of the analyzed antibody.

In the subsequent Western blotting, cells from cell culture or tissue samples which might contain the target protein are lysed in a 1% strength SDS solution,

and the proteins are denatured in the process. The lysates are fractionated according to size by electrophoresis on 8-15% strength denaturing polyacrylamide gels (contain 1% SDS) (SDS polyacrylamide gel electrophoresis, SDS-PAGE). The proteins are then transferred by one of a plurality of blotting methods (e.g. semi-dry electroblot; Biorad) to a specific membrane (e.g. nitrocellulose, Schleicher & Schüll). The desired protein can be visualized on this membrane. For this purpose, the membrane is first incubated with the antibody which recognizes the target protein (dilution approx. 1:20-1:200, depending on the specificity of said antibody), for 60 minutes. After a washing step, the membrane is incubated with a second antibody which is coupled to a marker (e.g. enzymes such as peroxidase or alkaline phosphatase) and which recognizes the first antibody. It is then possible to make the target protein visible on the membrane in a color or chemiluminescent reaction (e.g. ECL, Amersham Bioscience). An antibody with a high specificity for the target protein should in the ideal case only recognise the desired protein itself.

Localization of the target protein

Various methods are used to confirm the membrane localization, identified in the in silico approach, of the target protein. An important and well-established method using the antibodies described above is immunofluorescence (IF). For this purpose, cells of established cell lines which either synthesize the target protein (detection of the RNA by RT-PCR or of the protein by Western blotting) or else have been transfected with plasmid DNA are utilized. A wide variety of methods (e.g. electroporation, liposome-based transfection, calcium phosphate precipitation) are well established for transfection of cell lines with DNA (e.g. Lemoine et al., *Methods Mol. Biol.* 75: 441-7, 1997). The plasmid transfected into the cells, in immunofluorescence, may encode the unmodified

protein or else couple different amino acid markers to the target protein. The principle markers are, for example, the fluorescent green fluorescent protein (GFP) in various differentially fluorescent forms, short peptide sequences of 6-12 amino acids for which high-affinity and specific antibodies are available, or the short amino acid sequence Cys-Cys-X-X-Cys-Cys which can bind via its cysteines specific fluorescent substances (Invitrogen). Cells which synthesize the target protein are fixed, for example, with paraformaldehyde or methanol. The cells may then, if required, be permeabilized by incubation with detergents (e.g. 0.2% Triton X-100). The cells are then incubated with a primary antibody which is directed against the target protein or against one of the coupled markers. After a washing step, the mixture is incubated with a second antibody coupled to a fluorescent marker (e.g. fluorescein, Texas Red, Dako), which binds to the first antibody. The cells labeled in this way are then overlaid with glycerol and analyzed with the aid of a fluorescence microscope according to the manufacturer's information. Specific fluorescence emissions are achieved in this case by specific excitation depending on the substances employed. The analysis usually permits reliable localization of the target protein, the antibody quality and the target protein being confirmed in double stainings with, in addition to the target protein, also the coupled amino acid markers or other marker proteins whose localization has already been described in the literature being stained. GFP and its derivatives represent a special case, being excitable directly and themselves fluorescing. The membrane permeability which may be controlled through the use of detergents, in immunofluorescence, allows demonstration of whether an immunogenic epitope is located inside or outside the cell. The prediction of the selected proteins can thus be supported experimentally. An alternative possibility is to detect extracellular domains by means of flow

cytometry. For this purpose, cells are fixed under non-permeabilizing conditions (e.g. with PBS/Na azide/2% FCS/5 mM EDTA) and analyzed in a flow cytometer in accordance with the manufacturer's instructions. Only
5 extracellular epitopes can be recognized by the antibody to be analyzed in this method. A difference from immunofluorescence is that it is possible to distinguish between dead and living cells by using, for example, propidium iodide or Trypan blue, and thus
10 avoid false-positive results.

Another important detection is by immunohistochemistry (IHC) on specific tissue samples. The aim of this method is to identify the localization of a protein in
15 a functionally intact tissue aggregate. IHC serves specifically for (1) being able to estimate the amount of target protein in tumor and normal tissues, (2) analyzing how many cells in tumor and healthy tissues synthesize the target gene, and (3) defining the cell
20 type in a tissue (tumor, healthy cells) in which the target protein is detectable. Alternatively, the amounts of protein of a target gene may be quantified by tissue immunofluorescence using a digital camera and suitable software (e.g. Tillvision, Till-photonics,
25 Germany). The technology has frequently been published, and details of staining and microscopy can therefore be found, for example, in "Diagnostic Immunohistochemistry" by David J., MD Dabbs ISBN: 0443065667 or in "Microscopy, Immunohistochemistry, and Antigen
30 Retrieval Methods: For Light and Electron Microscopy" ISBN: 0306467704. It should be noted that, owing to the properties of antibodies, different protocols have to be used (an example is described below) in order to obtain a meaningful result.

35

Normally, histologically defined tumor tissues and, as reference, comparable healthy tissues are employed in IHC. It is also possible to use as positive and negative controls cell lines in which the presence of

the target gene is known through RT-PCR analyses. A background control must always be included.

5 Formalin-fixed (another fixation method, for example
with methanol, is also possible) and paraffin-embedded
tissue pieces with a thickness of 4 μ m are applied to a
glass support and deparaffinated with xylene, for
example. The samples are washed with TBS-T and blocked
10 in serum. This is followed by incubation with the first
antibody (dilution: 1:2 to 1:2000) for 1-18 hours, with
affinity-purified antibodies normally being used. A
washing step is followed by incubation with a second
antibody which is coupled to an alkaline phosphatase
15 (alternative: for example peroxidase) and directed
against the first antibody, for approx. 30-60 minutes.
This is followed by a color reaction using said
alkaline phosphatase (cf., for example, Shi et al.,
J. Histochem. Cytochem. 39: 741-748, 1991; Shin et al.,
Lab. Invest. 64: 693-702, 1991). To demonstrate anti-
20 body specificity, the reaction can be blocked by
previous addition of the immunogen.

Analysis of protein modifications

Secondary protein modifications such as, for example,
25 N- and O-glycosylations or myristilations may impair or
even completely prevent the accessibility of immuno-
genic epitopes and thus call into question the efficacy
of antibody therapies. Moreover, it has frequently been
demonstrated that the type and amount of secondary
30 modifications differ in normal and tumor tissues (e.g.
Durand & Seta, 2000; *Clin. Chem.* 46: 795-805; Hakomori,
1996; *Cancer Res.* 56: 5309-18). The analysis of these
modifications is therefore essential to the therapeutic
success of an antibody. Potential binding sites can be
35 predicted by specific algorithms.

Analysis of protein modifications usually takes place
by Western blotting (see above). Glycosylations which
usually have a size of several kDa, especially lead to

a larger total mass of the target protein, which can be fractionated in SDS-PAGE. To detect specific O- and N-glycosidic bonds, protein lysates are incubated prior to denaturation by SDS with O- or N-glycosylases (in accordance with their respective manufacturer's instructions, e.g. PNGase, endoglycosidase F, endoglycosidase H, Roche Diagnostics). This is followed by Western blotting as described above. Thus, if there is a reduction in the size of a target protein after incubation with a glycosidase, it is possible to detect a specific glycosylation and, in this way, also analyze the tumor specificity of a modification.

Functional analysis of the target gene

The function of the target molecule may be crucial for its therapeutic usefulness, so that functional analyses are an important component in the characterization of therapeutically utilizable molecules. The functional analysis may take place either in cells in cell culture experiments or else in vivo with the aid of animal models. This involves either switching off the gene of the target molecule by mutation (knockout) or inserting the target sequence into the cell or the organism (knockin). Thus it is possible to analyze functional modifications in a cellular context firstly by way of the loss of function of the gene to be analyzed (loss of function). In the second case, modifications caused by addition of the analyzed gene can be analyzed (gain of function).

30

a. Functional analysis in cells

Transfection. In order to analyze the gain of function, the gene of the target molecule must be transferred into the cell. For this purpose, cells which allow synthesis of the target molecule are transfected with a DNA. Normally, the gene of the target molecule here is under the control of a strong eukaryotic promoter (e.g. cytomegalovirus promoter; CMV). A wide variety of methods (e.g. electroporation, liposome-based

transfection, calcium phosphate precipitation) are well established for transfecting cell lines with DNA (e.g. Lemoine et al., *Methods Mol. Biol.* 75: 441-7, 1997). The gene may be synthesized either transiently, without
5 genomic integration, or else stably, with genomic integration after selection with neomycin, for example.

RNA interference (siRNA). An inhibition of expression of the target gene, which may induce a complete loss of
10 function of the target molecule in cells, may be generated by the RNA interference (siRNA) technology in cells (Hannon, GJ. 2002. RNA interference. *Nature* 418: 244-51; Czauderna et al. 2003. *Nucl. Acid Res.* 31: 670-82). For this purpose, cells are transfected with
15 short, double-stranded RNA molecules of approx. 20-25 nucleotides in length, which are specific for the target molecule. An enzymic process then results in degradation of the specific RNA of the target gene and thus in an inhibition of the function of the target
20 protein and consequently enables the target gene to be analyzed.

Cell lines which have been modified by means of transfection or siRNA may subsequently be analyzed in
25 different ways. The most common examples are listed below.

1. Proliferation and cell cycle behavior

A multiplicity of methods for analyzing cell
30 proliferation are established and are commercially supplied by various companies (e.g. Roche Diagnostics, Invitrogen; details of the assay methods are described in the numerous application protocols). The number of cells in cell culture experiments can be determined by simple
35 counting or by colorimetric assays which measure the metabolic activity of the cells (e.g. wst-1, Roche Diagnostics). Metabolic assay methods measure the number of cells in an experiment indirectly via enzymic markers. Cell proliferation may be measured directly by analyzing

2015201738 07 Apr 2015

the rate of DNA synthesis, for example by adding bromodeoxyuridine (BrdU), with the integrated BrdU being detected colorimetrically via specific antibodies.

5 2. Apoptosis and cytotoxicity

A large number of assay systems for detecting cellular apoptosis and cytotoxicity are available. A decisive characteristic is the specific, enzyme-dependent fragmentation of genomic DNA, which is irreversible and results in certain death of the cell. Methods for detecting these specific DNA fragments are commercially obtainable. An additional method available is the TUNEL assay which can detect DNA single-strand breaks also in tissue sections. Cytotoxicity is mainly detected via an altered cell permeability which serves as marker of the vitality state of cells. This involves on the one hand the analysis of markers which can typically be found intracellularly in the cell culture supernatant. On the other hand, it is also possible to analyze the absorbability of dye markers which are not absorbed by intact cells. The best-known examples of dye markers are Trypan blue and propidium iodide, a common intracellular marker is lactate dehydrogenase which can be detected enzymatically in the supernatant. Different assay systems of various commercial suppliers (e.g. Roche Diagnostics, Invitrogen) are available.

3. Migration assay

The ability of cells to migrate is analyzed in a specific migration assay, preferably with the aid of a Boyden chamber (Corning Costar) (Cinamon G., Alon R. J. Immunol. Methods. 2003 Feb; 273(1-2):53-62; Stockton et al. 2001. Mol. Biol. Cell. 12: 1937-56). For this purpose, cells are cultured on a filter with a specific pore size. Cells which can migrate are capable of migrating through this filter into another culture vessel below. Subsequent microscopic analysis then permits determination of a possibly altered migration

behavior induced by the gain of function or loss of function of the target molecule.

b. Functional analysis in animal models

5 A possible alternative of cell culture experiments for the analysis of target gene function are complicated in vivo experiments in animal models. Compared to the cell-based methods, these models have the advantage of being able to detect faulty developments or diseases
10 which are detectable only in the context of the whole organism. A multiplicity of models for human disorders are available by now (Abate-Shen & Shen. 2002. Trends in Genetics S1-5; Matsusue et al. 2003. J. Clin. Invest. 111:737-47). Various animal models such as, for
15 example, yeast, nematodes or zebra fish have since been characterized intensively. However, models which are preferred over other species are mammalian animal models such as, for example, mice (*Mus musculus*) because they offer the best possibility of reproducing
20 the biological processes in a human context. For mice, on the one hand transgenic methods which integrate new genes into the mouse genome have been established in recent years (gain of function; Jegstrup I. et al. 2003. Lab Anim. 2003 Jan.; 37(1):1-9). On the other
25 hand, other methodical approaches switch off genes in the mouse genome and thus induce a loss of function of a desired gene (knockout models, loss of function; Zambrowicz BP & Sands AT. 2003. Nat. Rev. Drug Discov. 2003 Jan; 2(1):38-51; Niwa H. 2001. Cell Struct. Funct. 2001 Jun; 26(3):137-48); technical details have been
30 published in large numbers.

After the mouse models have been generated, alterations induced by the transgene or by the loss of function of
35 a gene can be analyzed in the context of the whole organism (Balling R, 2001. Ann. Rev. Genomics Hum. Genet. 2:463-92). Thus it is possible to carry out, for example, behavior tests as well as to biochemically study established blood parameters. Histological

analyses, immunohistochemistry or electron microscopy enable alterations to be characterized at the cellular level. The specific expression pattern of a gene can be detected by in-situ hybridization (Peters T. et al. 2003. Hum. Mol. Genet 12:2109-20).

Example 3: Identification of SEQ ID NO: 1/2 as a diagnostic and therapeutic cancer target

SEQ ID NO: 1 (nucleic acid sequence) is encoded by a new gene on chromosome 6 (6q26-27) and represents the deduced protein sequence (SEQ ID NO: 2). An alternative open reading frame of this gene locus is SEQ ID NO: 267 which codes for the deduced protein sequence SEQ ID NO: 268. Both protein sequences show no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing a specific quantitative RT-PCR (primer pair SEQ ID NO: 3 and 4). The transcript was not detected in any of the normal tissues analyzed. Surprisingly, we detected very specifically substantial amounts of said transcript in almost all melanoma samples studied, although the gene is not expressed in normal skin as tissue of origin (fig. 1). The selectivity of this marker for melanomas was confirmed by a conventional RT-PCR (fig. 2). Surprisingly, we amplified in the process two fragments which reflect gene-specific variants (probably SEQ ID NO: 1 and SEQ ID NO: 267).

We thus demonstrate that this gene is an absolutely specific marker for melanoma cells and, due to its absence in each of the normal tissues studied, is suitable as biomarker for targeted therapeutic and diagnostic approaches.

In particular it is possible to utilize according to the invention extracellular portions of SEQ ID NO: 2 or 268 as target structure of monoclonal antibodies. This applies inter alia to the following epitopes: amino acids 1-50 based on SEQ ID NO: 2, amino acids 1-12

based on SEQ ID NO: 268, amino acids 70-88 based on SEQ ID NO: 2, amino acids 33-129 based on SEQ ID NO: 268, and SEQ ID NO: 281.

According to the invention, other target-oriented approaches such as vaccines and therapies with small compounds, which have only this gene as target structure and thus do not affect any healthy cells, are also therapeutically conceivable. Said gene may also be utilized diagnostically owing to its selectivity for tumor cells.

Example 4: Identification of SEQ ID NO: 5/6 as diagnostic and therapeutic cancer target

SEQ ID NO: 5 (nucleic acid sequence) is encoded by a new gene on chromosome 11 (11q12.1) and represents the deduced protein sequence (SEQ ID NO: 6). An alternative open reading frame of this gene locus is SEQ ID NO: 269 which codes for the deduced protein sequence SEQ ID NO: 270. Both protein sequences show no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcript in healthy tissue and in carcinoma samples (in each case pool of samples) was studied after establishing a gene-specific quantitative RT-PCR (primer pair SEQ ID NO: 7 and 8). We detected no specific RNA at all or else only small amounts thereof in the healthy tissues we studied, with the exception of testis (fig. 3; A quantitative RT-PCR; B gel image). Consequently, there is a high probability of the locus expressing a germ cell-specific gene product. However, the gene is activated in many tumor samples, and specific RNA was detectable in substantial amounts (fig. 3). The highest prevalence and level of expression were found in renal cell tumors. But specific transcripts were also detectable in gastric, pancreatic, ENT and lung tumors (fig. 4; A quantitative RT-PCR; B gel image). Even repeated examinations of the corresponding normal tissues were unable to detect gene-specific transcripts. In order to additionally

prove expression from this gene locus, a Northern blot was additionally carried out. For this purpose, a probe was prepared in a specific PCR of primers SEQ ID NO: 7 and 8 with incorporation of digoxigenin-dUTP (Roche Diagnostics) according to the manufacturer's instructions. The probe was then hybridized with 2 µg (fig. 5, lane 1) and 1 µg (fig. 5, lane 2), respectively, of total RNA from testis tissue and the digoxigenin of said probe was subsequently detected in a specific color reaction. An approx. 3.1 kB gene-specific fragment was detected in the experiment (fig. 5) and thus additionally confirmed expression of this locus. Said gene locus is thus a typical representative of the class of the "cancer/testis antigens" which are expressed in normal tissues virtually exclusively in the germ cells of the testis. In tumors, however, cancer/testis antigens are frequently switched on, although they are not expressed in the underlying somatic normal tissue cells. Several members of this functionally and structurally heterogeneous class are already tested for specific immunotherapeutic approaches with cancers in phase I/II studies, owing to their attractive selective tissue distribution (e.g. Scanlan MJ, Gure AO, Jungbluth AA, Old LJ, Chen YT. 2002. Immunol. Rev. 2002 Oct; 188:22-32). Antibodies may be produced by utilizing the peptides according to SEQ ID NO: 282 and 283. In particular, according to the invention it is possible to utilize the extracellular domains of SEQ ID NO: 6 and SEQ ID NO: 270 as target structures of monoclonal antibodies.

Example 5: Identification of LOC203413 as diagnostic and therapeutic cancer target

The gene or protein of the gene locus LOC203413 (nucleic acid sequence: SEQ ID NO: 9; amino acid sequence: SEQ ID NO: 10) is a gene on the X chromosome (Xq24), which has not been characterized previously. Aside from a transmembrane domain, it has no further

functional motifs and no homologies to previously known proteins.

According to the invention, the amount of transcript in healthy tissue and in carcinoma samples (pool of samples, number indicated in the figure) was studied after establishing an LOC203413-specific quantitative RT-PCR (primer pair SEQ ID NO: 11 and 12) (fig. 6; A: quantitative evaluation, B: image after gel-electrophoretic fractionation). LOC203413-specific RNA

cannot be detected in any of the healthy tissues we studied, with the exception of testis. Consequently, it is highly probable that LOC203413 is a germ cell-specific gene product. As fig. 6 reveals, LOC203413-specific transcripts were detectable in gastric, pancreatic, esophageal, mammary, ovarian and prostate carcinomas, with high expression being observed in particular in gastric and mammary carcinomas. For a more detailed analysis, healthy gastric samples and gastric carcinoma samples were additionally characterized in a quantitative RT-PCR (fig. 7A). LOC203413 was expressed in 70% of the carcinomas, whereas no significant expression was detectable in any of the healthy gastric samples. The MKN45 cell line which is derived from a gastric carcinoma also expresses LOC203413. In addition, specific expression was detected in 2/3rds of pancreatic tumors studied and in 40% of liver carcinomas (fig. 7B).

LOC203413 is thus a typical representative of the class of cancer/testis antigens which are expressed in normal tissues exclusively in the germ cells of the testis. In tumors, however, cancer/testis antigens are frequently switched on, although they are not expressed in the underlying somatic normal tissue cells. Several members of this functionally and structurally heterogeneous class are already tested for specific immunotherapeutic approaches with cancers in phase I/II studies, owing to their attractive selective tissue distribution (e.g. Scanlan MJ, Gure AO, Jungbluth AA, Old LJ, Chen YT. 2002. Immunol. Rev. 2002 Oct; 188:22-32).

2015201738 07 Apr 2015

In particular it is possible to utilize according to the invention the extracellular domain of LOC203413 as target structure of monoclonal antibodies. Thus the amino acids 22-113 (SEQ ID NO: 284) are of interest as epitopes. Conserved N-glycosylation motifs are located in the sequence at amino acid positions 34 and 83, based on SEQ ID NO: 10, which motifs may be suitable in particular for producing tumor-specific antibodies. LOC203413-specific antibodies were produced by using the peptides listed under SEQ ID NO: 285 and 286. According to the invention, other target-oriented approaches such as vaccines and therapies with small compounds, which have only this gene as target structure and thus do not affect any healthy cells, are also therapeutically conceivable. Said gene may also be utilized diagnostically owing to its selectivity for tumor cells.

Example 6: Identification of LOC90625 as a diagnostic and therapeutic cancer target

The gene LOC90625 (nucleic acid sequence: SEQ ID NO: 13) is a gene on chromosome 21 (21q22.3), which has not been characterized previously. It encodes a protein (amino acid sequence: SEQ ID NO: 14) having a trans-membrane domain but otherwise no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples (pool of samples, the number is indicated in the figure) was investigated after establishing an LOC90625-specific quantitative RT-PCR (primer pair SEQ ID NO: 15 and 16) (fig. 8). LOC90625 is expressed very selectively in healthy tissue, with specific transcripts being detectable especially in testis. In all other healthy tissues analyzed LOC90625-specific expression was detectable only at a low level, if at all (fig. 8). Surprisingly, we detected LOC90625-specific overexpression in some types of tumors.

LOC90625 was strongly overexpressed in particular in prostate, esophageal and pancreatic carcinomas, in comparison to the respective healthy tissue samples (figs. 8 and 9A).

5 LOC90625 is a selectively expressed antigen which is obviously increasingly expressed in proliferating tissues. Thus a selective overexpression in tumors can be observed which is therapeutically utilizable. The extracellular domain of LOC90625 in particular can
10 be utilized according to the invention as target structure of monoclonal antibodies. Said structure may be, for example, 1-19 (SEQ ID NO: 287) or else the amino acids 40-160 (SEQ ID NO: 288). LOC203413-specific antibodies were produced by using the peptides
15 according to SEQ ID NO: 289 and 290.

Example 7: Identification of the FAM26A protein as a diagnostic and therapeutic cancer target

The FAM26A gene (SEQ ID NO: 17; NM_182494) which is
20 located on chromosome 10 (10q24) encodes the gene product of SEQ ID NO: 18 (NP_872300). FAM26A has several transmembrane domains, with an N-glycosylation motif being located at amino acid position 142. The deduced protein sequence displays a distant homology to
25 the PMP/claudin family.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in tumor samples was investigated after establishing an FAM26A-specific quantitative RT-PCR (primer pair SEQ ID NO: 19 and 20)
30 (fig. 10). Surprisingly, we were able to detect overexpression of FAM26A in various tumors. FAM26A was expressed at a distinctly higher level in particular in ovarian, gastric, esophageal, pancreatic and liver tumors, in comparison with the corresponding healthy
35 tissue. According to the invention, selectively high expression of FAM26A in various tumor tissues may be utilized for molecular diagnostic methods such as, for example, RT-PCR for detecting tumor cells in tissue biopsies.

In order to further verify the expression data, FAM26A-specific antibodies were produced by immunization of animals. Polyclonal antibodies were produced by using the peptides listed under SEQ ID NO: 291 and 292. The specificity of the antibodies was demonstrated by Western blot analysis (fig. 11A: SEQ ID NO: 291; B: SEQ ID NO: 292). For this purpose, COS cells were transfected with an FAM26 fragment-encoding plasmid construct. The Western blot showed a specific signal with both antibodies, which was not detectable in the respective controls (fig. 11). We detected FAM26A also in various cervical, ovarian and pancreatic tumors, using a SEQ ID NO: 292-specific antibody (fig. 12), as well as in the cell lines SW480, EFO 27 and SNU 16 which were in each case RT-PCR-positive, using a SEQ ID NO: 291-specific antibody (fig. 13A). Here we found, in addition to an approx. 50 kDa specific band, also a weaker band at approx. 40 kDa. The latter corresponds to about the expected size. The major fragment at 50 kDa represents a post-translationally modified protein. The endogenous FAM26A protein was moreover detected in SW480 cells by means of immunofluorescence using a SEQ ID NO: 292-specific antibody. The analysis reveals localization in the plasma membrane (fig. 13B). In order to analyze localization of FAM26A in a tissue assemblage, healthy testis samples were characterized immunohistologically. In testis, the FAM26A protein was detected specifically in the membrane of spermatocytes, and due to the results, a membrane localization of FAM26A appears likely (fig. 14). This was also confirmed in tumor samples (fig. 15).

The extracellular domains of FAM26A in particular may be utilized according to the invention as target structures of monoclonal antibodies. These are, based on SEQ ID NO: 17, the amino acids 38-48 (SEQ ID NO: 293) and the amino acids 129-181 (SEQ ID NO: 294). Alternatively, the C-terminal amino acids 199-334 (SEQ ID NO: 295) may also be preferred epitopes for

producing antibodies for diagnostic or therapeutic purposes. In addition, the N-glycosylation motif at position 142 may be an interesting point of attack for therapeutic antibodies.

Example 8: Identification of SEMA5B as diagnostic and therapeutic cancer target

The gene semaphorin 5B (SEMA5B; SEQ ID NO: 21) which encodes the protein of SEQ ID NO: 22 is located on chromosome 3 (3q21.1). SEMA5B is a type I transmembrane protein and belongs to the family of semaphorins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples (pool of samples, the number is indicated in the figure) was investigated after establishing an SEMA5B-specific quantitative RT-PCR (primer pair SEQ ID NO: 23 and 24) (fig. 16). We found that, in healthy tissue, SEMA5B is very selectively restricted to testis and skin. In all other healthy tissues analyzed SEMA5B-specific expression was detectable at low level or not at all (fig. 16). In contrast, we surprisingly found SEMA5B-specific overexpression in some types of tumors, in particular in kidney carcinomas and breast tumors (fig. 17A and B), in comparison to the respective healthy tissues.

Said selective overexpression in tumors can be utilized therapeutically.

The extracellular domain of SEMA5B (aa 20-1035; SEQ ID NO: 296) in particular may be utilized according to the invention as target structure of antibodies. SEMA5B is a type I transmembrane domain protein (TM aa 1035-1057) whose C terminus is located inside the cell (aa 1058-1151). SEMA5B-specific antibodies were produced by using the peptides according to SEQ ID NO: 297 and 298.

Example 9: Identification of GJB5 as a diagnostic and therapeutic cancer target

The protein GJB5 (nucleic acid sequence: SEQ ID NO: 25; amino acid sequence: SEQ ID NO: 26) is a member of the

connexin family. The gene consists of two exons and is located on chromosome 1 (1p35.1). The deduced amino acid sequence codes for a protein of 273 amino acids. Connexins have an important function in cell-cell contacts via "gap junctions" which are used for exchanging small cytoplasmic molecules, ions and secondary transmitters and thus enable individual cells to communicate with each other. Gap junctions consist of several connexin subunits which form a membrane channel. 11 different members of the connexins have been described to date, all of which are located in a gene cluster on chromosome 1 (Richard, G.; Nature Genet. 20: 366-369, 1998). GBJ5 has four transmembrane domains, with the N and C termini of the protein being located inside the cell.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated (pool of samples, the number is indicated in the figure) after establishing a GBJ5-specific quantitative RT-PCR (primer pair SEQ ID NO: 27, 28). Our studies reveal differential distribution of expression in normal tissues. We found GBJ5 transcripts to be expressed virtually exclusively in the esophagus and in the skin, with transcription being very weak or not detectable in all other tissues analyzed (fig. 18). Very strong tumor-specific overexpression was observed in esophageal, colon, gastric and pancreatic carcinomas (fig. 18). This was confirmed by analyzing individual samples of the four carcinomas (fig. 19 A-D). In addition, the GBJ5-specific transcript can clearly be detected in the established cell lines LoVo, MKN45 and NCI-N87 (fig. 19 A-D).

The extracellular domains of GBJ5 in particular may be utilized according to the invention as target structure of therapeutic antibodies. Based on SEQ ID NO: 26, the amino acids 41-75 (SEQ ID NO: 299) and the region between amino acids 150 and 187 (SEQ ID NO: 300) are located extracellularly. GBJ5-specific antibodies were

produced by using the peptides according to SEQ ID NO: 301 and 302.

Example 10: Identification of KLK5 as a diagnostic and therapeutic cancer target

The gene KLK5 (SEQ ID NO: 29) and its translation product (SEQ ID NO: 30) is a member of the kallikrein family, a group of serine proteases with very different physiological functions. The gene is located on chromosome 19 (19q13.3-13.4) and codes for a serine protease. KLK5 is synthesized as pro form and is activated by proteolysis in the stratum corneum (Brattsand, M et al; *J. Biol. Chem.* 274: 1999). The active protease (aa 67-293) is secreted and is involved in the process of desquamation. The propeptide (aa 30-67) remains bound to the cell surface via the transmembrane domain (aa 1-29) (Ekholm, E et al; *Jour Investigative Dermatol*, 114; 2000).

According to the invention the distribution of KLK5-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing a KLK5-specific quantitative RT-PCR (primer pair SEQ ID NO: 31, 32) (fig. 20). In most normal tissues expression of KLK5 is at a very low to non-existent level, with moderate expression of KLK5 being found only in testis, esophagus, skin and prostate. We detected significant overexpression of KLK5 in esophageal carcinomas, cervical and in ENT tumors, in comparison with the corresponding normal tissues of origin (fig. 20, 21). Distinctly weaker but detectable KLK5-specific expression was moreover detected in some tumors of other tissues (e.g. in gastric and pancreatic carcinomas).

The extracellular domain of KLK5 in particular may be utilized according to the invention as target structure of therapeutic antibodies (SEQ ID NO: 303). The region of the propeptide (amino acids 30 to 67) is particularly suitable for this. KLK5-specific anti-

bodies were produced by using the peptide listed under SEQ ID NO: 304.

Example 11: Identification of LOC352765 as a diagnostic and therapeutic cancer target

The LOC352765 gene locus is located on chromosome 9 (9q34.12). The gene (SEQ ID NO: 33) encodes the gene product of SEQ ID NO: 34. The LOC352765 protein has a transmembrane domain at the N terminus. The hypothetical protein displays no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples (pool of samples) was investigated after establishing an LOC352765-specific quantitative RT-PCR (primer pair SEQ ID NO: 35 and 36) (fig. 22). LOC352765 is expressed very selectively in healthy tissue, and we found specific transcripts to be detectable only in testis, skin and bladder. In contrast, LOC352765-specific overexpression was detected in some types of tumors. Particularly in breast tumors, expression was higher than in the normal tissue with the highest level of expression. We also found LOC352765 to be distinctly overexpressed in colon and ovarian carcinomas and in ENT tumors (figs. 22, 23).

Owing to its selective overexpression in tumors, LOC352765 can be utilized therapeutically. The extracellular domain of LOC352765 (amino acids 44-211, SEQ ID NO: 34) in particular may be utilized according to the invention as target structure of antibodies and other targeted forms of therapy. Specific antibodies were produced by using the peptides according to SEQ ID NO: 305 and 306.

Example 12: Identification of SVCT1 as a diagnostic and therapeutic cancer target

The gene SVCT1 (SEQ ID NO: 37) is located on chromosome 7 (7q33) and codes for the gene product of SEQ ID NO: 38. The SVCT1 protein has four transmembrane

domains and displays no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples (pool of samples) was investigated after establishing an SVCT1-specific quantitative RT-PCR (primer pair SEQ ID NO: 39 and 40) (fig. 24). SVCT1 in healthy tissue is restricted selectively to kidney, testis, thymus and mammary gland. In contrast, SVCT1-specific overexpression was surprisingly detected in some types of tumors. SVCT1 is strongly overexpressed in particular in carcinomas of the kidney, esophagus and pancreas and in ENT tumors (figs. 24, 25), and that is not only in comparison with the corresponding healthy tissue of origin but also with respect to the normal tissue with the highest level of expression over all. SVCT1 can be therapeutically utilized owing to its selective overexpression in tumors. The extracellular domains of SVCT1 in particular may be utilized according to the invention as target structures of antibodies and for other targeted forms of therapy. Specific antibodies were produced by using the peptides according to SEQ ID NO: 307 and 308.

Example 13: Identification of LOC199953 as a diagnostic and therapeutic cancer target

The gene or protein of the LOC199953 gene locus (nucleic acid sequence: SEQ ID NO: 41; amino acid sequence: SEQ ID NO: 42) is located on chromosome 1 (1q36.22). The protein has several transmembrane domains. Alternative open reading frames of this gene locus are SEQ ID NO: 271 with its gene product SEQ ID NO: 272 and SEQ ID NO: 273 with the corresponding gene product SEQ ID NO: 274. Other than that, the hypothetical protein displays no further homologies to previously known protein domains.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an LOC199953-

specific quantitative RT-PCR (primer pair SEQ ID NO: 43 and 44). LOC199953 is selectively expressed in healthy tissues and overexpressed in some tumors. In particular, it was possible to identify overexpression in ENT and kidney carcinomas (fig. 26) in approx. 50% of the tumor samples, in comparison with normal tissues.

According to the invention, the extracellular domains of LOC199953 may be utilized as target structure of antibodies.

Example 14: Identification of TMEM31 as a diagnostic and therapeutic cancer target

The gene TMEM31 (SEQ ID NO: 45) of the LOC203562 gene locus is located on chromosome X (Xq22.2). The gene codes for the protein of SEQ ID NO: 46. Said protein has two transmembrane domains and otherwise displays no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing a TMEM31-specific quantitative RT-PCR (primer pair SEQ ID NO: 47 and 48). In healthy tissues, TMEM31 is very selectively restricted especially to testis (fig. 27).

Surprisingly, we also found expression in some types of tumors, whereas no expression was detectable in the corresponding normal tissues. Said tumors are in particular carcinomas of the kidney, colon, stomach, breast, liver and lung and ENT carcinomas (figs. 27, 28).

TMEM31 is thus a typical representative of the class of cancer/testis antigens which are expressed in normal tissues exclusively in the germ cells of the testis. In tumors, however, cancer/testis antigens are frequently switched on, although they are not expressed in the underlying somatic normal tissue cells. Several members of this functionally and structurally heterogeneous class are already tested for specific immunotherapeutic approaches with cancers in phase I/II studies, owing to

their attractive selective tissue distribution (e.g. Scanlan MJ, Gure AO, Jungbluth AA, Old LJ, Chen YT. 2002. Immunol. Rev. 2002 Oct; 188:22-32).

The extracellular TMEM31 domains may be utilized according to the invention as target structure of antibodies.

Example 15: Identification of FLJ25132 as a diagnostic and therapeutic cancer target

The FLJ25132 gene/protein (nucleic acid sequence: SEQ ID NO: 49; amino acid sequence: SEQ ID NO: 50) is located on chromosome 17 (17q25.3). FLJ25132 has a transmembrane domain but otherwise does not display any homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an FLJ25132-specific quantitative RT-PCR (primer pair SEQ ID NO: 51 and 52). FLJ25132 is partially overexpressed in the carcinoma samples studied by us, in comparison to healthy tissue (fig. 29). Distinct overexpression of FLJ25132 was detected in particular in ovarian and in prostate carcinomas.

The extracellular FLJ25132 domains may be utilized according to the invention as target structure of antibodies.

Example 16: Identification of LOC143724, LOC284263, LOC283435 and LOC349260 as diagnostic and therapeutic cancer targets

The gene loci (with the correspondingly encoded genes and gene products), LOC143724, LOC284263, LOC283435 and LOC349260, are combined, owing to their similar profiles.

The gene with SEQ ID NO: 53, which is present in the LOC143724 gene locus on chromosome 11 (11q13.1), encodes the gene product SEQ ID NO: 54. SEQ ID NO: 275 with its gene product SEQ ID NO: 276 represents an alternative open reading frame of this gene locus,

which is either a separate transcript or a splice variant of SEQ ID NO: 53. The primers according to SEQ ID NO: 55 and 56 were used for gene-specific amplification of said gene.

- 5 The gene with SEQ ID NO: 89, which is present in the LOC284263 gene locus on chromosome 18 (18q21.1), encodes the gene product with SEQ ID NO: 90. The primers according to SEQ ID NO: 91 and 92 were used for gene-specific amplification of said gene.
- 10 The gene with SEQ ID NO: 117, which is present in the LOC283435 gene locus on chromosome 12 (12q24.32), encodes the gene product with SEQ ID NO: 118. The primers according to SEQ ID NO: 119 and 120 were used for gene-specific amplification of said gene.
- 15 The gene with SEQ ID NO: 121, which is present in the LOC349260 gene locus on chromosome 9 (9q11.2), encodes the gene product with SEQ ID NO: 122. The primers according to SEQ ID NO: 123 and 124 were used for gene-specific amplification of said gene.
- 20 All proteins have transmembrane domains and, in addition, do not display any homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples
25 was investigated after establishing specific quantitative RT-PCR analyses. None of the four genes were detected in the healthy tissues which are investigated, with the exception of testis. Consequently, there is a high probability of said genes
30 being germ cell-specific. However, surprisingly significant expression is found in various tumor samples.

The four genes are thus typical representatives of the class of cancer/testis antigens which are expressed in
35 normal tissues exclusively in the germ cells of the testis. In tumors, however, cancer/testis antigens are frequently switched on, although they are not expressed in the underlying somatic normal tissue cells. Several members of this functionally and structurally

heterogeneous class are already tested for specific immunotherapeutic approaches with cancers in phase I/II studies, owing to their attractive selective tissue distribution (e.g. Scanlan MJ, Gure AO, Jungbluth AA, Old LJ, Chen YT. 2002. Immunol. Rev. 2002 Oct; 188:22-32).

The extracellular domains of the four genes may be utilized according to the invention as target structure of antibodies.

Example 17: Identification of the sequence according to SEQ ID NO: 57 as a diagnostic and therapeutic cancer target

The sequence according to SEQ ID NO: 57 is derived from a gene on chromosome 1 (1p21.3) and encodes the protein sequence according to SEQ ID NO: 58. SEQ ID NO: 277 with its gene product SEQ ID NO: 278 represents an alternative transcript of said gene locus. The transmembrane protein does not display any homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing a specific quantitative RT-PCR (primer pair SEQ ID NO: 59 and 60).

SEQ ID NO: 57 is selectively expressed in the healthy tissues studied by us (fig. 30). Specific transcripts were detectable in nearly all types of tumors analyzed and overexpressed in particular in liver, ENT and kidney tumors. This was confirmed in the analysis of individual tumor samples in comparison with healthy tissue samples (fig. 31).

The extracellular domains of the sequence according to SEQ ID NO: 58 may be utilized according to the invention as target structure of antibodies, in particular with amino acids 20-38 and 90-133 being located extracellularly.

Example 18: Identification of LOC119395 as a diagnostic and therapeutic cancer target

The gene with SEQ ID NO: 61, which is present in the LOC119395 gene locus on chromosome 17 (17q25.3), encodes a gene product with SEQ ID NO: 62. The transmembrane protein displays no homologies to previously known proteins.

According to the invention the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an LOC119395-specific quantitative RT-PCR (primer pair SEQ ID NO: 63 and 64) (fig. 32). LOC119395 is very selectively expressed in the healthy tissues studied by us and is detectable only in a few tissues (fig. 32). In contrast, LOC119395-specific transcripts were detectable in nearly all types of tumors analyzed. In parts distinct, tumor-selective overexpression of LOC119395 was observed in particular in gastric, ovarian and prostate carcinomas. This was confirmed in the analysis of individual tumor samples in comparison with healthy tissue samples (fig. 33). It was possible to detect overexpression of LOC119395 in mammary carcinomas and esophageal tumors in comparison with the respective healthy tissue. Tumor-selective expression was identified in colon carcinomas and gastric carcinomas (fig. 33).

The extracellular LOC119395 domain (amino acids 44-129) may be utilized according to the invention as target structure of antibodies.

Example 19: Identification of LOC121838 as a diagnostic and therapeutic cancer target

The gene which is located in the LOC121838 gene locus on chromosome 13 (13q14.11) and has the transcript of SEQ ID NO: 65 encodes the protein with SEQ ID NO: 66. The transmembrane protein displays no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an LOC121838-specific quantitative RT-PCR (primer pair SEQ ID NO: 67

and 68) (fig. 34A). LOC121838 is very selectively expressed in the healthy tissues studied by us and is detectable only in a few tissues (fig. 34A and B). In contrast, LOC121838-specific transcripts were
5 detectable in many types of tumors analyzed. We found distinct tumor-selective overexpression of LOC121838 in particular in ovarian and esophageal carcinomas. The extracellular LOC121838 domains may be utilized according to the invention as target structure of
10 antibodies.

Example 20: Identification of LOC221103 as a diagnostic and therapeutic cancer target

The gene which is localized in the LOC221103 gene locus
15 on chromosome 11 (11q12.3) and has the transcript of SEQ ID NO: 69 encodes the protein with SEQ ID NO: 70. The transmembrane protein displays no homologies to previously known proteins.

According to the invention, the amount of gene-specific
20 transcripts in healthy tissue and in carcinoma samples was investigated after establishing an LOC221103-specific quantitative RT-PCR (primer pair SEQ ID NO: 71 and 72). In the healthy tissues studied by us, LOC221103 is expressed only in the liver and otherwise
25 not detectable (fig. 35). Surprisingly, LOC221103-specific transcripts are overexpressed in liver carcinomas (fig. 36).

The extracellular LOC221103 domains may be utilized according to the invention as target structure of
30 antibodies.

Example 21: Identification of LOC338579 as a diagnostic and therapeutic cancer target

The gene which is localized in the LOC338579 gene locus
35 on chromosome 10 (10q11.21) and has the transcript of SEQ ID NO: 73 encodes the protein with SEQ ID NO: 74. The transmembrane protein displays no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an LOC338579-specific quantitative RT-PCR (primer pair SEQ ID NO: 75 and 76). We found expression in healthy tissues only in testis and, at a lower level, in the liver and the thymus. Surprisingly, we found LOC338579 overexpression in colon carcinomas and liver carcinomas in comparison with the healthy tissue (fig. 37).

The extracellular LOC338579 domains may be utilized according to the invention as target structure of antibodies.

Example 22: Identification of LOC90342 as a diagnostic and therapeutic cancer target

The gene which is located in the LOC90342 gene locus on chromosome 2 (2q11.2) and has the transcript of SEQ ID NO: 77 encodes the protein with SEQ ID NO: 78. The transmembrane protein includes a calcium-binding motif (CalB) which is conserved in protein kinase C and in various phospholipases.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an LOC90342-specific quantitative RT-PCR (primer pair SEQ ID NO: 79 and 80) (fig. 38). We found LOC90342 only in a small number of healthy tissues, most of which are of little relevance with regard to toxicity (fig. 38). In contrast, we found LOC90342-specific transcripts in a multiplicity of the types of tumors analyzed. In parts distinctly tumor-selective overexpression of LOC90342 was observed in particular in gastric, liver, pancreatic, prostate, ovarian and lung carcinomas.

The membrane protein has a single transmembrane domain (aa 707-726). The extracellular LOC90342 domain may be utilized according to the invention as target structure of therapeutic antibodies.

Example 23: Identification of LRFN1 as a diagnostic and therapeutic cancer target

LRFN1 (SEQ ID NO: 81) is a gene which is localized on chromosome 19 (19q13.2). The gene codes for the protein of SEQ ID NO: 82. Said protein includes a transmembrane domain and displays homologies to the Myb DNA-binding domain and to a C2-type immunoglobulin domain.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an LRFN1-specific quantitative RT-PCR (primer pair SEQ ID NO: 83 and 84). LRFN1 is very weakly expressed in most of the normal tissues studied, except for activated PBMC and brain (fig. 39). In contrast, we found LRFN1-specific transcripts to be increasingly detectable in some of the types of tumors analyzed. We found distinct tumor-selective overexpression of LRFN1 in particular in gastric, pancreatic, esophageal and mammary carcinomas, in comparison with the corresponding normal tissues.

The protein includes a transmembrane domain (aa 448-470). The extracellular LRFN1 domains may be utilized according to the invention as target structure of therapeutic antibodies.

Example 24: Identification of LOC285916 as a diagnostic and therapeutic cancer target

The gene which is localized in the LOC285916 gene locus on chromosome 7 (7p22.3) and has the transcript of SEQ ID NO: 85 encodes the protein with SEQ ID NO: 86. The transmembrane protein displays no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an LOC285916-specific quantitative RT-PCR (primer pair SEQ ID NO: 87 and 88). In the healthy tissues studied by us, LOC285916 is expressed selectively in testis, with no or only little expression being detected by us in all other tissues studied (fig. 40A). Surprisingly, we

found LOC285916-specific transcripts in all types of tumors tested. Distinct tumor-specific overexpression was detectable in particular in mammary, esophageal, renal, ENT and lung carcinomas (figs. 40A and B).

- 5 The extracellular LOC285916 domains (amino acids 42 to 93) may be utilized according to the invention as target structure of antibodies.

10 **Example 25: Identification of MGC71744 as a diagnostic and therapeutic cancer target**

The MGC71744 gene with SEQ ID NO: 93 on chromosome 17 (17p13.2) encodes the protein with SEQ ID NO: 94. The transmembrane protein displays no homologies to previously known proteins.

- 15 According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples (pool of samples) was studied after establishing an MGC71744-specific quantitative RT-PCR (primer pair SEQ ID NO: 95 and 96) (fig. 41). MGC71744 is hardly
20 expressed in healthy tissue. We found small amounts of specific transcripts only in the lung and in the spleen. The level of MGC71744-specific expression in all other healthy tissues analyzed was low or not detectable at all (fig. 41A). In contrast, we
25 surprisingly found MGC71744-specific overexpression in some types of tumors, in particular in carcinomas of the kidney (figs. 41A & B), in comparison with healthy tissue.

- 30 The extracellular domain of MGC71744 (N terminus, aa 67-85) in particular may be utilized according to the invention as target structure of antibodies.

Example 26: Identification of LOC342982 as a diagnostic and therapeutic cancer target

- 35 The gene which is localized in the LOC342982 gene locus on chromosome 19 (19p13.13) and has the transcript of SEQ ID NO: 97 encodes the protein with SEQ ID NO: 98. The transmembrane protein displays homologies to the carbohydrate binding domain of C-type lectins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples (pool of samples) was investigated after establishing an LOC342982-specific quantitative RT-PCR (primer pair
5 SEQ ID NO: 99 and 100). LOC342982-specific RNA is selectively expressed, with only a low level of expression or no expression being detectable in many normal tissues analyzed (fig. 42). In contrast, nearly
10 all of the classes of tumors tested exhibited overexpression which was partly tumor-specific. Primarily pancreatic, kidney, lung and mammary carcinomas exhibit very strong expression of LOC342982-specific RNA (fig. 42).

The extracellular domain of LOC342982 (amino acids
15 178-339) in particular may be utilized according to the invention as target structure of monoclonal antibodies.

Example 27: Identification of LOC343169/OR6F1 as a diagnostic and therapeutic cancer target

20 The gene OR6F1 which is localized in the LOC343169 gene locus on chromosome 1 (1q44) and has the transcript of SEQ ID NO: 101 encodes the protein with SEQ ID NO: 102. OR6F1 has several transmembrane domains and belongs to the family of olfactory receptors and thus to the large
25 family of G protein-coupled receptors.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples (pool of samples) was investigated after establishing an LOC343169/OR6F1-specific quantitative RT-PCR (primer
30 pair SEQ ID NO: 103 and 104) (fig. 43A). LOC343169/OR6F1 is very selectively expressed in healthy tissue, with specific transcripts being detectable especially in testis and spleen. The level of LOC343169/OR6F1-specific expression was low or not
35 detectable at all in all other healthy tissues analyzed (fig. 43A). In contrast, LOC343169/OR6F1-specific overexpression was surprisingly detected in some types of tumors. Tumor-specific overexpression of LOC343169/OR6F1 is seen in particular in mammary,

ovarian, kidney, prostate, pancreatic and liver carcinomas (fig. 43A). An analysis of individual samples confirmed overexpression in ovarian carcinomas. LOC343169/OR6F1 is a selectively expressed antigen
5 which is obviously increasingly expressed in proliferating tissues. Thus selective overexpression in tumors can be observed which is therapeutically utilizable. The extracellular domains in particular may be utilized according to the invention as target
10 structures of monoclonal antibodies.

Example 28: Identification of LOC340204 as a diagnostic and therapeutic cancer target

The gene which is localized in the LOC340204 gene locus
15 on chromosome 6 (6p21.31) and has the transcript of SEQ ID NO: 105 encodes the protein with SEQ ID NO: 106. Said protein has a transmembrane domain. Moreover said protein displays strong homology to a "colipase" domain. A cofactor function for pancreatic lipase is
20 attributed to colipase. SEQ ID NO: 279 with its gene product SEQ ID NO: 280 represents an alternative transcript of said gene locus, which could be both a separate transcript and a splice variant of SEQ ID NO: 105.

25 According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an LOC340204-specific quantitative RT-PCR (primer pair SEQ ID NO: 107 and 108). LOC340204 is selectively expressed in
30 healthy tissues and strongly overexpressed in some tumors. Distinct overexpression in tumor samples in comparison with various normal tissues was detected in particular in gastric, pancreatic, ovarian, lung and esophageal carcinomas (fig. 44).

35 The extracellular LOC340204 domains may be utilized according to the invention as target structure of monoclonal antibodies.

Example 29: Identification of LOC340067 as a diagnostic and therapeutic cancer target

The gene which is localized in the LOC340067 gene locus on chromosome 5 (5q22.3) and has the transcript of SEQ ID NO: 109 encodes the protein with SEQ ID NO: 110. The transmembrane protein displays no homologies to other protein domains.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing a quantitative RT-PCR (primer pair SEQ ID NO: 111 and 112) specific for LOC340067. LOC340067 is selectively expressed in healthy tissues and strongly overexpressed in some tumors (fig. 45). Distinct overexpression in tumor samples in comparison with various healthy tissues was detected in particular in pancreatic, mammary, liver, ovarian, lung and kidney carcinomas.

The extracellular LOC340067 domain may be utilized according to the invention as target structure of monoclonal antibodies.

Example 30: Identification of LOC342780 as a diagnostic and therapeutic cancer target

The gene which is localized in the LOC342780 gene locus on chromosome 18 (18q21.32) and has the transcript of SEQ ID NO: 309 encodes the protein with SEQ ID NO: 310. The transmembrane protein includes an acyltransferase domain which is present in many C. elegans proteins which have previously not been characterized in detail.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples (pool of samples, the number is indicated in the figure) was investigated after establishing an LOC342780-specific quantitative RT-PCR (primer pair SEQ ID NO: 311 and 312). LOC342780 is very selectively expressed in healthy tissue, with specific transcripts being detectable especially in the prostate, stomach, testis, lung and the mammary gland (fig. 46). In contrast, LOC342780-specific expression was

2015201738 07 Apr 2015

surprisingly detected in all types of tumors analyzed. Tumor-specific overexpression of LOC342780 is seen in particular in mammary, ovarian, kidney and liver carcinomas (fig. 46).

5 LOC342780 is a selectively expressed antigen which is obviously increasingly expressed in proliferating tissues. Thus selective overexpression in tumors can be observed which is therapeutically utilizable. The extracellularly located amino acids 76-89, 316-345,
10 399-493 and 650-665 (based on SEQ ID NO: 310) may be utilized according to the invention as target structures of monoclonal antibodies.

**Example 31: Identification of LOC339511 as a diagnostic
15 and therapeutic cancer target**

The sequence according to SEQ ID NO: 113 is derived from a gene which is located on chromosome 1 (1q23.1). The gene encodes the protein of SEQ ID NO: 114. The transmembrane protein displays homologies to the group
20 of olfactory 7-transmembrane receptors.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing a quantitative RT-PCR (primer pair SEQ ID NO: 115 and 116) specific for
25 LOC339511. In healthy tissues, LOC339511 is selectively expressed in the liver (fig. 47A). In the carcinoma samples, LOC339511-specific transcripts were identified in liver tumors, with weak expression being moreover detectable in colon carcinomas, mammary and lung
30 carcinomas. When comparing liver-specific expression in tumor and in healthy tissue, increased expression was detected in some tumor samples (fig. 47B).

The extracellular domains of SEQ ID NO: 113 may be utilized according to the invention as target
35 structures of monoclonal antibodies. In particular, the extracellularly located amino acid residues 1-23, 82-100, 167-175 and 226-236 are therefore particularly suitable for producing monoclonal antibodies.

Example 32: Identification of C14orf37 as a diagnostic and therapeutic cancer target

C14orf37 (SEQ ID NO: 125) is a gene which is localized on chromosome 14 (14q22.3) and which encodes the gene product with SEQ ID NO: 126. The transmembrane protein displays no homologies to previously known proteins.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing a quantitative RT-PCR (primer pair SEQ ID NO: 127 and 128) specific for C14orf37. C14orf37 is expressed in various healthy tissues, and strongest in testis (fig. 48). A distinct overexpression in comparison with various healthy tissues was detected in particular in kidney carcinomas.

The extracellular domain of SEQ ID NO: 126 may be utilized according to the invention as target structure of monoclonal antibodies.

Example 33: Identification of ATP1A4 as a diagnostic and therapeutic cancer target

The ATP1A4 gene (SEQ ID NO: 129) is located on chromosome 1 (1q21-23). The gene codes for a protein with SEQ ID NO: 130. ATP1A4 is an integral transmembrane protein with eight transmembrane domains, which is located in the plasma membrane. ATP1A4 is part of a protein complex, with the catalytical part of the sodium/potassium ATPase being present at the N terminus (Woo et al., J. 2000. Biol. Chem. 275, 20693-99). ATP1A4 displays strong homologies to numerous other representatives of the cation ATPase family.

According to the invention, the amount of gene-specific transcripts in healthy tissue and in carcinoma samples was investigated after establishing an ATP1A4-specific quantitative RT-PCR (primer pair SEQ ID NO: 131 and 132). In healthy tissues, ATP1A4 is selectively expressed especially in testis (fig. 49). Strong overexpression of ATP1A4 was detected in some tumor samples in comparison with the respective healthy tissue.

Distinct overexpression in tumor samples in comparison with healthy tissues was detected in particular in pancreatic, mammary, liver and kidney carcinomas (fig. 49), with expression in pancreatic and mammary carcinomas being very high over all.

The extracellular domains of ATP1A4 may be utilized according to the invention as target structure of monoclonal antibodies. The following amino acid residues, based on SEQ ID NO: 130, are located extracellularly: amino acid residues 129-137, 321-329, 816-857 and 977-990.

Example 34: Identification of SEQ ID NO: 133 to 264 as a diagnostic and therapeutic cancer target

The sequences according to SEQ ID NO: 133-266 are 33 genes (nucleic acid sequence, amino acid sequence), together with the respective PCR primers for specific RT-PCR reactions. All proteins have one or more transmembrane domains, but there is little information on homologies to protein domains.

According to the invention, the amount of the particular gene-specific transcripts in healthy tissue and in carcinoma samples was investigated for these genes in specific quantitative RT-PCR reactions. For all of the genes, overexpression which was partially strong in comparison with the respective healthy tissue was detected in tumor samples.

All genes of this group are therapeutically and diagnostically utilizable. The extracellular domains may be utilized here according to the invention as target structure of antibodies.

The claims defining the invention are as follows:

1. A pharmaceutical composition when used for treating a cancer disease characterized by an increased expression of a tumor-associated antigen, comprising one or more components selected from the group consisting of:
 - (i) a tumor-associated antigen or a part thereof,
 - (ii) a nucleic acid which codes for a tumor-associated antigen or a part thereof,
 - (iii) an antibody which binds to a tumor-associated antigen or a part thereof,
 - (iv) an antisense nucleic acid which hybridizes specifically with a nucleic acid coding for a tumor-associated antigen,
 - (v) a host cell which expresses a tumor-associated antigen or a part thereof, and
 - (vi) isolated complexes between a tumor-associated antigen or a part thereof and an HLA molecule, wherein said part comprises at least 6 consecutive amino acids of the tumor-associated antigen, said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
 - (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
 - (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).
2. The pharmaceutical composition as claimed in claim 1, in which the nucleic acid of (ii) is present in an expression vector.
3. The pharmaceutical composition as claimed in claim 1, in which the host cell secretes the tumor-associated antigen or the part thereof.

4. The pharmaceutical composition as claimed in claim 1, in which the host cell additionally expresses an HLA molecule which binds to the tumor-associated antigen or the part thereof.
5. The pharmaceutical composition as claimed in claim 4, in which the host cell expresses the HLA molecule and/or the tumor-associated antigen or the part thereof in a recombinant manner.
6. The pharmaceutical composition as claimed in claim 4, in which the host cell expresses the HLA molecule endogenously.
7. The pharmaceutical composition as claimed in claim 1, 4 or 6, in which the host cell is an antigen-presenting cell, preferably a dendritic cell, a monocyte or a macrophage.
8. The pharmaceutical composition as claimed in claim 1, in which the antibody is a monoclonal antibody.
9. The pharmaceutical composition as claimed in claim 1, in which the antibody is a chimeric or humanized antibody or an antigen-binding fragment of an antibody.
10. The pharmaceutical composition as claimed in claim 1, in which the antibody is coupled to a therapeutic or diagnostic agent.
11. The pharmaceutical composition as claimed in any one of claims 1-10, further comprising a pharmaceutically acceptable carrier and/or an adjuvant.
12. The pharmaceutical composition as claimed in any one of claims 1 to 11, in which the cancer disease is gastric cancer, colon cancer, rectal cancer,

renal cancer, breast cancer, prostate cancer, uterus cancer, ovarian cancer, endometrial cancer, esophagus cancer, blood cancer, liver cancer, pancreatic cancer, skin cancer, brain cancer, lung cancer, a lymphoma, or a neuroblastoma, a lung tumor, a breast tumor, a prostate tumor, a colon tumor, a renal cell carcinoma, a cervical carcinoma, a colon carcinoma, or a mamma carcinoma, or metastases of said cancer types or tumors.

13. The pharmaceutical composition as claimed in any one of claims 1-12, in which the tumor-associated antigen comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 14 and 287-290 of the sequence listing.
14. A method of diagnosing a cancer disease characterized by an increased expression of a tumor-associated antigen, which method comprises
 - (i) detection of a nucleic acid which codes for the tumor-associated antigen, and/or
 - (ii) detection of the tumor-associated antigen, and/or
 - (iii) detection of an antibody to the tumor-associated antigen and/or
 - (iv) detection of cytotoxic or T helper lymphocytes which are specific to the tumor-associated antigen or to a part thereof in a biological sample isolated from a patient, wherein the part comprises at least 6 consecutive amino acids of the tumor-associated antigen, said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
 - (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
 - (b) a nucleic acid which is at least 90%

identical in sequence to the nucleic acid of (a).

15. The method as claimed in claim 14, in which the detection comprises
 - (i) contacting the biological sample with an agent which binds specifically to the nucleic acid coding for the tumor-associated antigen, to the tumor-associated antigen, to the antibody or to the cytotoxic or T helper lymphocytes, and
 - (ii) detecting the formation of a complex between the agent and the nucleic acid, the tumor-associated antigen, the antibody or the cytotoxic or T helper lymphocytes.
16. The method as claimed in claim 14 or 15, in which the nucleic acid is detected using a polynucleotide probe which hybridizes specifically to said nucleic acid or by selectively amplifying said nucleic acid or a part thereof, which is specific for said nucleic acid.
17. The method as claimed in claim 14 or 15, in which the tumor-associated antigen is detected using an antibody binding specifically to said tumor-associated antigen.
18. The method as claimed in claim 14 or 15, in which the antibody is detected using a protein or peptide binding specifically to said antibody.
19. A method for determining regression, course or onset of a cancer disease characterized by an increased expression of a tumor-associated antigen, which method comprises monitoring a sample from a patient who has said disease or is suspected of falling ill with said disease, with respect to one or more parameters selected from the group consisting of:
 - (i) the amount of nucleic acid which codes for

the tumor-associated antigen,
(ii) the amount of the tumor-associated antigen,
(iii) the amount of antibodies which bind to the tumor-associated antigen, and
(iv) the amount of cytolytic or cytokine-releasing T cells which are specific for a complex between the tumor-associated antigen or a part thereof comprising at least 6 consecutive amino acids of the tumor-associated antigen,
said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
(a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
(b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).

20. The method as claimed in claim 19, in which the amount of the nucleic acid or is monitored using a polynucleotide probe which hybridizes specifically to said nucleic acid or by selectively amplifying said nucleic acid or a part thereof which is specific for said nucleic acid.
21. The method as claimed in claim 19, in which the amount of the tumor-associated antigen is monitored using an antibody binding specifically to said tumor-associated antigen.
22. The method as claimed in claim 19, in which the amount of antibodies is monitored using a protein or peptide binding specifically to the antibody.
23. The method as claimed in any one of claims 16-18 and 20-22, in which the polynucleotide probe, the antibody, or the protein or peptide is labeled in a detectable manner.

24. A method of treating a cancer disease characterized by an increased expression of a tumor-associated antigen, which method comprises administration of a pharmaceutical composition as claimed in any of claims 1-13, said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
- (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13, and
 - (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).
25. A method of treating, diagnosing or monitoring a cancer disease characterized by an increased expression of a tumor-associated antigen, which method comprises administering an antibody binding to said tumor-associated antigen and coupled to a therapeutic or diagnostic agent, said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
- (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
 - (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).
26. The method as claimed in any one of claims 17, 21 or 25, in which the antibody is a monoclonal antibody.
27. The method as claimed in any one of claims 17, 21 or 25, in which the antibody is a chimeric or humanized antibody, or an antigen-binding fragment of an antibody.
28. A method of treating a patient having a cancer disease characterized by an increased expression

of a tumor-associated antigen, which method comprises:

- (i) removing a sample containing immunoreactive cells from said patient,
 - (ii) contacting said sample with a host cell expressing said tumor-associated antigen or a part thereof comprising at least 6 consecutive amino acids of the tumor-associated antigen, under conditions which favor production of cytolytic or cytokine-releasing T cells against said tumor-associated antigen or the part thereof, and
 - (iii) introducing the cytolytic or cytokine-releasing T cells into the patient in an amount suitable for lysing cells expressing the tumor-associated antigen or the part thereof,
- said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
- (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
 - (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).

- 29. The method as claimed in claim 28, in which the host cell expresses an HLA molecule binding to the tumor-associated antigen or to the part thereof recombinantly or endogenously.
- 30. The method as claimed in claim 28 or 29, in which the host cells are nonproliferative.
- 31. A method of inhibiting the development of cancer in a patient, said cancer being characterized by an increased expression of a tumor associated antigen as defined in any one of claims 1 to 13, which method comprises administering an effective amount of a pharmaceutical composition as claimed in any one of claims 1-13.

32. The method as claimed in any one of claims 14-31, in which the tumor-associated antigen comprises an amino acid sequence according to SEQ ID NO: 13 of the sequence listing.
33. A kit when used for detecting expression of a tumor-associated antigen in tumor tissue, which kit comprises agents for detection
- (i) of the nucleic acid which codes for the tumor-associated antigen,
 - (ii) of the tumor-associated antigen,
 - (iii) of antibodies which bind to the tumor-associated antigen, and/or
 - (iv) of T cells which are specific for a complex between the tumor-associated antigen or a part thereof comprising at least 6 consecutive amino acids of the tumor-associated antigen and an MHC molecule,
- said tumor-associated antigen having a sequence encoded by a nucleic acid which is selected from the group consisting of:
- (a) a nucleic acid which comprises a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
 - (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).
34. A pharmaceutical composition when used for treating or preventing a cancer disease, said pharmaceutical composition comprising RNA interference (RNAi) which inhibits expression or activity of the tumor antigen according to SEQ ID NO: 14 of the sequence listing.
35. The pharmaceutical composition as claimed in claim 34, in which RNAi comprises a "short hairpin" structure (shRNA).

36. A method of treating, diagnosing or monitoring a metastasizing tumor characterized by an increased expression of at least one tumor antigen, which method comprises administering an antibody which binds to at least one tumor antigen and which is coupled to a therapeutic or diagnostic agent, said at least one tumor antigen having a sequence encoded by a nucleic acid consisting of:
- (a) a nucleic acid comprising a nucleic acid sequence according to SEQ ID NO: 13 of the sequence listing, and
 - (b) a nucleic acid which is at least 90% identical in sequence to the nucleic acid of (a).
37. The method as claimed in claim 36, in which the antibody is a monoclonal antibody.
38. The method as claimed in claim 36, in which the antibody is a chimeric or humanized antibody or an antigen-binding fragment of an antibody.

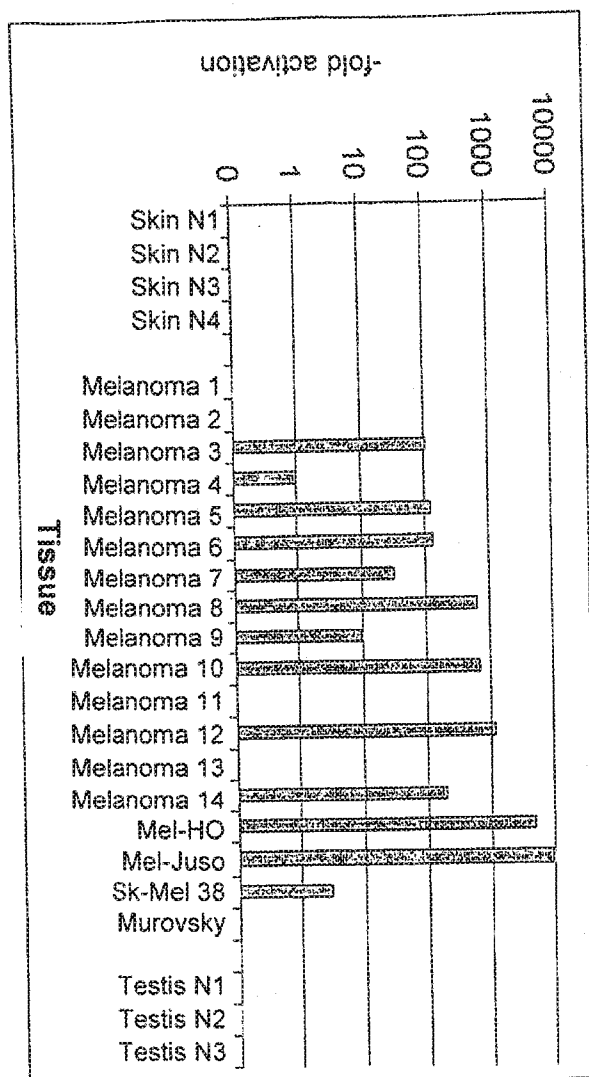


Fig. 1

Fig. 2

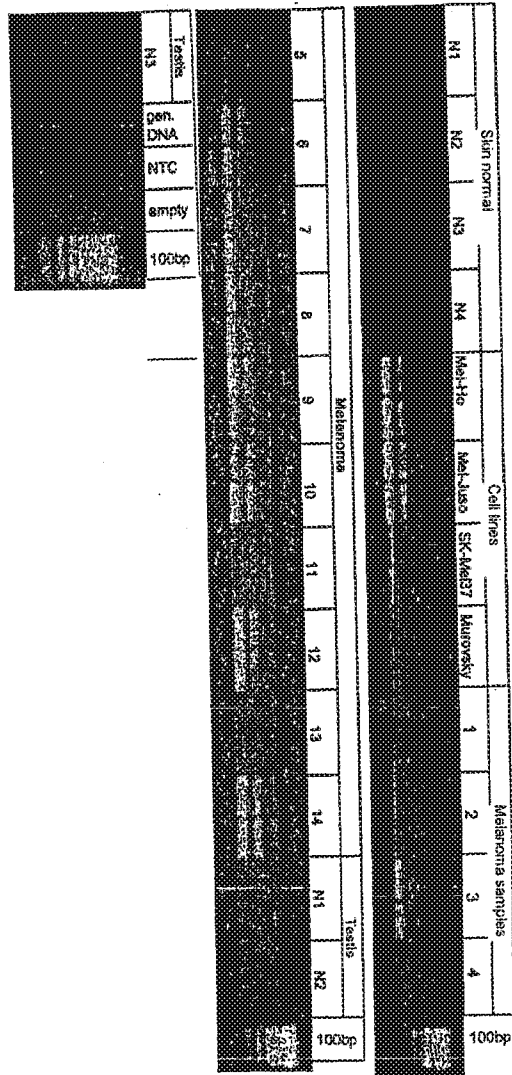


Fig. 3

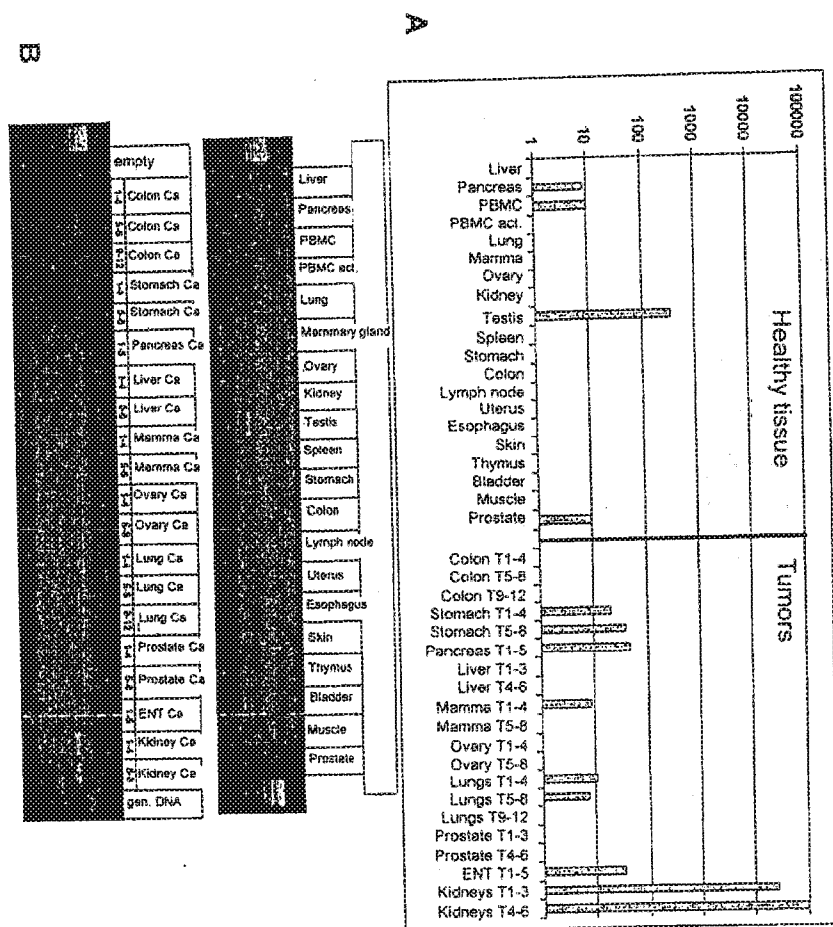
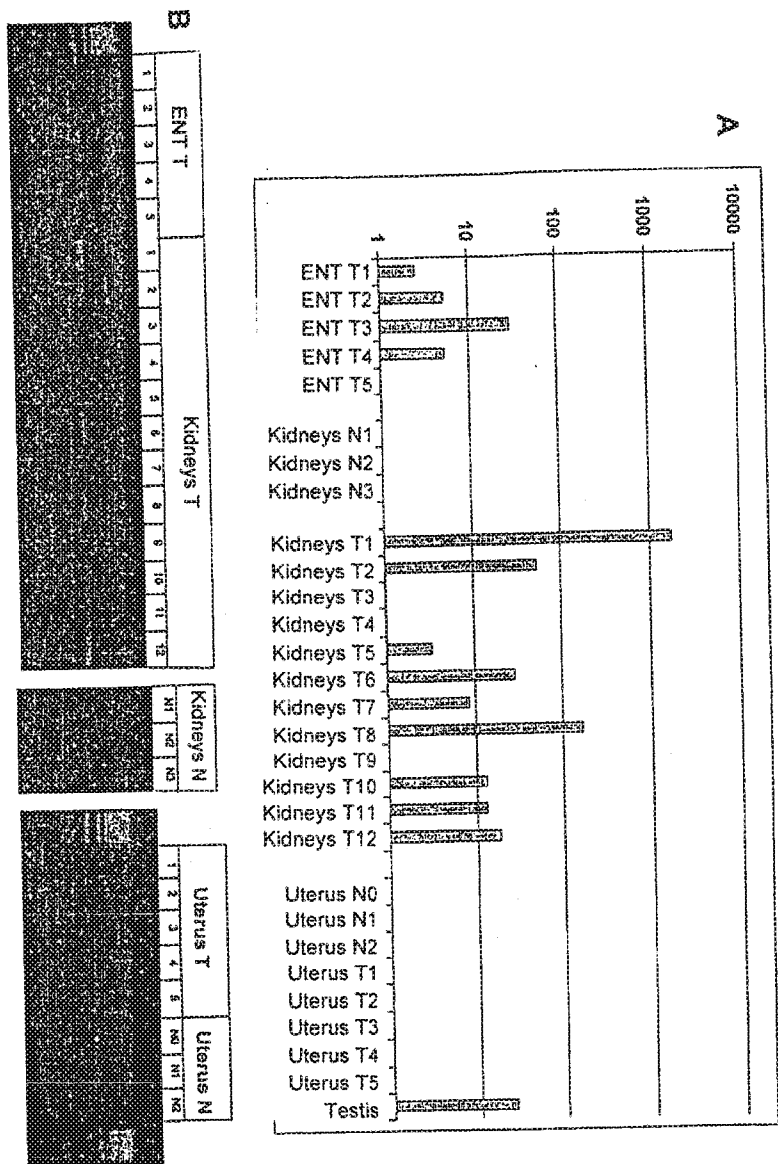


Fig. 4



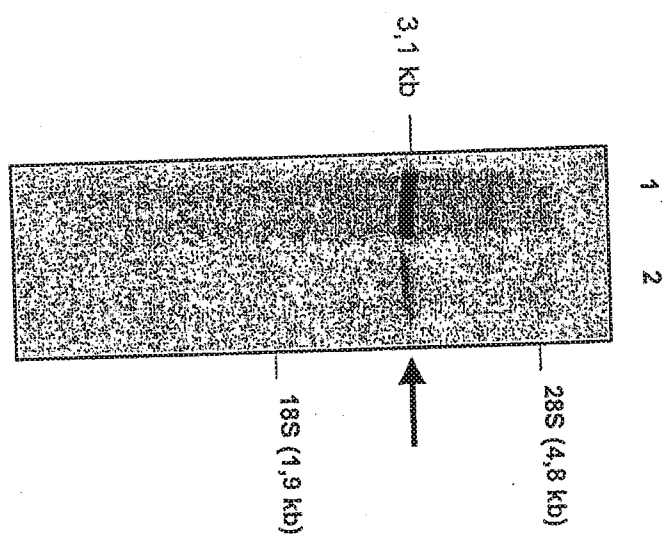


Fig. 5

6/50

A

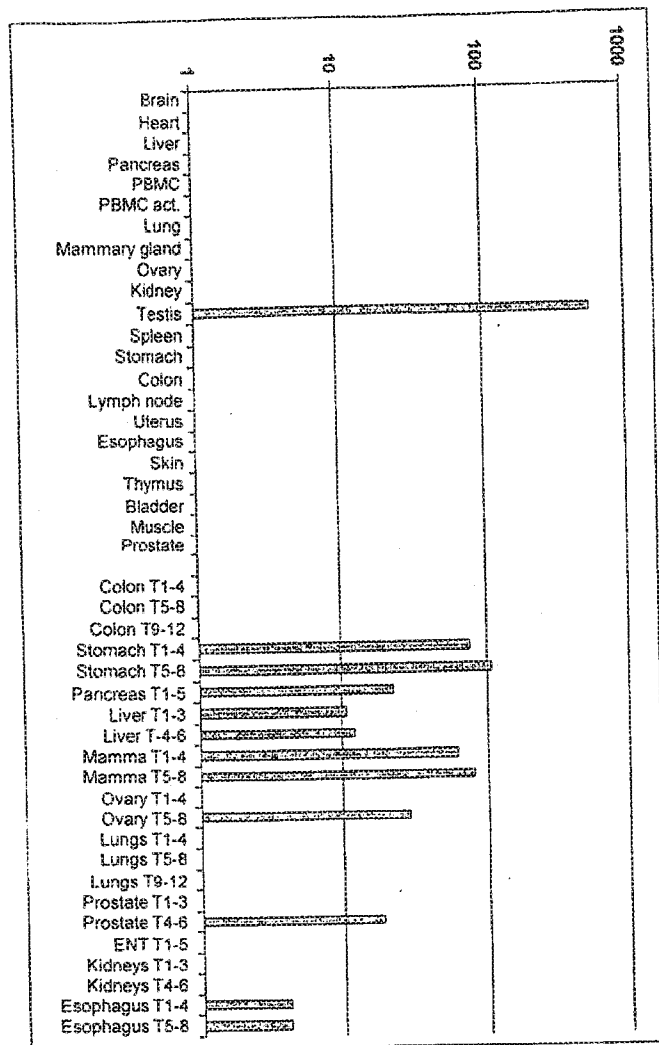


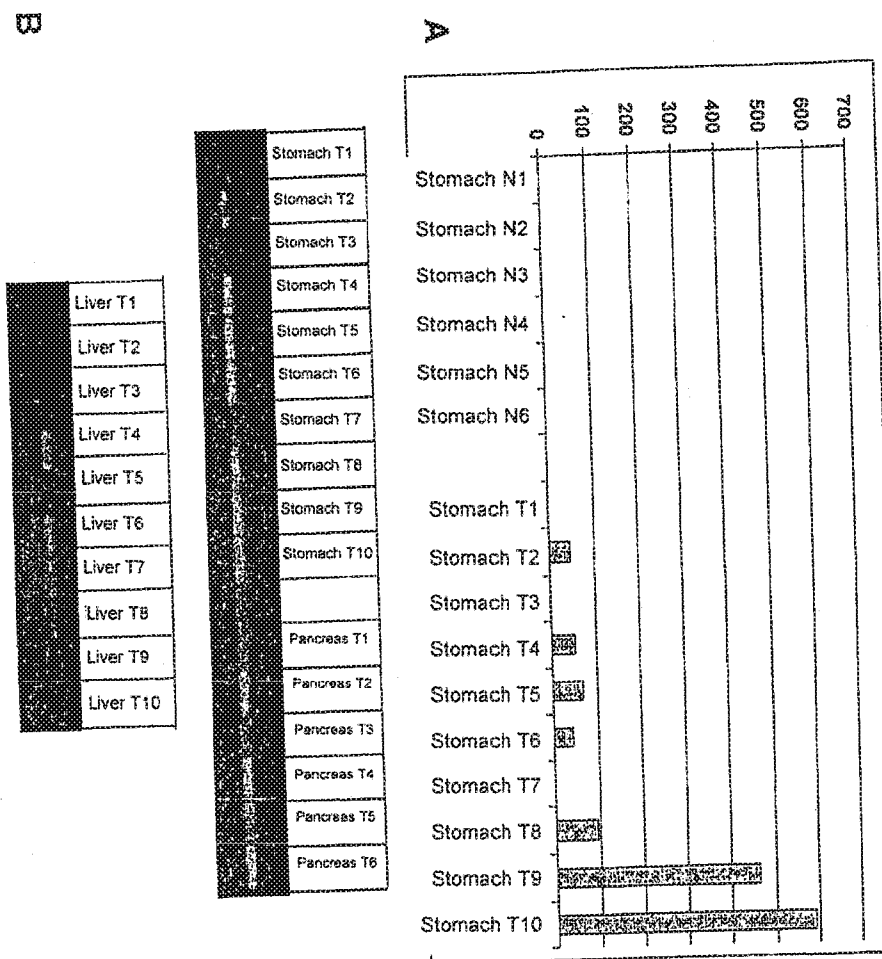
Fig. 6

B

Lungs T1-4	Colon T1-4	Stomach N	Brain N
Lungs T1-4	Colon T1-4	Stomach N	Brain N
Lungs T5-8	Colon T5-8	Colon N	Heart N
Lungs T5-8	Colon T5-8	Colon N	Heart N
Lungs T9-12	Colon T9-12	Lymph node N	Liver N
Lungs T9-12	Colon T9-12	Lymph node N	Liver N
Prostate T1-4	Stomach T1-4	Uterus N	Pancreas N
Prostate T1-4	Stomach T1-4	Uterus N	Pancreas N
Prostate T5-8	Stomach T5-8	Esophagus N	PBMC
Prostate T5-8	Stomach T5-8	Esophagus N	PBMC
ENT T1-5	Pancreas T1-5	Skin N	PBMC act.
ENT T1-5	Pancreas T1-5	Skin N	PBMC act.
Kidneys T1-4	Liver T1-4	Thymus N	Lung N
Kidneys T1-4	Liver T1-4	Thymus N	Lung N
Kidneys T5-8	Liver T5-8	Bladder N	Ovary N
Kidneys T5-8	Liver T5-8	Bladder N	Ovary N
genom. DNA	Mamma T1-4	Muscle N	Kidney N
genom. DNA	Mamma T1-4	Muscle N	Kidney N
Internal Cont.	Mamma T5-8	Neg C.	Testis N
Internal Cont.	Mamma T5-8	Neg C.	Testis N
	Ovary T1-4	empty	Spleen N
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	Ovary T5-8		empty

Fig. 6

Fig. 7



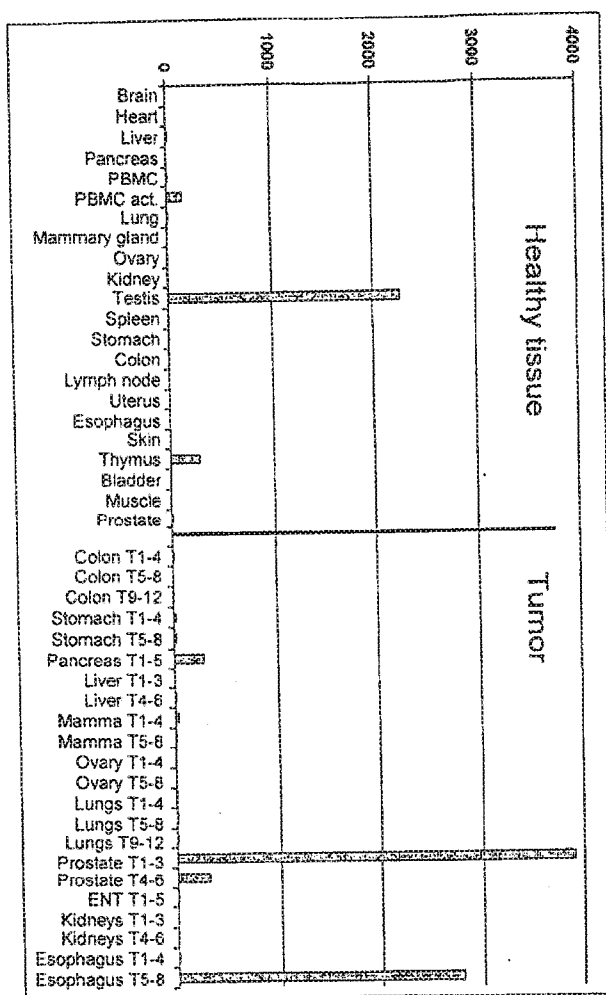


Fig. 8

Fig. 9

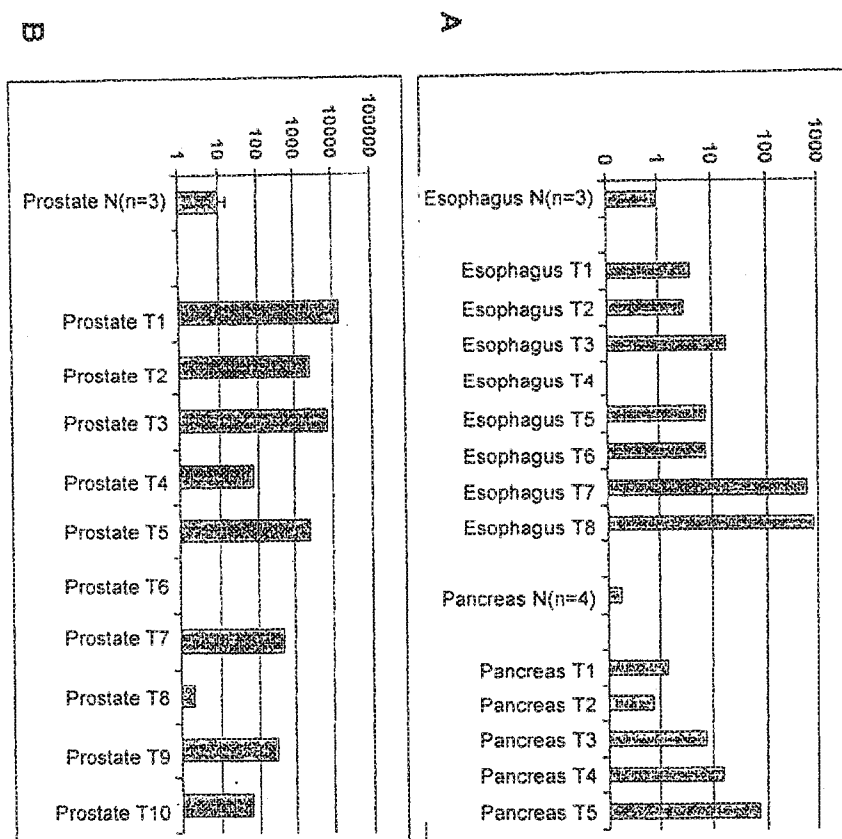


Fig. 10

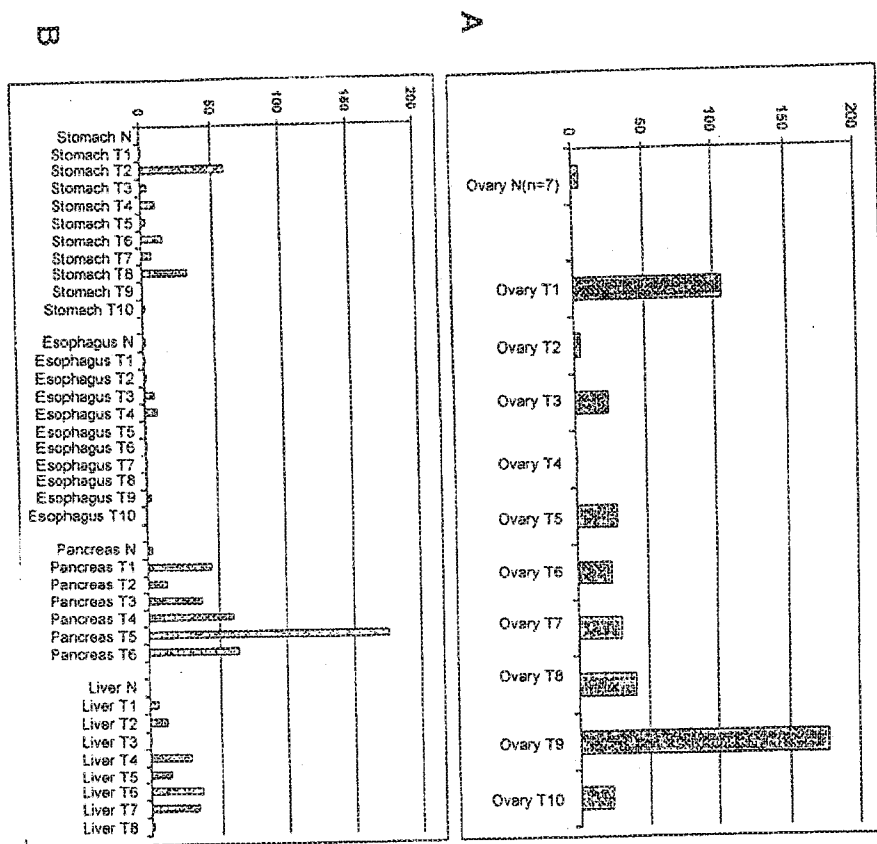


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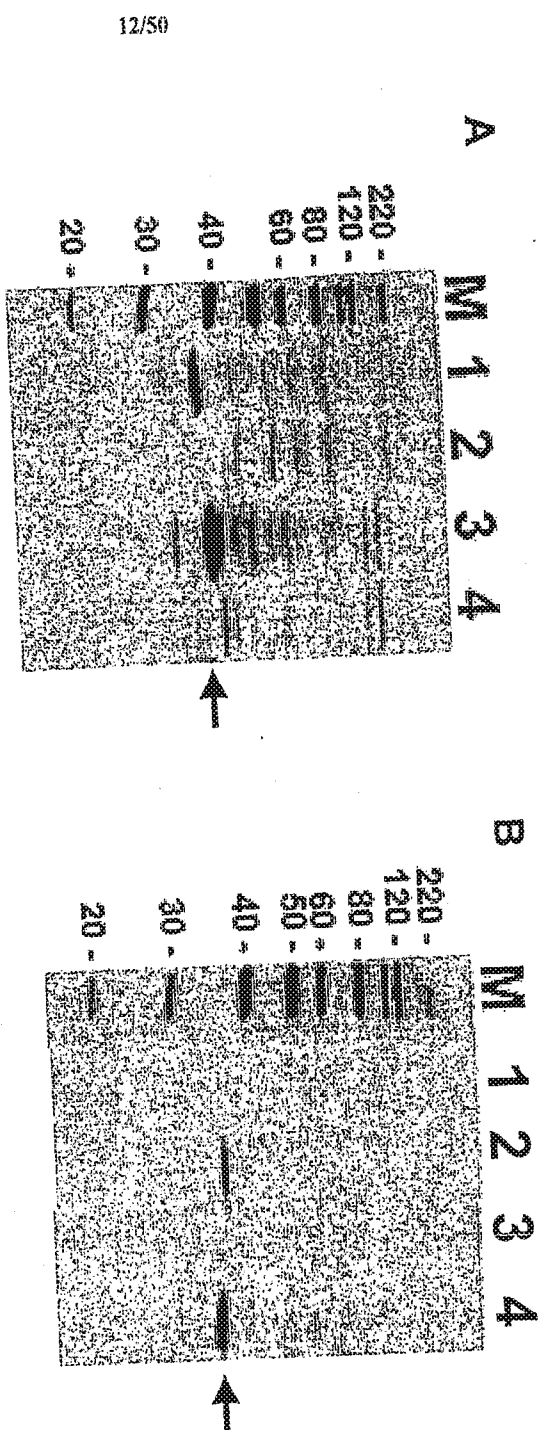


Fig. 12

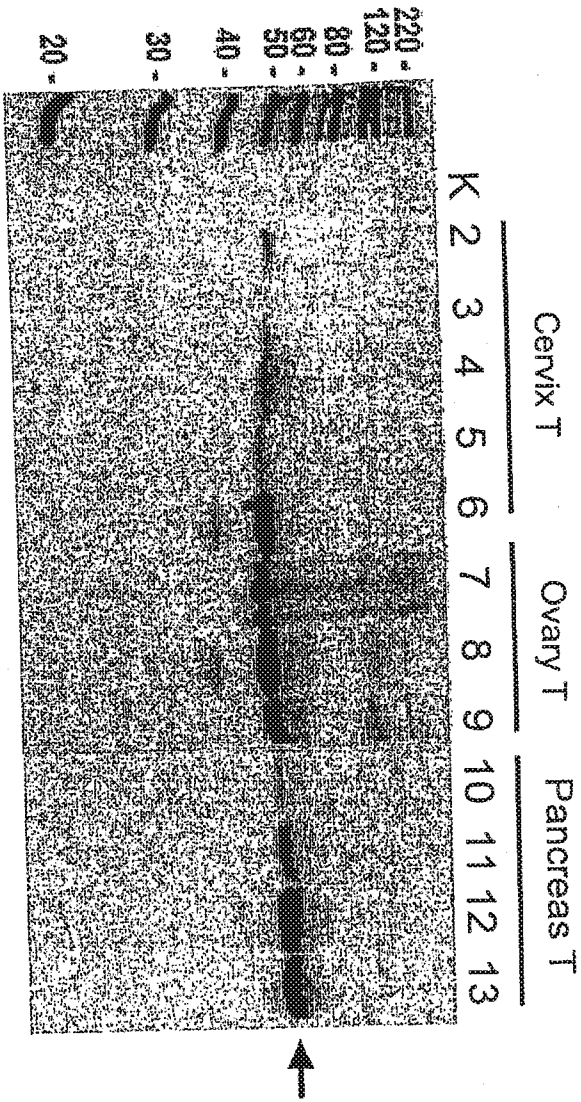


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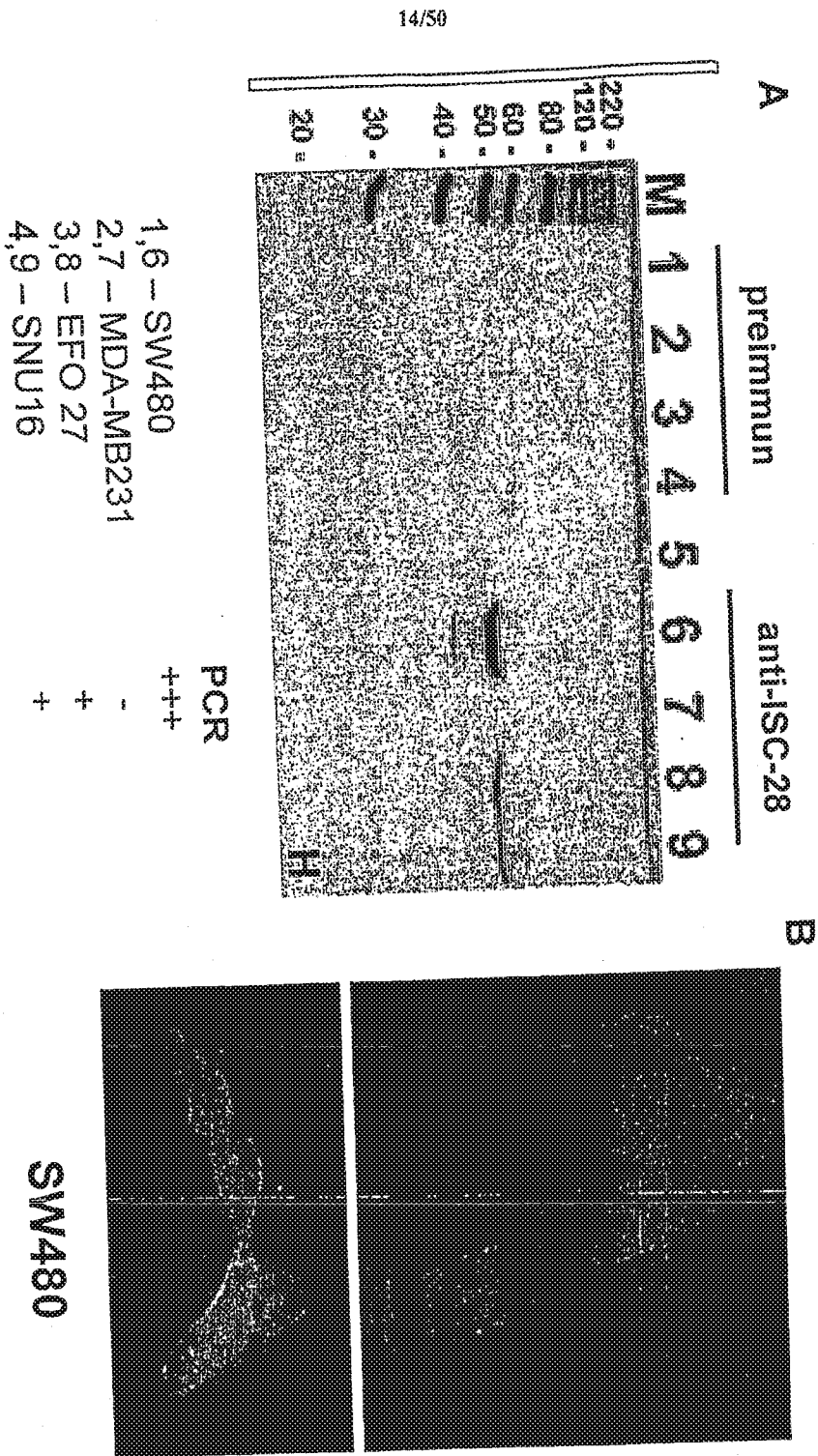
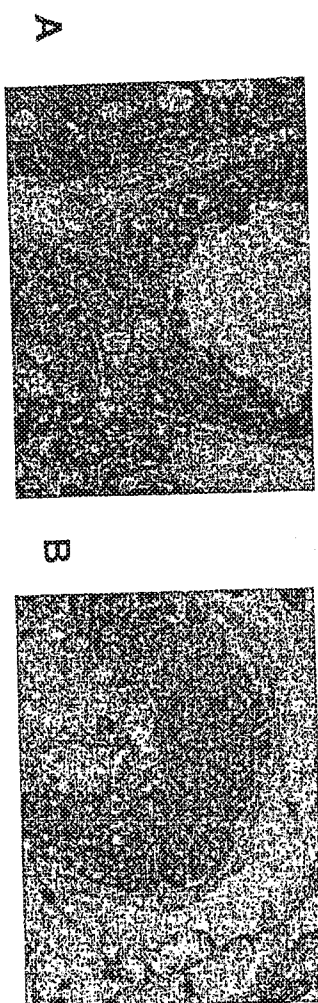
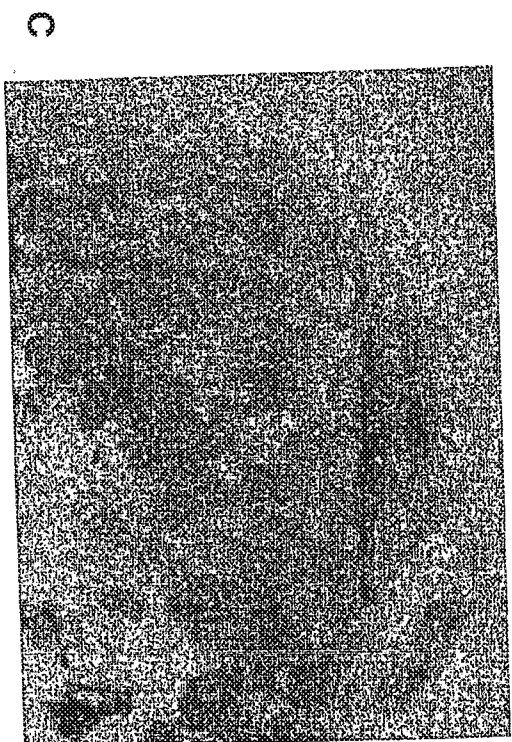


Fig. 14



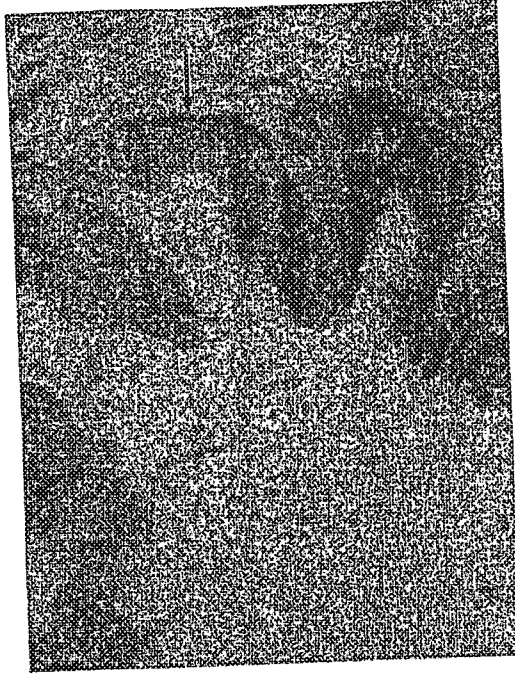
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A



B

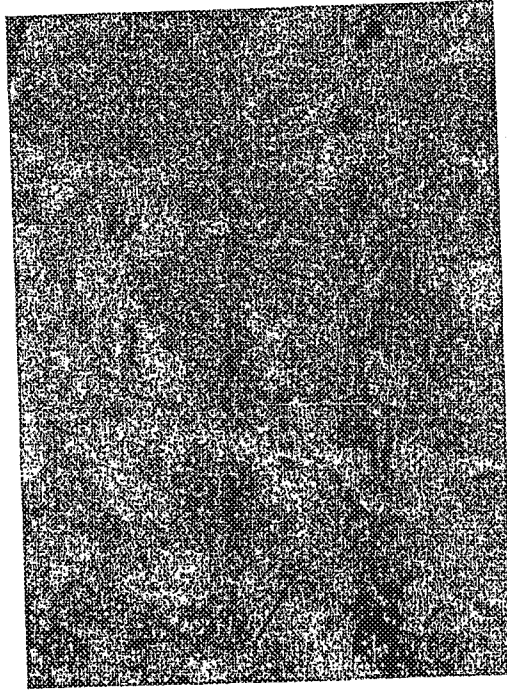


Fig. 15

17/50

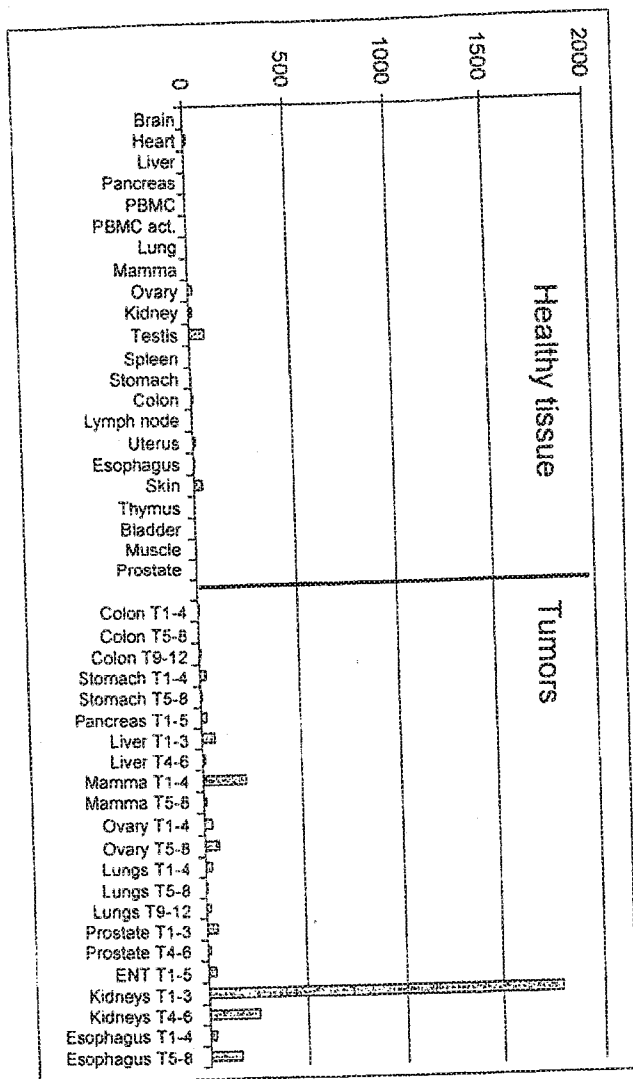
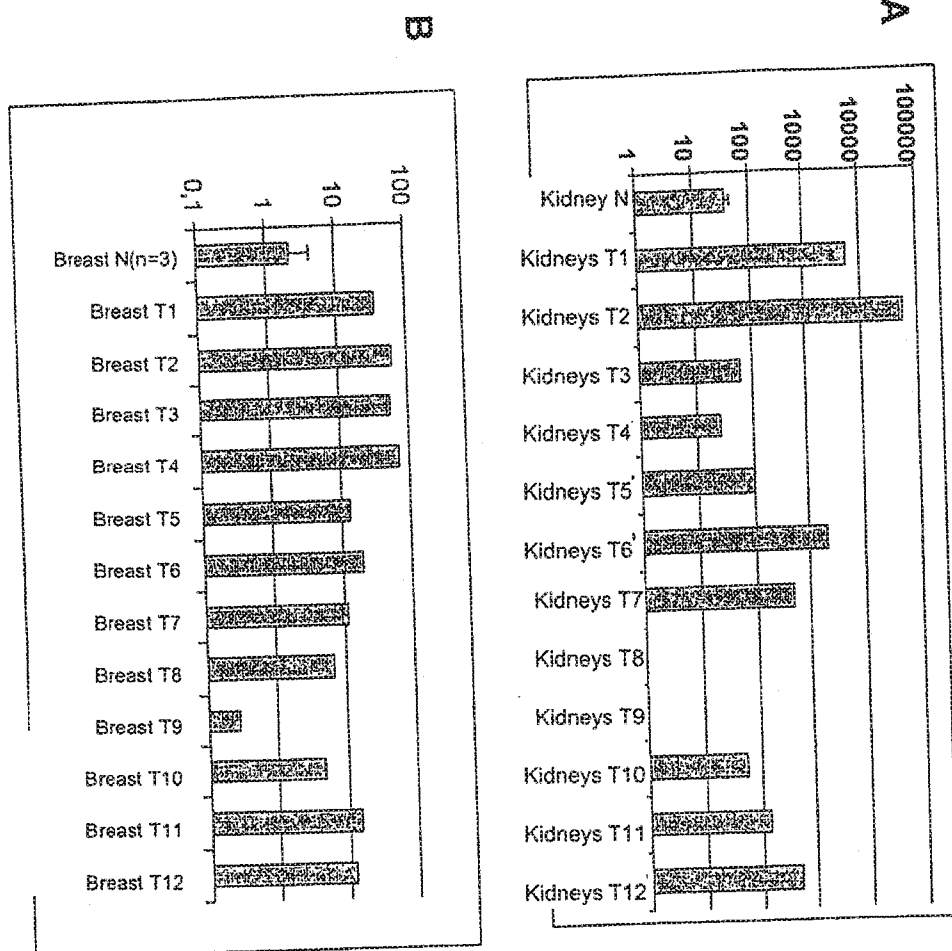


Fig. 16

Fig. 17



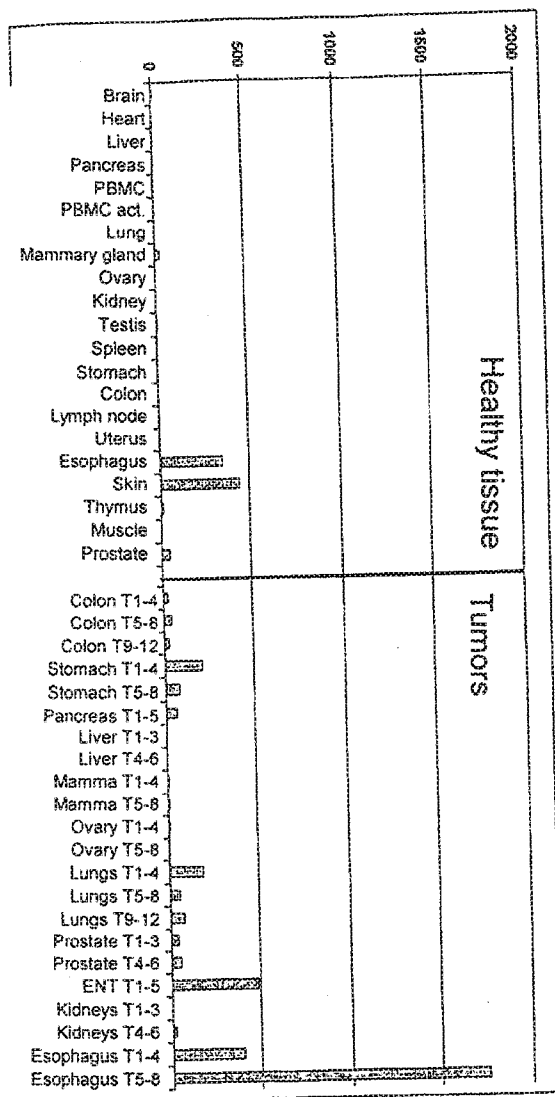
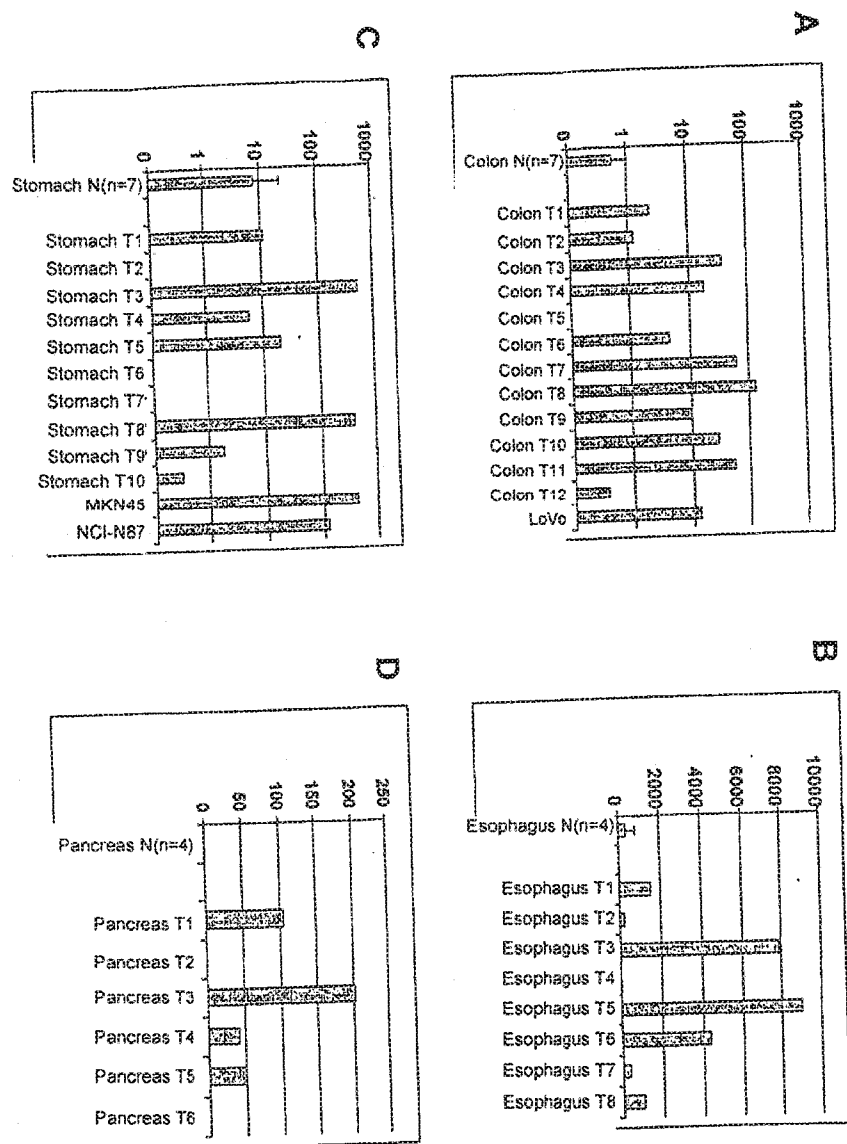


Fig. 18

Fig. 19



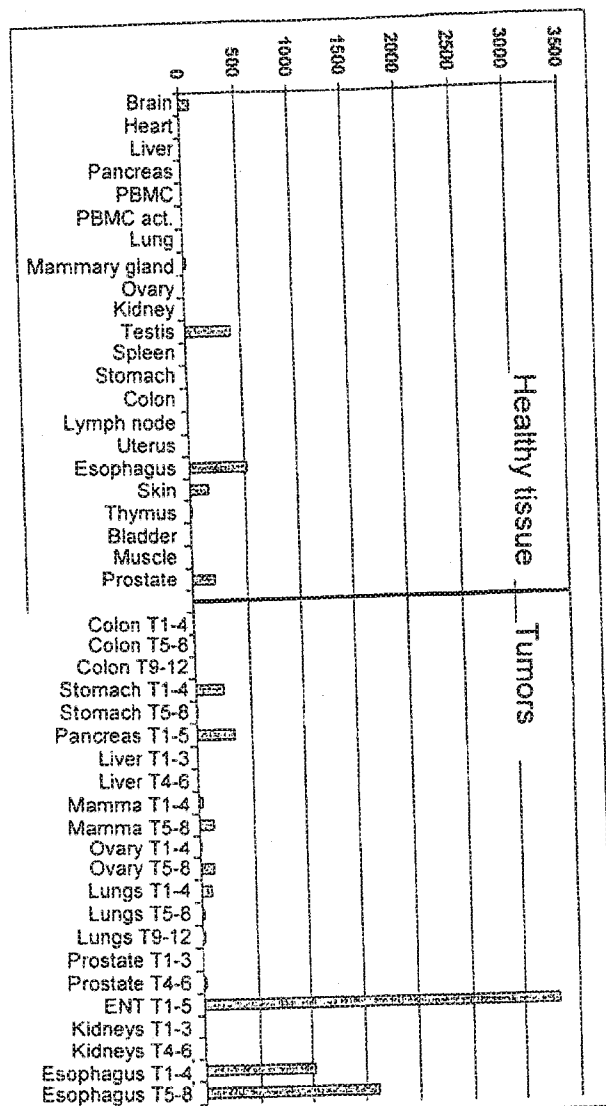


Fig. 20

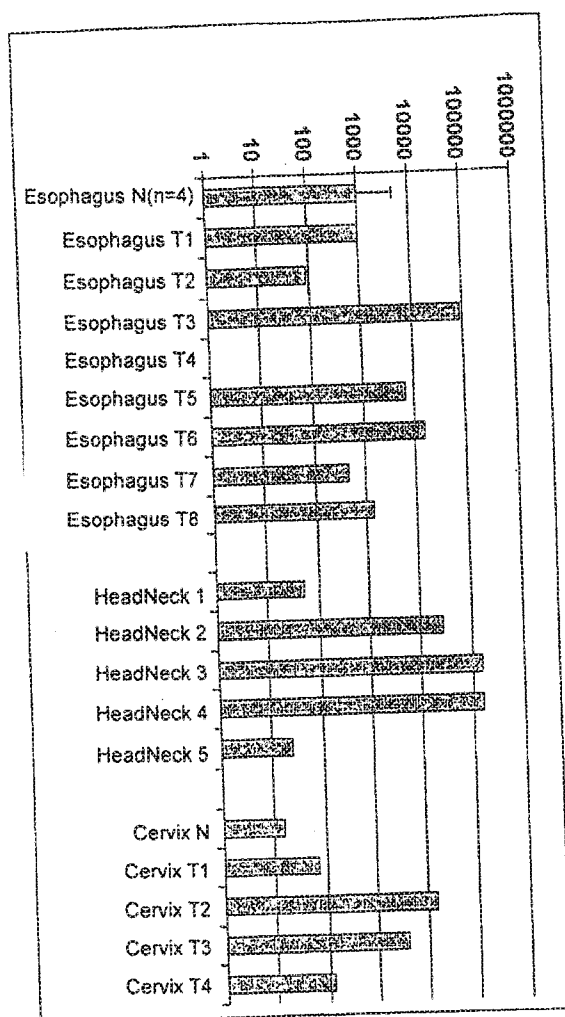


Fig. 21

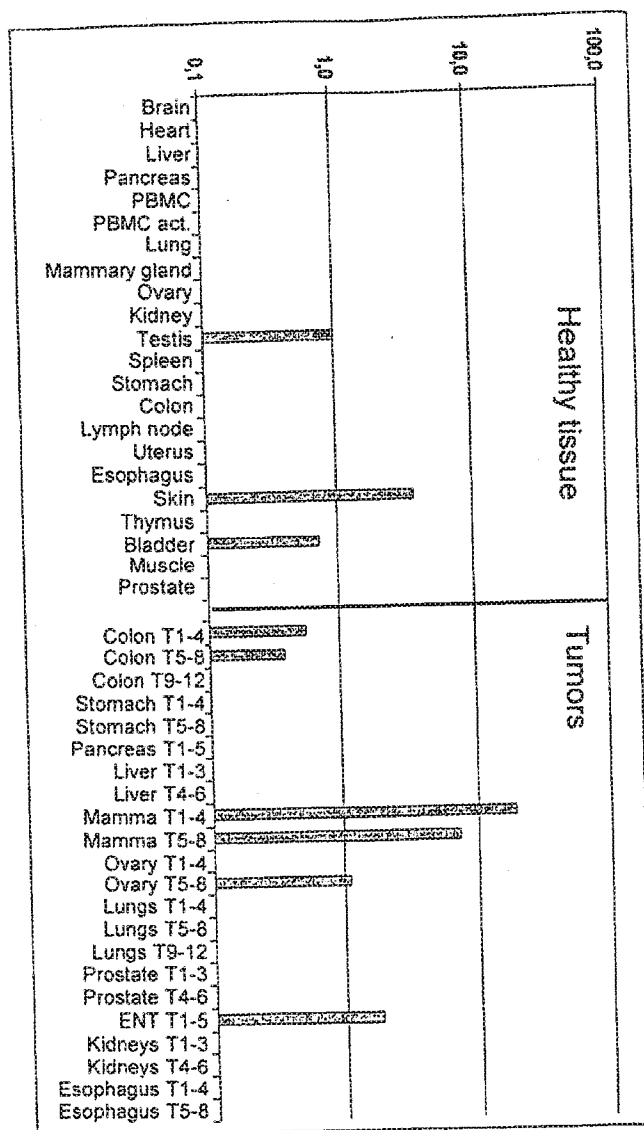


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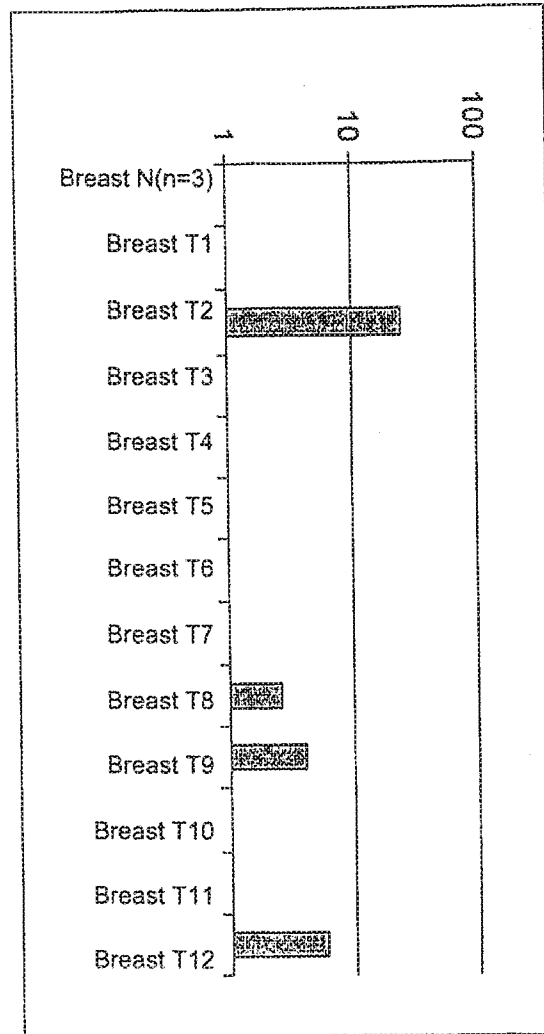


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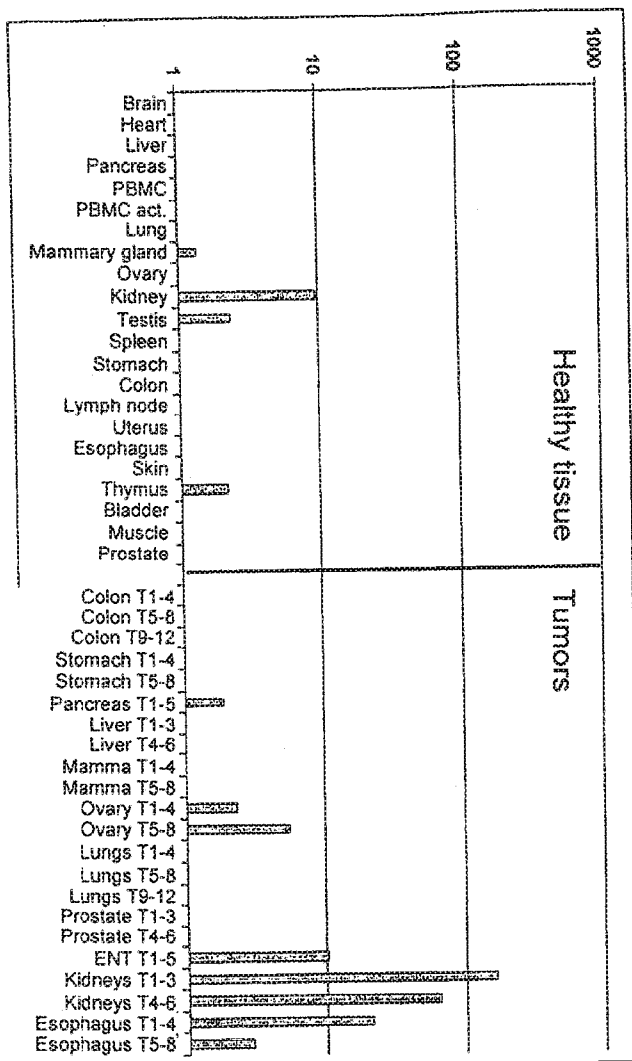
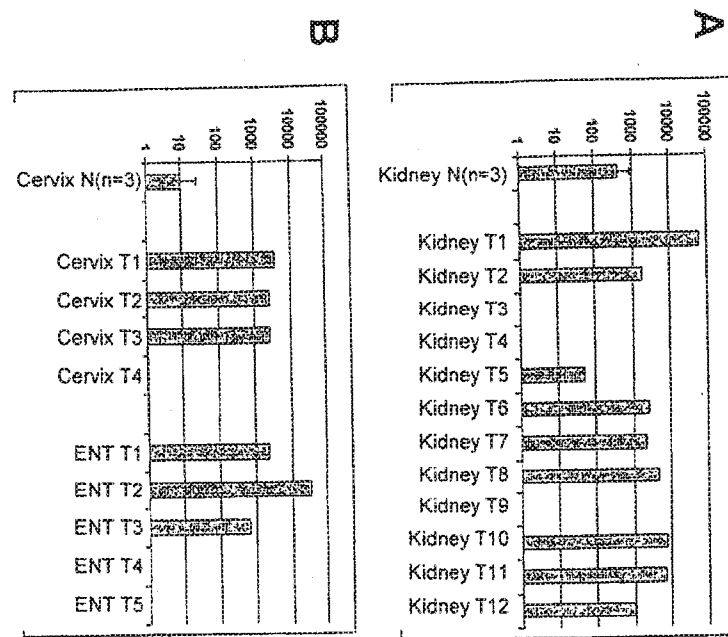


Fig. 24

Fig. 25



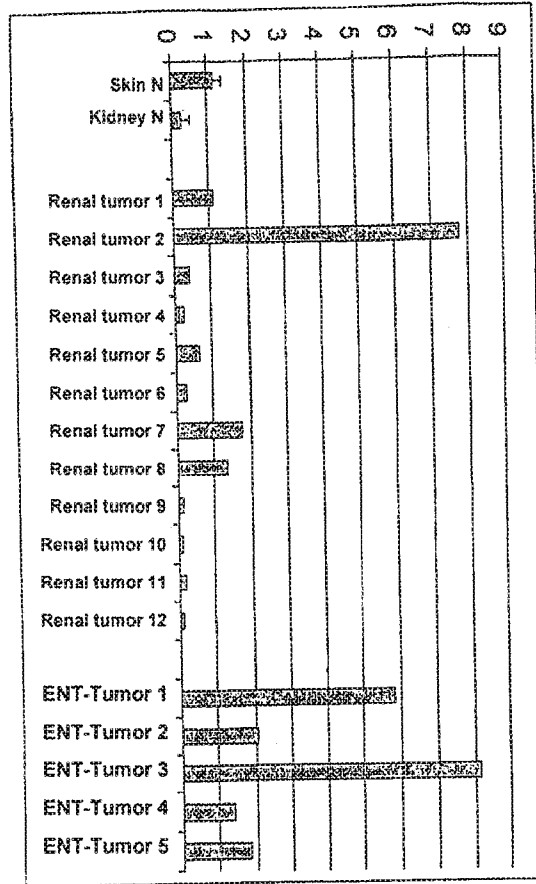


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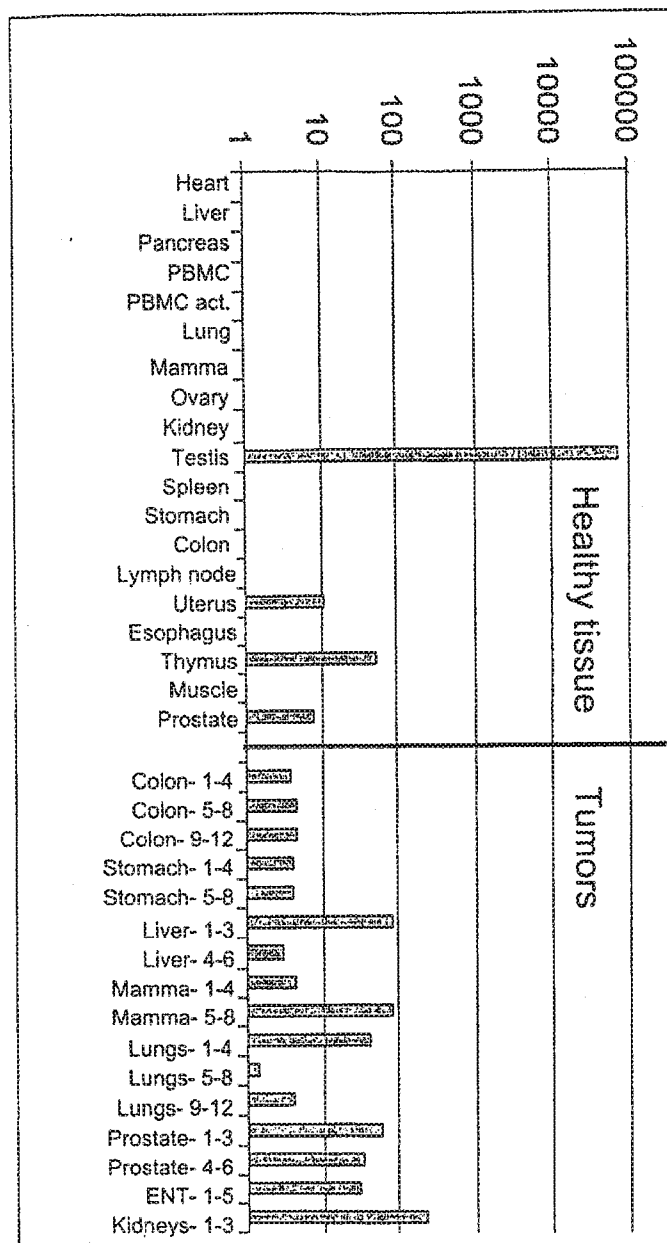


Fig. 27

Fig. 28

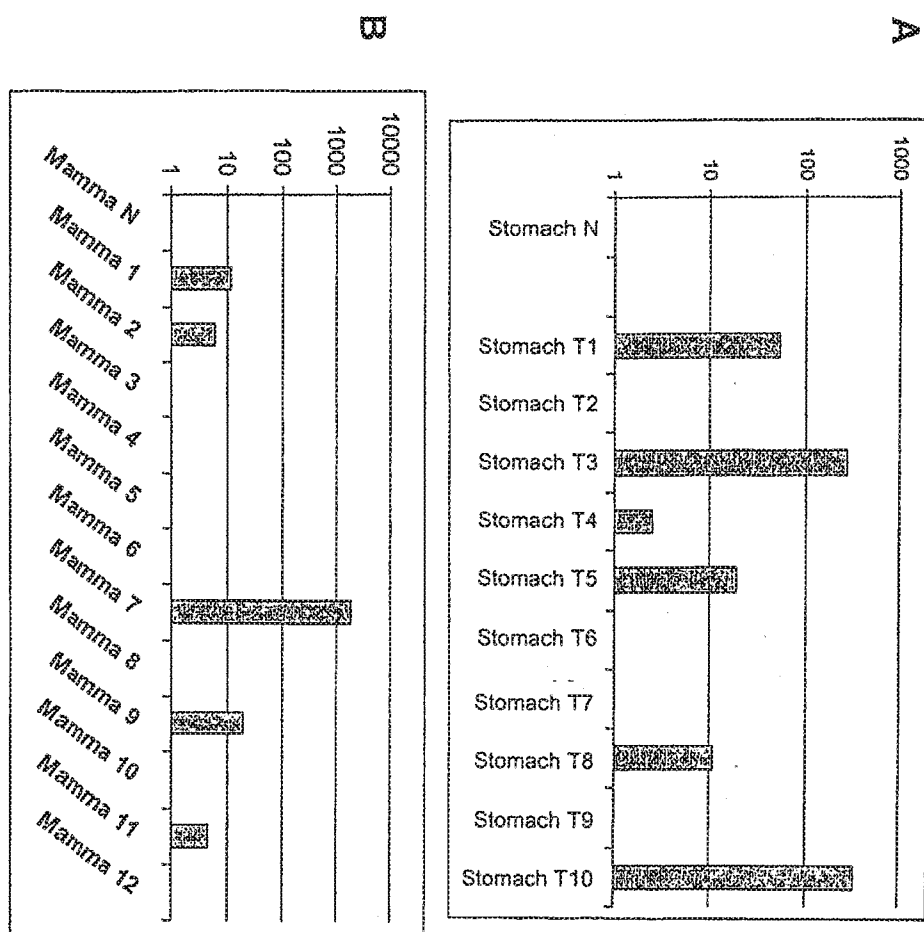
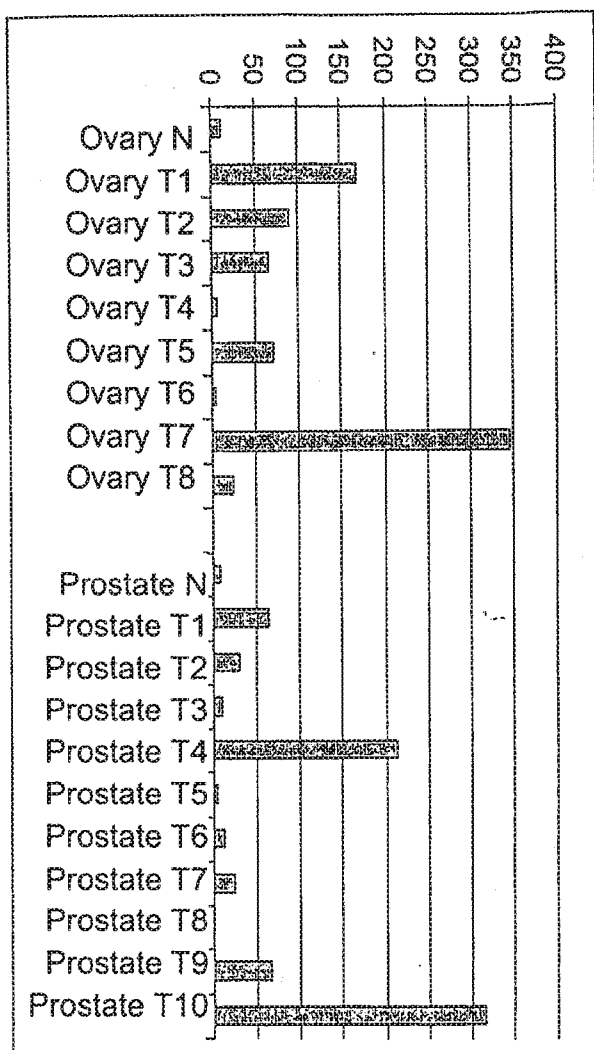


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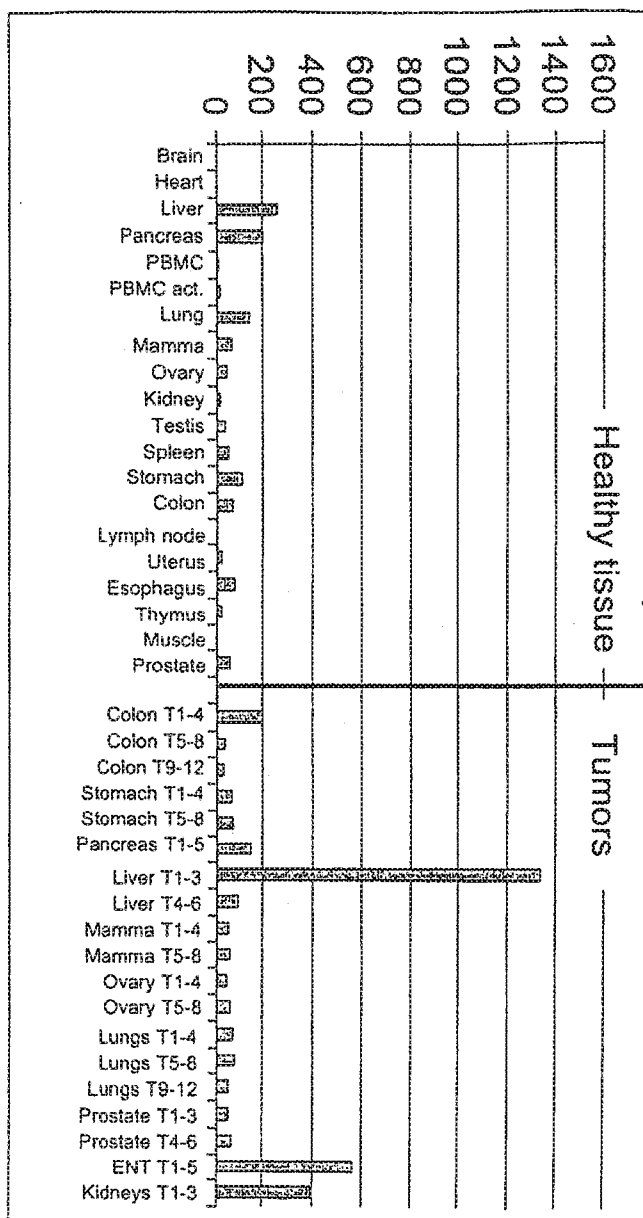
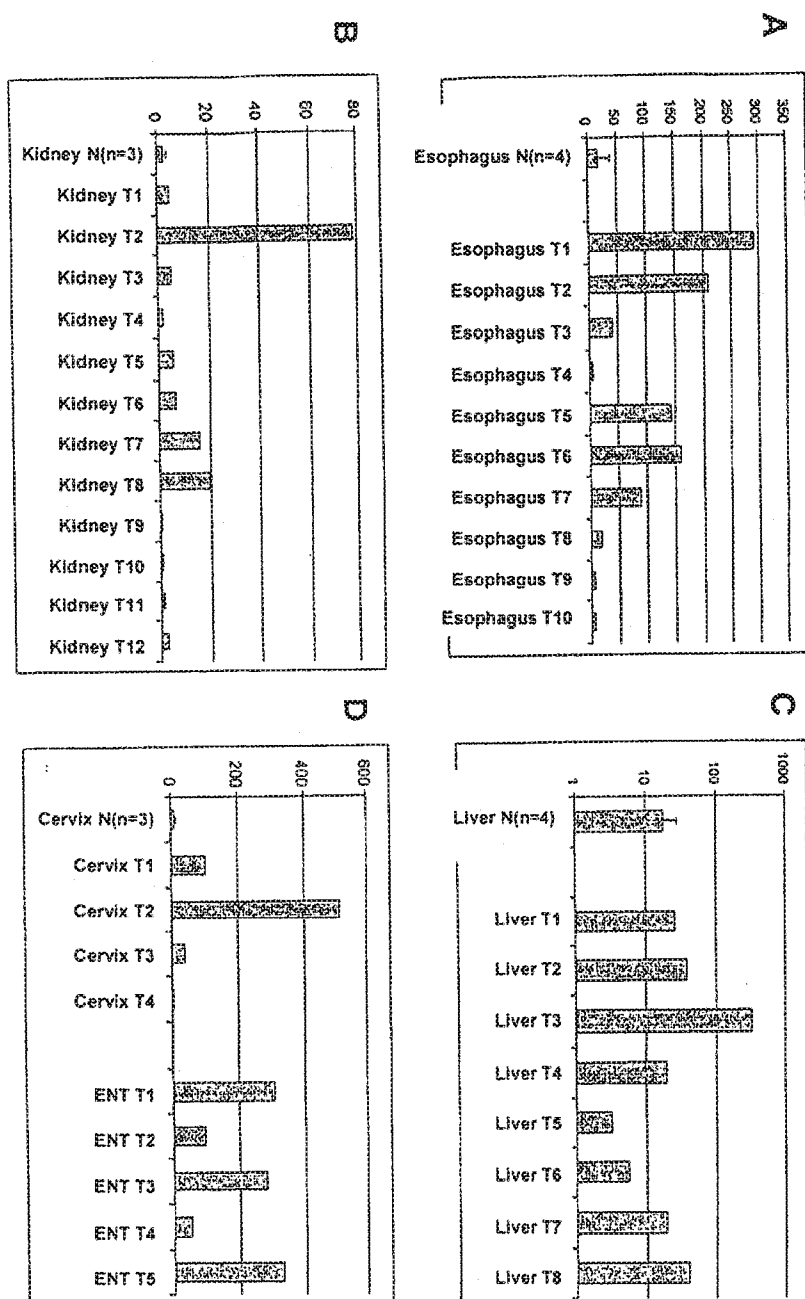


Fig. 30

Fig. 31



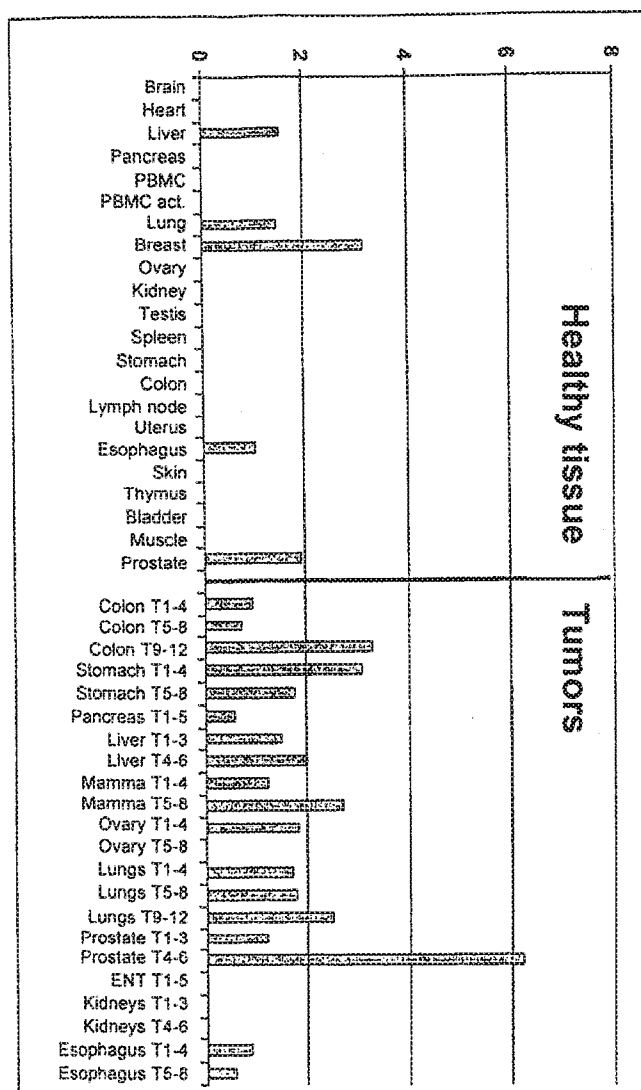


Fig. 32

Fig. 33

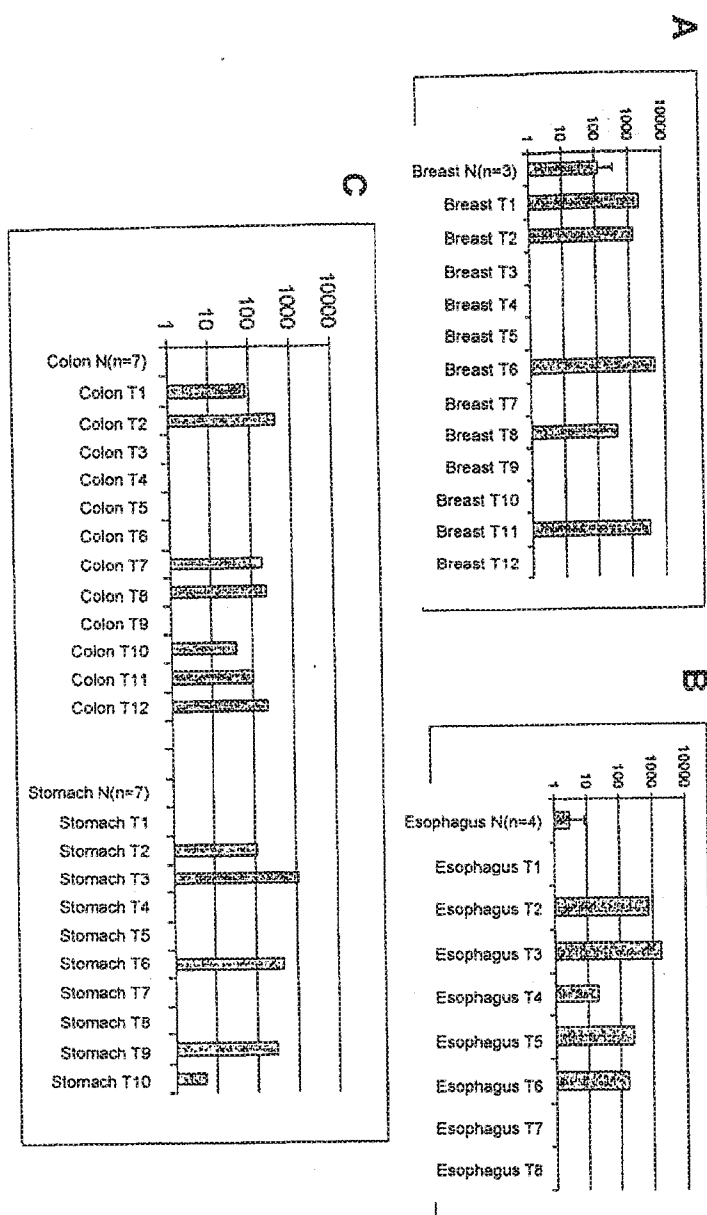
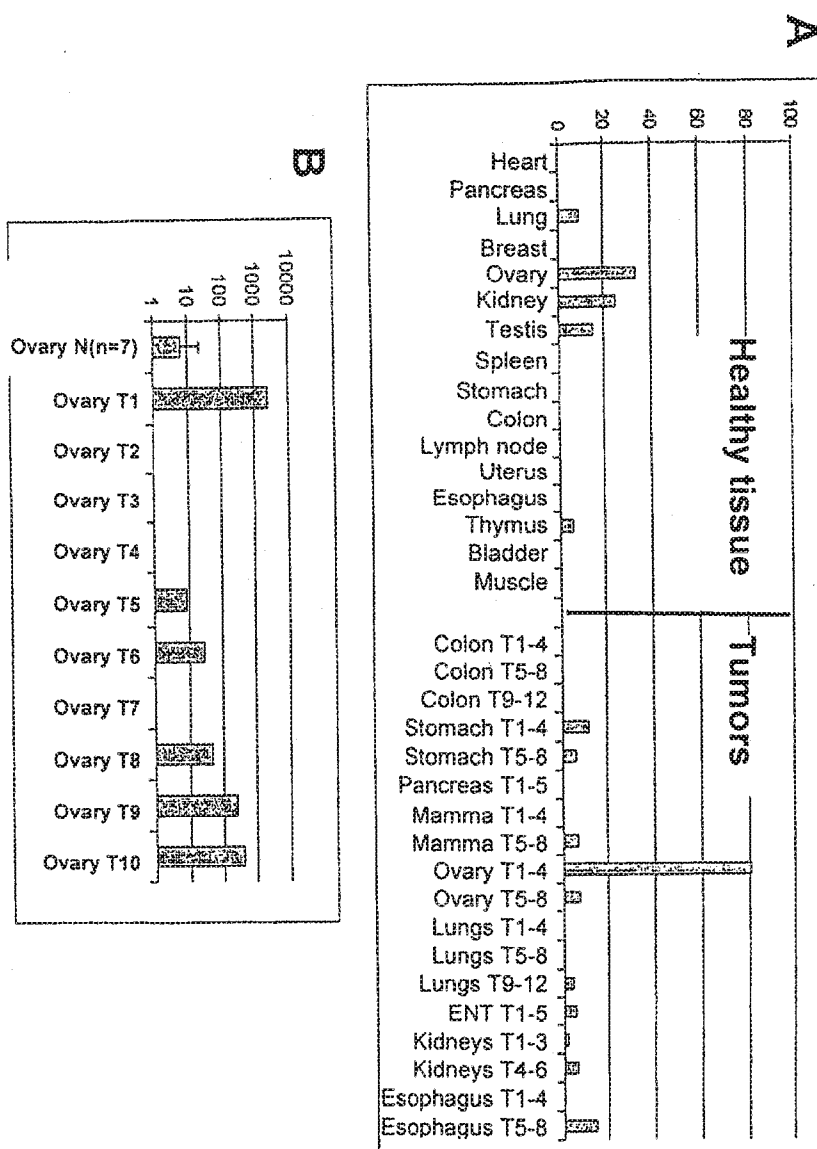


Fig. 34



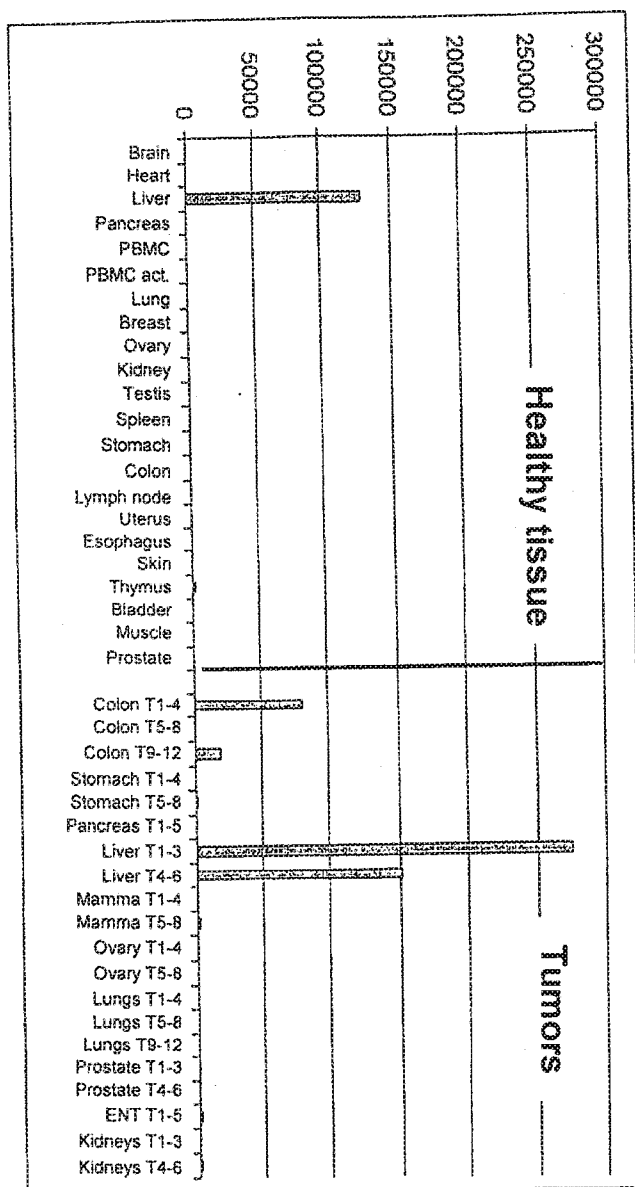


Fig. 35

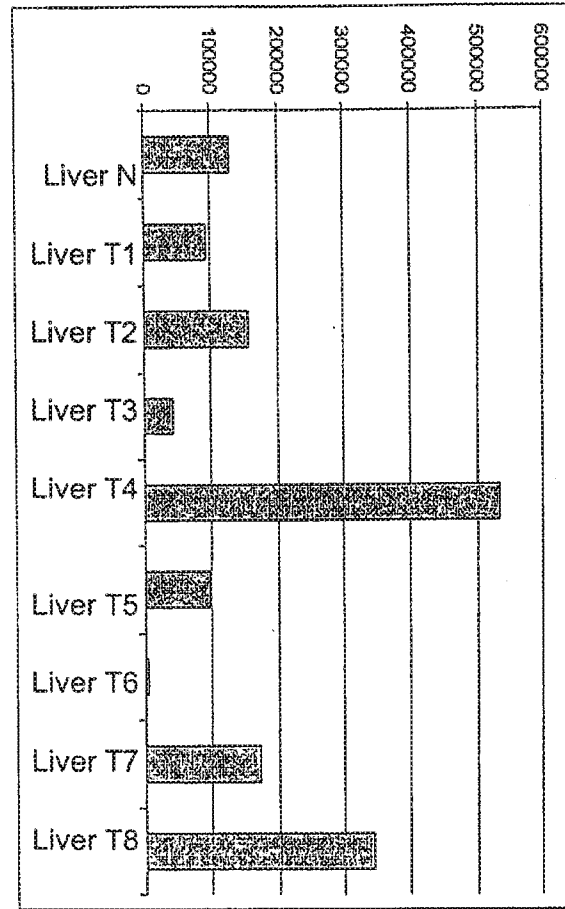


Fig. 36

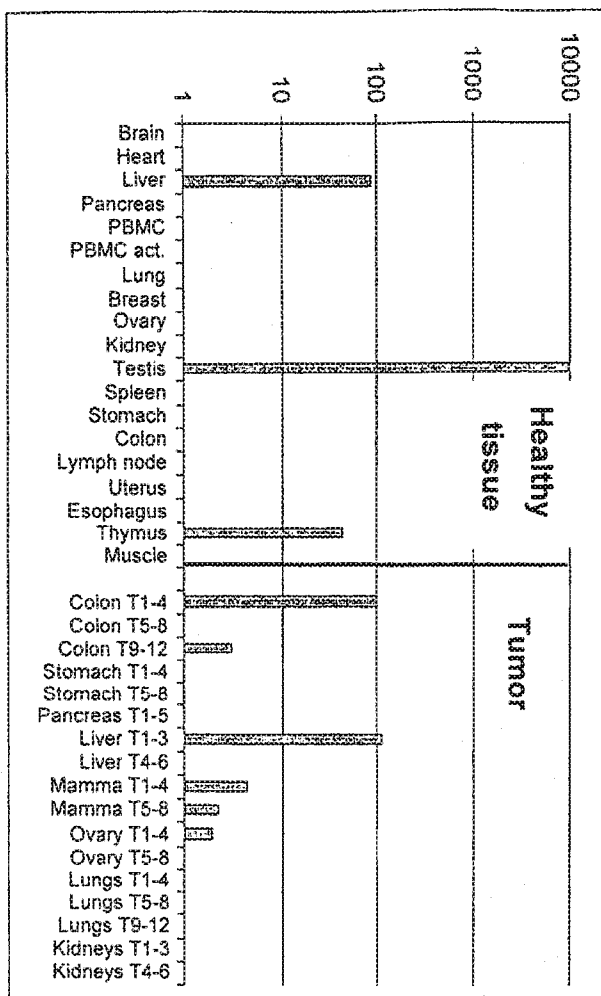


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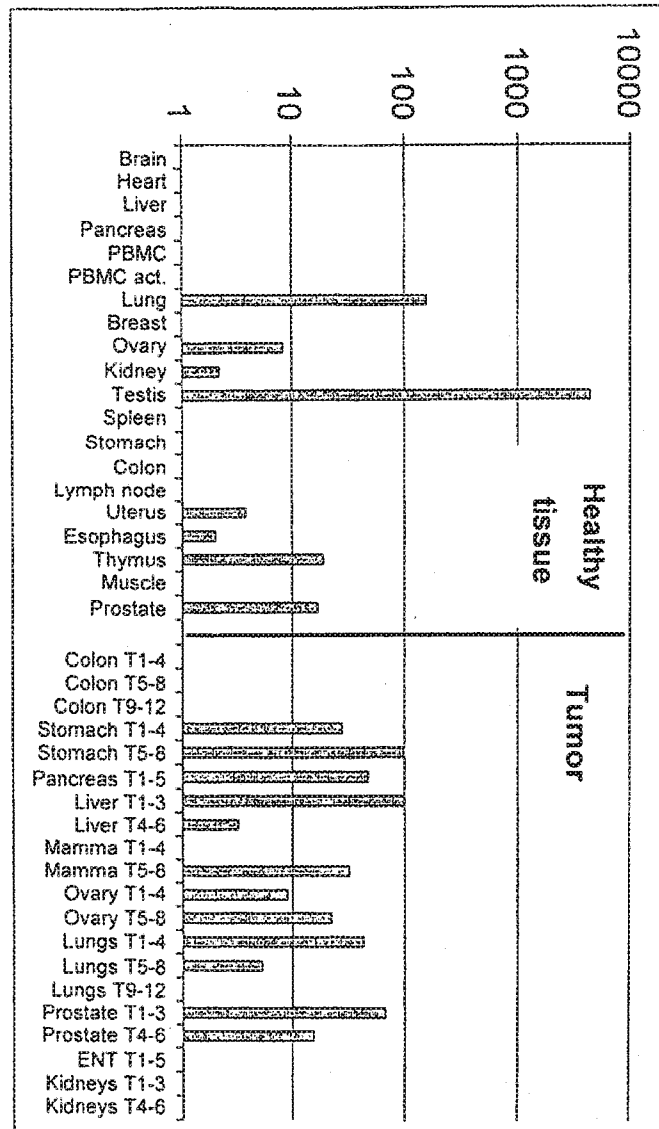


Fig. 38

40/50

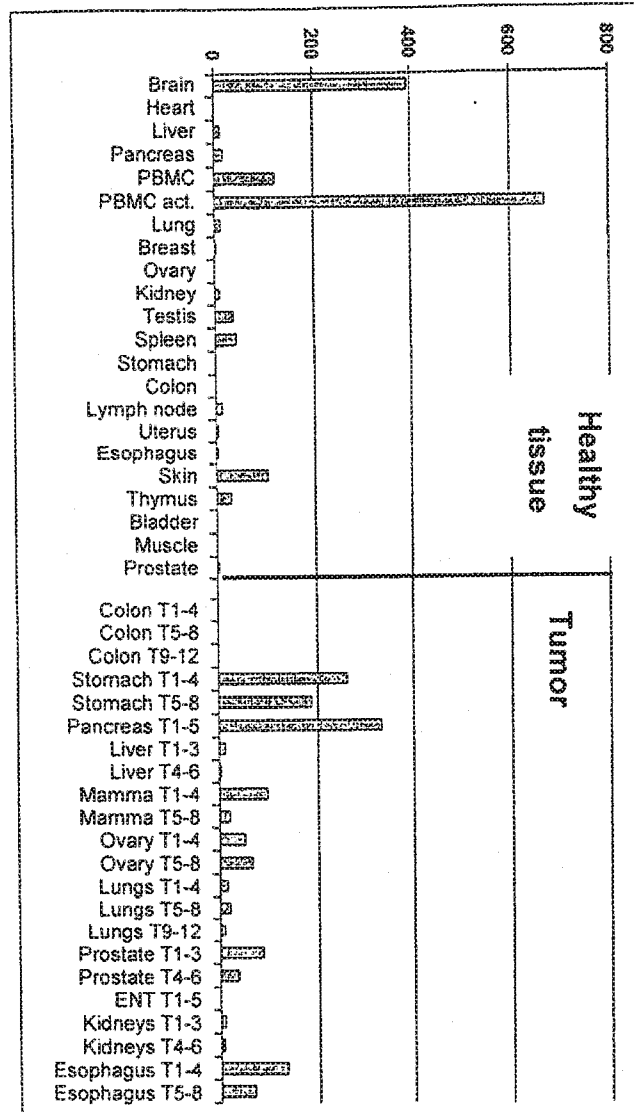


Fig. 39

Fig. 40

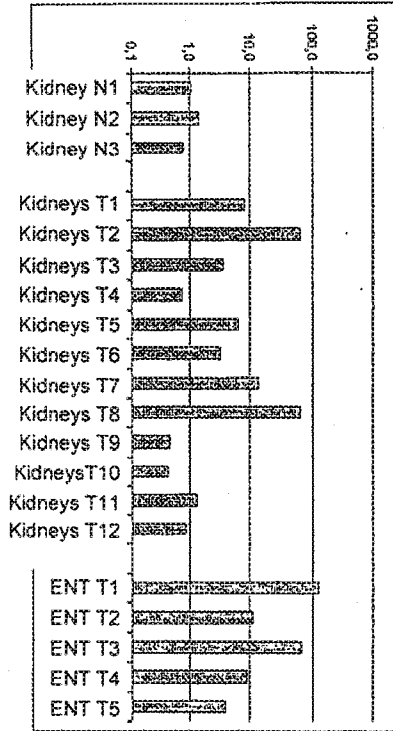
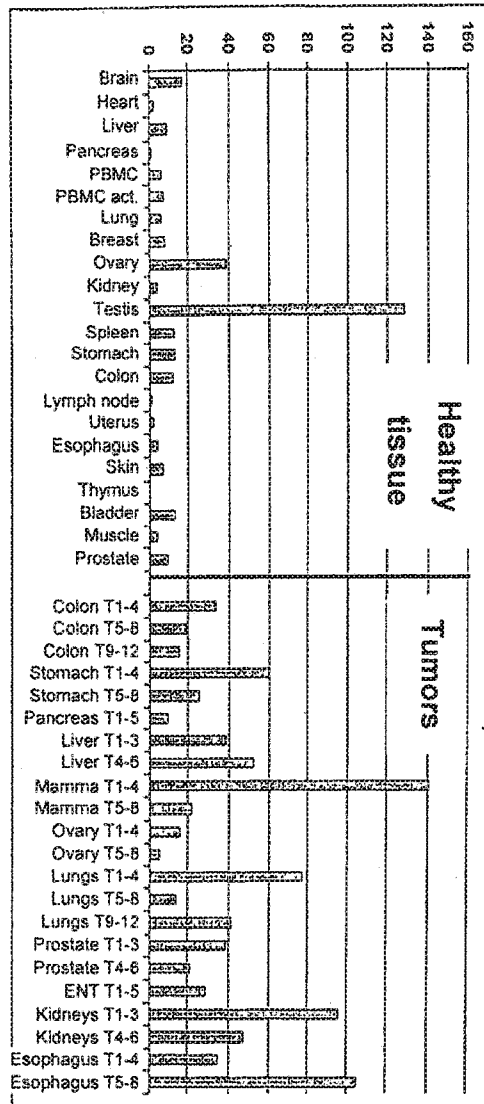
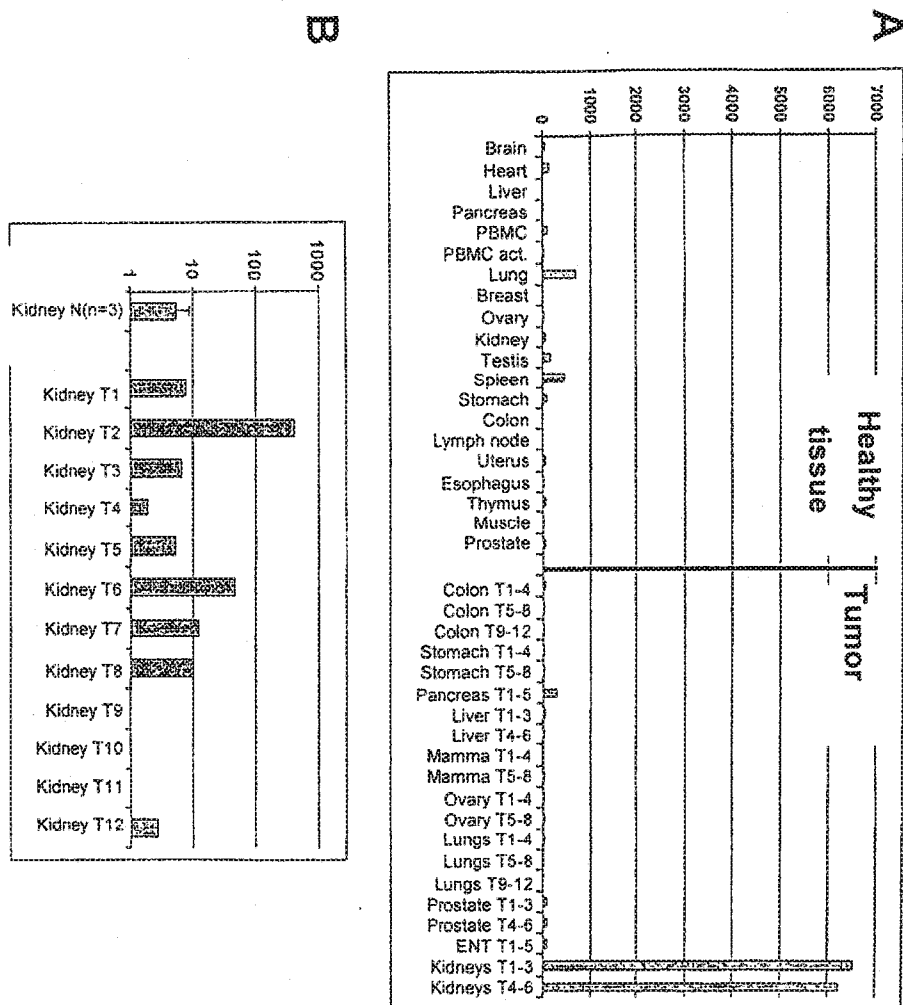


Fig. 41



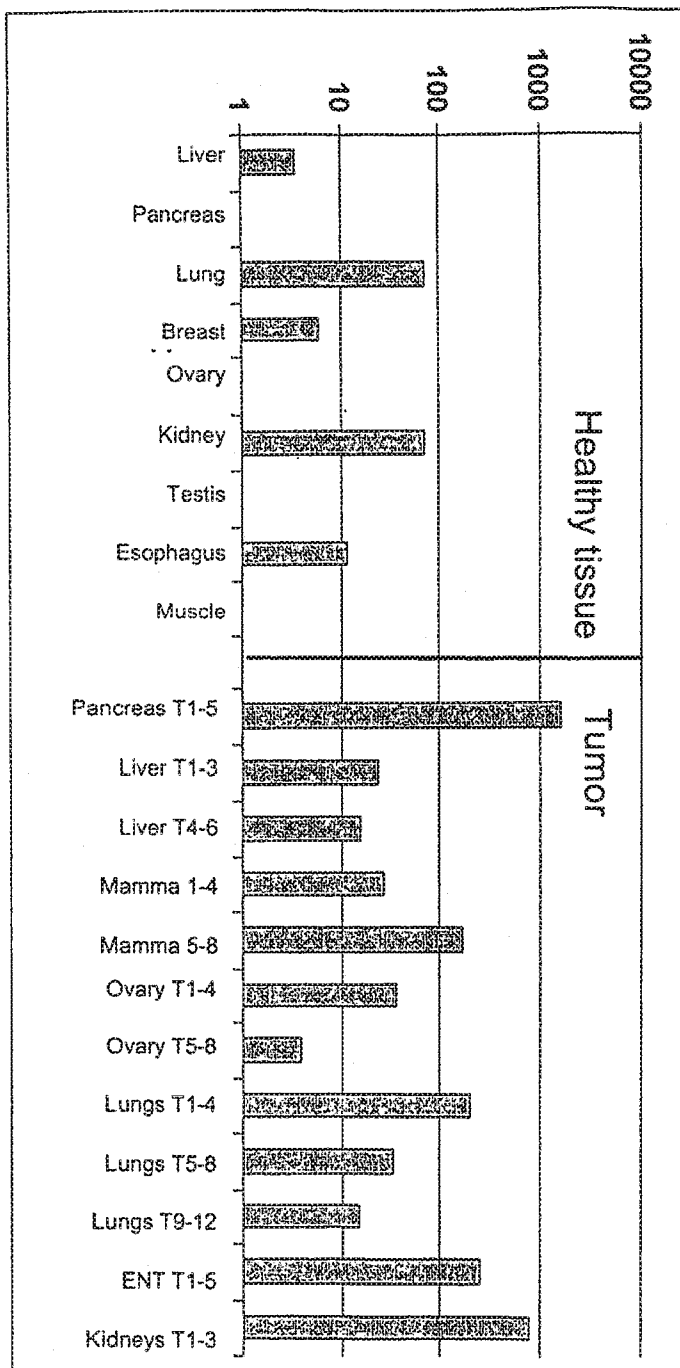


Fig. 42

A Fig. 43

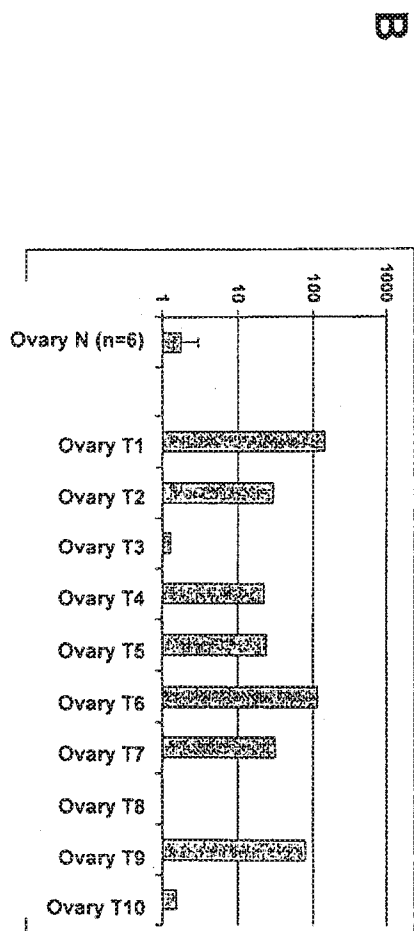
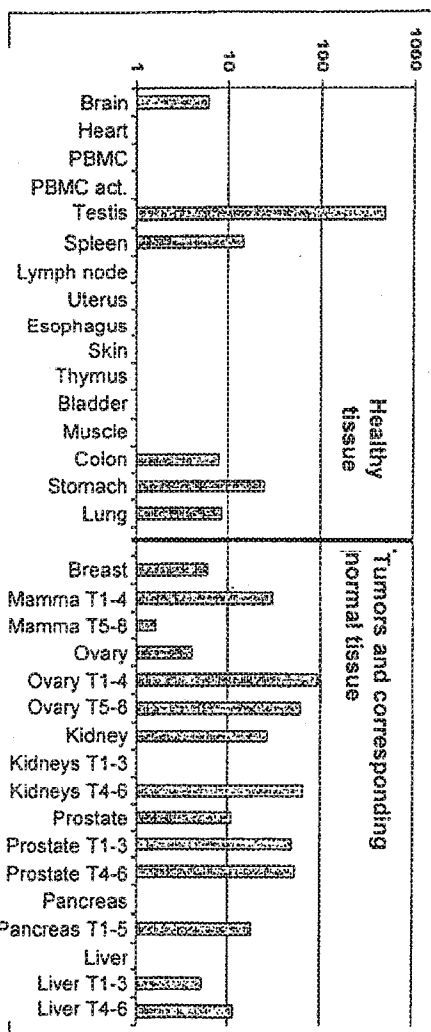
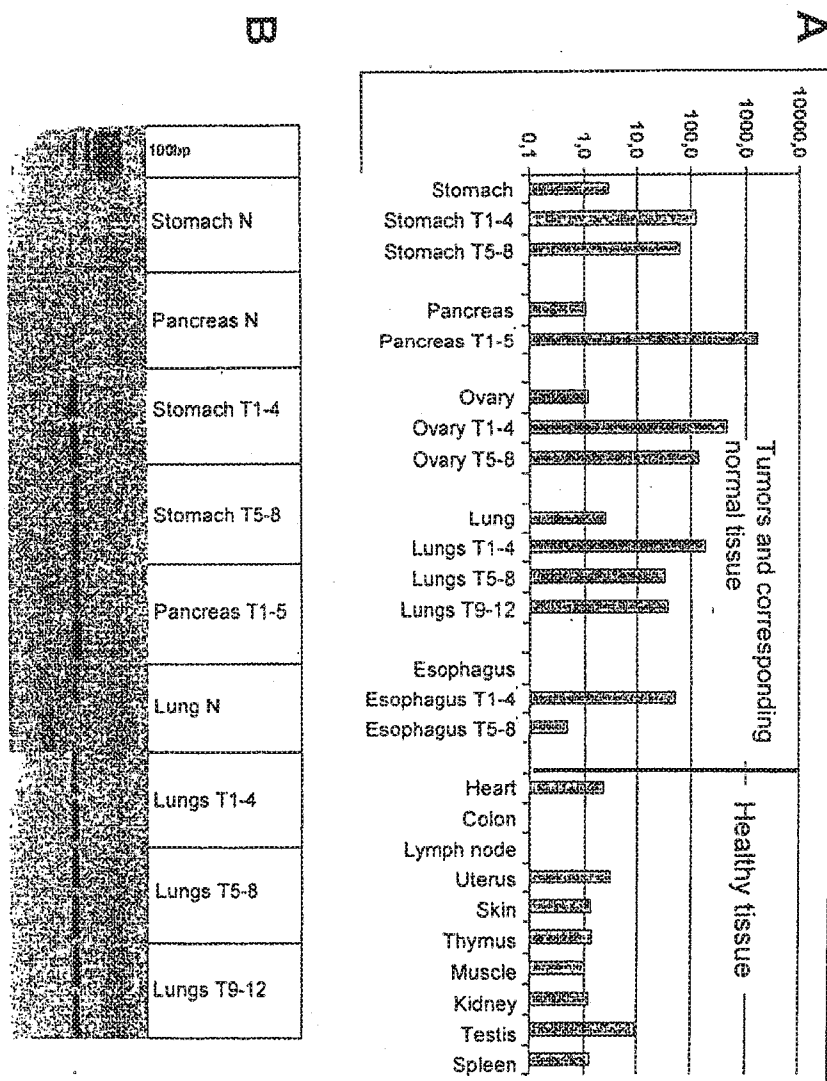


Fig. 44



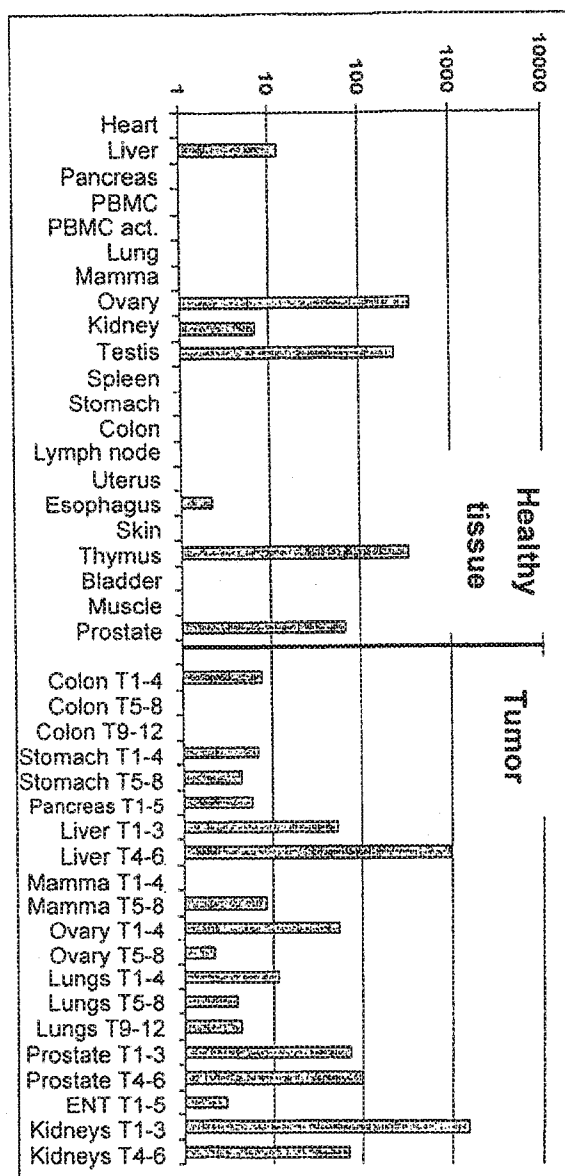


Fig. 45

47/50

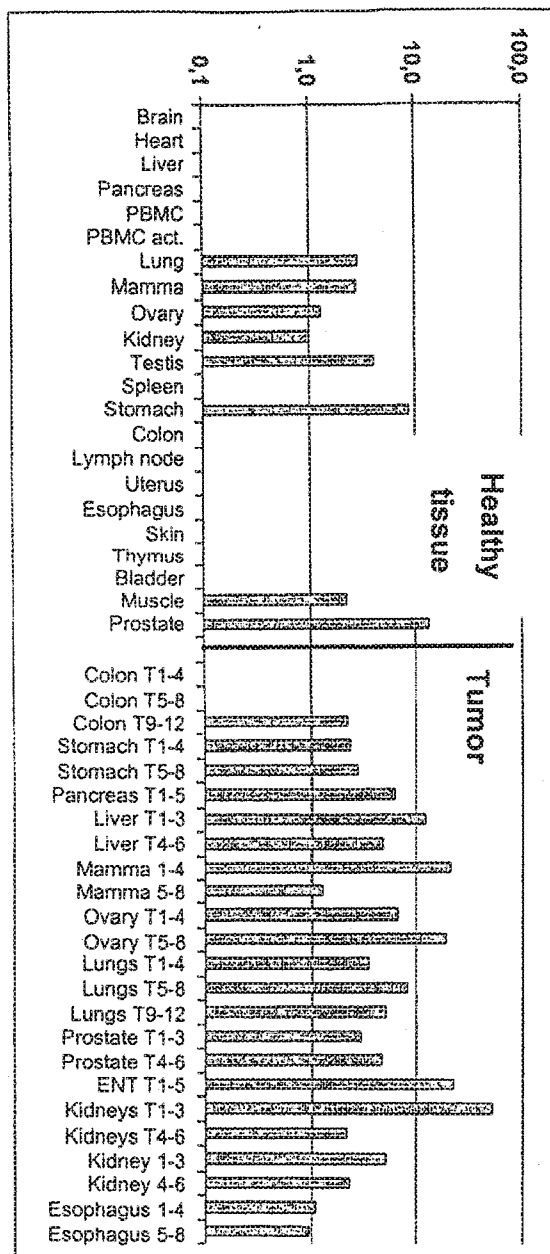
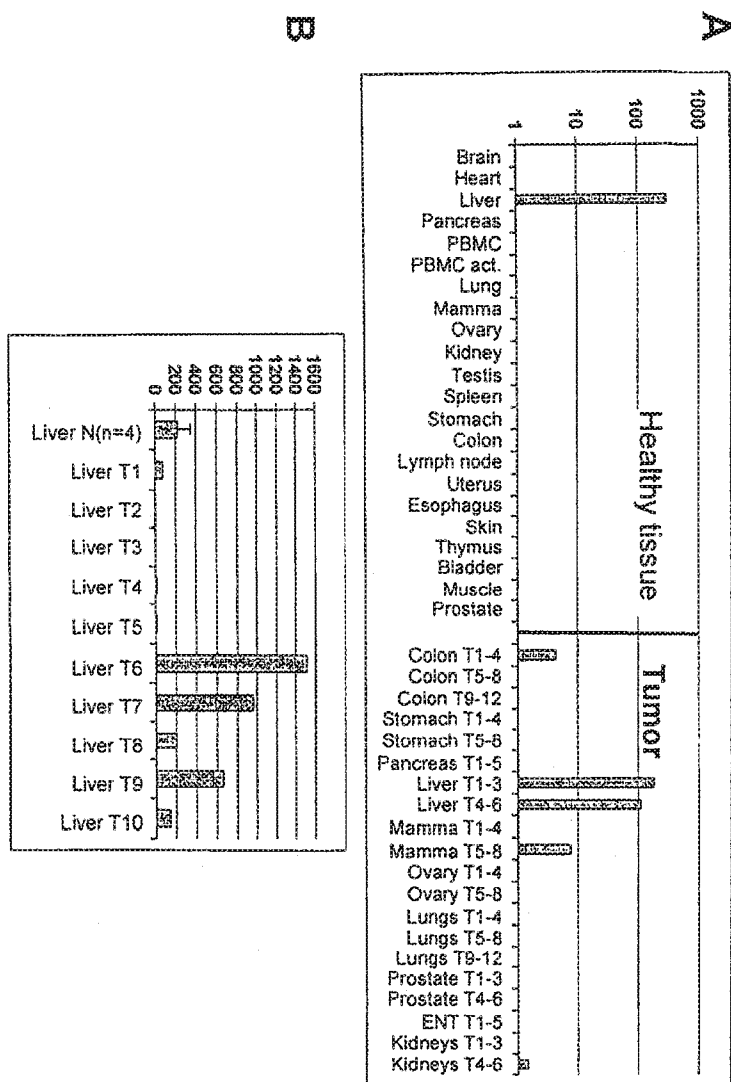


Fig. 46

Fig. 47



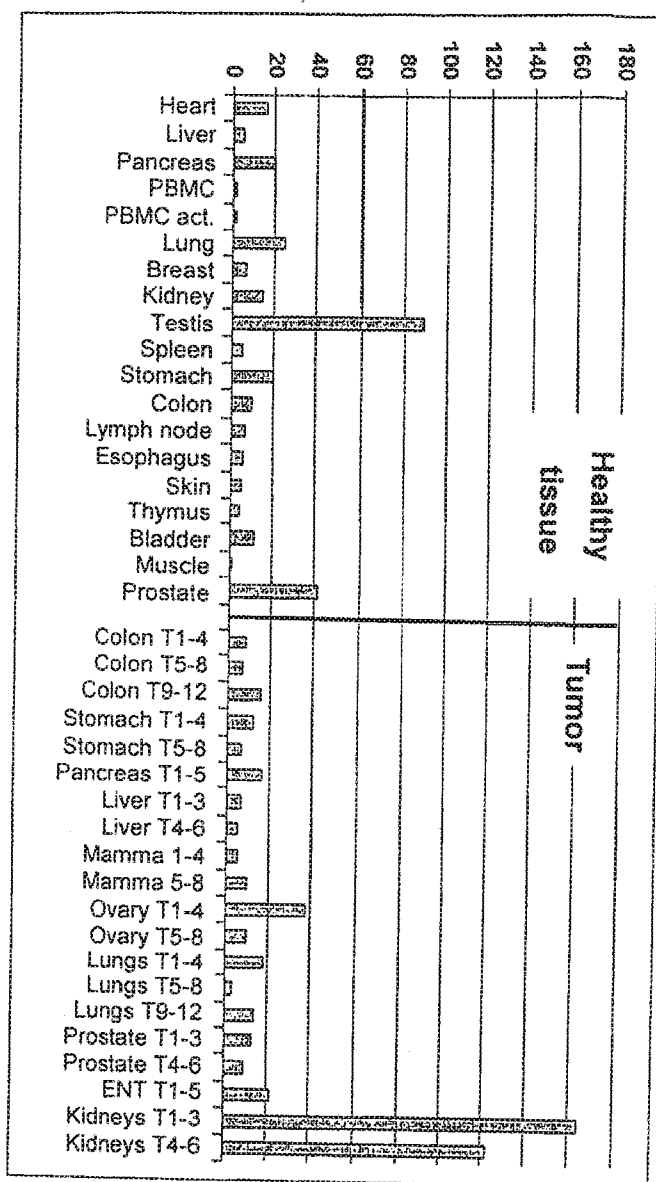
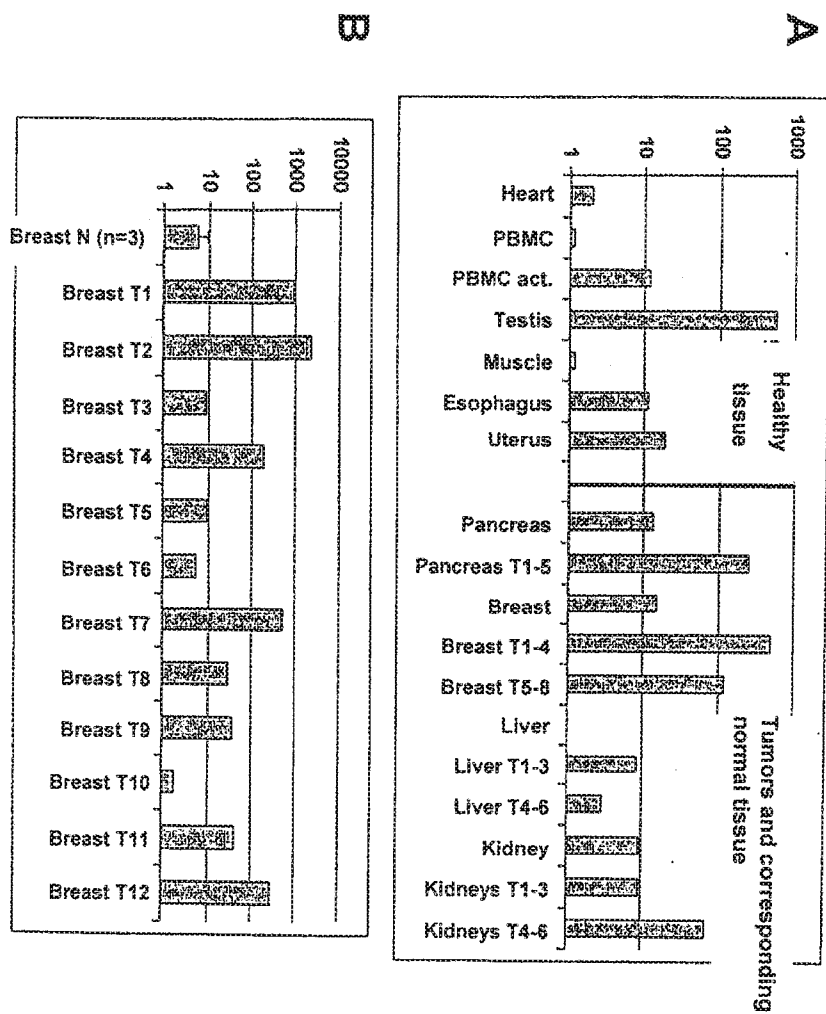


Fig. 48

Fig. 49



50/50

2015201738 07 Apr 2015

1/223

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07 Apr 2015 2015201738

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gtctgcacag	ccctgctctt	tctccttgcc	ctggccatct	taggcatctt	ccatgttgct	2640

2015201738 07 Apr 2015

4/223

342-10PCT.txt
 tgctcctgtg tctgggtgtc cttcatacct gcccacatgc atgcccacag caaagacacc 2700
 atggccatgg aggtctttgt catcttggca tcagcaggag gcctcatgtc ctccctcttc 2760
 ttttccaaat gctacatcat cttctccat cctgaaaaga acacaaaaga ccaaagtgtt 2820
 ggccggcatc atcgcaagtg ggaaaaactg aagtga 2856

<210> 6
 <211> 951
 <212> PRT
 <213> Homo sapiens

<400> 6

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

Phe Thr Asp His Pro Glu Leu Ala Val Pro Leu Phe Leu Val Phe Leu
 20 25 30

Ser Phe Tyr Leu Val Thr Phe Leu Gly Asn Gly Gly Met Ile Ile Leu
 35 40 45

Ile Gln Val Asp Ala Gln Leu His Thr Pro Val Tyr Phe Phe Leu Ser
 50 55 60

His Leu Ala Phe Leu Asp Ala Cys Cys Ala Ser Val Ile Thr Pro Gln
 65 70 75 80

Ile Leu Ala Thr Leu Ala Thr Asp Lys Thr Val Ile Ser Tyr Gly Cys
 85 90 95

Arg Ala Val Gln Phe Ser Phe Phe Thr Ile Cys Ala Gly Thr Glu Cys
 100 105 110

Tyr Leu Leu Ser Val Met Ala Tyr Asp Arg Phe Val Ala Ile Ser Asn
 115 120 125

Pro Leu His Cys Asn Met Thr Met Thr Pro Gly Thr Cys Arg Val Phe
 130 135 140

Leu Ala Ser Ala Phe Ile Cys Gly Val Ser Gly Ala Ile Leu His Thr
 145 150 155 160

Thr Cys Thr Phe Thr Leu Ser Phe Cys Cys Asp Asn Gln Ile Asn Phe
 165 170 175

Phe Phe Cys Asp Leu Pro Pro Leu Leu Lys Leu Ala Cys Ser Ser Met
 180 185 190

Thr Gln Thr Glu Ile Val Ile Leu Leu Cys Ala Lys Cys Met Phe Leu
 195 200 205

2015201738 07 Apr 2015

5/223

342-10PCT.txt

Ala Asn Val Met Val Ile Leu Ile Cys Tyr Met Leu Ile Ile Arg Ala
210 215 220

Ile Leu Arg Val Lys Ser Ala Gly Gly Leu Leu Ile Ala Ser Ala His
225 230 235 240

Phe Asp Ala Tyr Val Tyr Glu Thr Gly Ile Asn Tyr Asn Thr Val Tyr
245 250 255

Gly Ser Gly Lys Ala Val Gly Trp Ser Trp Arg Ser Leu Arg Glu Thr
260 265 270

Asn His Met Arg Pro Gly Asn Thr Ser Lys His Ser Ala Ala Gln Leu
275 280 285

His Gln Cys Leu Ile Gln Gln Val Gly Arg Trp Pro Leu Gln Ser Met
290 295 300

Pro Phe Pro Val Ser Ala Gly Pro Pro Tyr Lys Ser Val Gln Pro Leu
305 310 315 320

Pro Gly Asp Pro Arg Pro Leu Leu Cys Ile Thr Gly Leu Phe Leu Thr
325 330 335

Leu Lys Met Met Gly Cys Gly Pro Arg Arg Pro Arg Asp Arg Lys Ser
340 345 350

Asp Phe Phe Ile Asn Thr Asp Pro Gly Ala Gly Ser Pro Glu Glu Gln
355 360 365

Arg Cys Gly Trp Glu Gly His Pro Ser His Ser Tyr Thr Leu Gly Leu
370 375 380

Ser Leu Pro Val Asn Phe Gly Leu Lys Cys Pro Trp Trp Thr Leu Ser
385 390 395 400

Gly Pro Pro Ala Thr Cys Gln Arg Pro Asp Leu Gln Thr Pro Ser Pro
405 410 415

Pro Lys Glu Ile Cys Ser Ser Gly Leu Arg Pro Leu Thr His Ser Ala
420 425 430

Gly Pro Asp Arg Ser Gln Val Pro Ala Ala Ser Gly Ala Ala Thr Met
435 440 445

Leu Thr Lys Gly Leu Pro Asp Ile Thr Val Gly Leu Gln Ile Tyr Asp
450 455 460

Ser Cys Ile Ser Gly Ile Gln Ala Leu Gly Ser Thr Leu Ala Leu Leu
465 470 475 480

2015201738 07 Apr 2015

6/223

342-10PCT.txt

Ser Asn Gln Leu Pro 485 Pro Thr Thr Asn Tyr 490 Ala Cys Gly Ser Gln Gln 495

His Leu Leu Gly 500 Val Val Gly Gly Met 505 Thr Phe Leu Glu Ser 510 Glu Pro

Met Ser Glu 515 Leu Leu Ser Ile Tyr 520 Arg Val Pro Gln Gly 525 Gln Arg Leu

Thr Lys 530 Asn Phe Glu Val Lys 535 Glu Leu Val Cys Thr 540 Tyr Leu Val Gly

Gln 545 Leu Pro Tyr Gly Leu 550 Val Ser Tyr Asp Asn 555 Ser Asn Phe Glu Trp 560

Leu Asp Gln Gln Leu 565 Gln Lys Gln Ile Gly 570 Gly Glu Gly Leu Pro Val 575

Gly Ala Ala Pro 580 Ser Arg Val Ala Arg 585 Gln Gln Ser Asp Glu 590 Glu Ala

Val Gly Gly 595 Val Gln Gly Tyr Arg 600 Trp Ser Gly Leu Gly 605 Ala Ser Ile

Gln Ser 610 Ala Arg Glu Gly Ala 615 Trp His Arg Thr Gly 620 Leu Glu Asn Met

Thr 625 Thr Ala His Leu Ser 630 Ala Phe Lys Leu Pro 635 Asp Leu Thr Ala Thr 640

Tyr Gln Ala Tyr Leu 645 Ala Ala Lys Ala Leu Trp Val Ala Tyr Gln 655 Asn

Leu Met Ser Cys 660 Ser Glu Arg Glu Gly 665 Pro Phe Leu Gly Gly 670 Thr Tyr

Ala Asn Ala Trp Glu Ala Arg Leu 680 Ser Gln Val Asn Phe 685 Thr Thr Lys

Ala Gln Glu Glu Val Phe 695 Phe Ala Lys Asp Gly Glu 700 Val Leu Thr Thr

Phe Asp Ile Lys Asn 710 Ile Tyr Val Leu Pro Asp 715 Leu Ser Gly Gln Thr 720

Ala Ile Val Gly His 725 Phe Asp Phe Arg Ala 730 Pro Ser Gly Lys Glu 735 Leu

Leu Leu Asp Asp 740 Ser Ala Ile Val Trp 745 Ala Glu Gly Pro Leu 750 Lys Ile

7/223

342-10PCT.txt

Arg Ala Glu Arg Thr Leu Arg Thr Lys Thr Thr Gln His Leu Ser His
755 760 765

Pro Lys Leu Gln Glu Ser Leu Pro Leu Ser Ala Thr Lys Asn Val Leu
770 775 780

Trp Lys Pro Gly Ser Gln Pro Tyr Leu Arg Ser Gln Asn Ala Ala Thr
785 790 795 800

Lys Ala Phe Pro Asp Pro Glu Glu Lys Ser Gln Cys His Gln Phe Leu
805 810 815

Phe Leu Pro Ser Asp Ser Val Ala Cys Gln Lys Cys Ser Asp Asn Gln
820 825 830

Trp Pro Asn Val Gln Lys Gly Glu Cys Ile Pro Lys Thr Leu Asp Phe
835 840 845

Leu Phe Tyr His Lys Pro Leu Asp Thr Ala Leu Ala Val Cys Thr Ala
850 855 860

Leu Leu Phe Leu Leu Ala Leu Ala Ile Leu Gly Ile Phe His Val Val
865 870 875 880

Cys Ser Cys Val Trp Val Ser Phe Ile Pro Ala His Met His Ala His
885 890 895

Ser Lys Asp Thr Met Ala Met Glu Val Phe Val Ile Leu Ala Ser Ala
900 905 910

Gly Gly Leu Met Ser Ser Leu Phe Phe Ser Lys Cys Tyr Ile Ile Leu
915 920 925

Leu His Pro Glu Lys Asn Thr Lys Asp Gln Met Phe Gly Arg His His
930 935 940

Arg Lys Trp Glu Lys Leu Lys
945 950

<210> 7
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 7
agtggtgtg acgctgctgc ta

<210> 8
<211> 22
<212> DNA
<213> Artificial Sequence

2015201738 07 Apr 2015

8/223

342-10PCT.txt

<220>
<223> Oligonucleotide

<400> 8
tcttcttggg ctttggtggt ga

22

<210> 9
<211> 543
<212> DNA
<213> Homo sapiens

<400> 9
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aatccaggc ggctagaggc cactgcttc ccaactacca gctgaggggg tccgtcccga 120
gaaggagaa gaggccgaag aggaaacatg aacttctatt tactcctagc gagcagcatt 180
ctgtgtgcct tgattgtctt ctggaaatat cgccgcttcc agagaaacac tggcgaaatg 240
tcatcaaatt caactgctct tgcactagtg agaccctctt cttctgggtt aattaacagc 300
aatacagaca acaatcttgc agtctacgac ctctctcggg atattttaaa taatttccca 360
cactcaatag ccaggcagaa gcgaatattg gtaaacctca gtatggtgga aaacaagctg 420
gttgaactgg aacatactct acttagcaag ggtttcagag gtgcatcacc tcaccggaaa 480
tccacctaaa agcgtacagg atgtaatgcc agtggtggaa atcattaaag acactttgag 540
tag 543

<210> 10
<211> 113
<212> PRT
<213> Homo sapiens

<400> 10

Met Asn Phe Tyr Leu Leu Leu Ala Ser Ser Ile Leu Cys Ala Leu Ile
1 5 10 15

Val Phe Trp Lys Tyr Arg Arg Phe Gln Arg Asn Thr Gly Glu Met Ser
20 25 30

Ser Asn Ser Thr Ala Leu Ala Leu Val Arg Pro Ser Ser Ser Gly Leu
35 40 45

Ile Asn Ser Asn Thr Asp Asn Asn Leu Ala Val Tyr Asp Leu Ser Arg
50 55 60

Asp Ile Leu Asn Asn Phe Pro His Ser Ile Ala Arg Gln Lys Arg Ile
65 70 75 80

Leu Val Asn Leu Ser Met Val Glu Asn Lys Leu Val Glu Leu Glu His
85 90 95

Thr Leu Leu Ser Lys Gly Phe Arg Gly Ala Ser Pro His Arg Lys Ser
100 105 110

342-10PCT.txt

Thr

<210> 11
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 11
gtgtgccttg attgtcttct gg

22

<210> 12
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 12
cctggctatt gagtgtggg

19

<210> 13
<211> 2761
<212> DNA
<213> Homo sapiens

<400> 13
ctaggcctca gtctgtctgc atccagggtgc ttatttaaacc agtgtgttgc tccacaccgc 60
ctcgtgttgt ctgttggcgc gctctccggg ttccaaccaa tgcaagagcc ttggggctgg 120
ccctgaaacc tgcgaggggc ttccgtccac gtccccagtg gacctaccac ccctccatct 180
gggaaagcag gccacagcag ccggacaaag gaagctcctc agcctctagt cgcctctctg 240
tgcatgcaca tcggtcactg atctcgccca ctggcacaga cgtgtttatc ggccaaactg 300
accctcaca aaagctacca ccgaagtggc caggccccta cactgtgata ctacgacac 360
caactgcagt gagagtccga ggactcccca actggatcca tcgcaccagg gtcaagctca 420
ccccaaggc agcttcttcc tccaaaacat taacagctaa gtgtttgtct gggccaattt 480
ctcctaccaa gtttaaatta accaacattt ttttcttaaa accaaaacac aaggaagact 540
aaccacgtgc ttccaggaat ggctgtatc tacccaacca ctttctatac ctctcttcca 600
acaaaagtc ttaatatggg aatatccctc accacgatcc taatactgtc agtagctgtc 660
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ggggagatgc aacaatactt tacttaccat actcatatag aaagatcctg ttatggaaac 780
ttaatcgagg aatgtgttga atcaggaaag agttattata aagtaaagaa tctaggagta 840
tgtggcagtc gtaatggggc tatttgcccc agagggaagc agtggctttg cttcaccaaa 900
attggacaat ggggagtaaa cactcagggtg cttgaggaca taaagagaga acagattata 960

2015201738 07 Apr 2015

10/223

342-10PCT.txt

gccaaagcca aagcctcaaa accaacaact	ccccctgaaa atcgcccgcg gcattttccat	1020
tccttttatac aaaaactata agcagatgca	tcccttccta agccaggaaa aaatctgttt	1080
gtagatctag gagaaccatt gtgcttacca	tgaatgtgtc caattgttgg gtatgcgggg	1140
gagctttatg agtgaacagt ggctgtggga	cgggatatagac attccccctt acttacaggc	1200
atcccaaaac cccagactca ctttcaactcc	tcaggaatgc ccgcagtcct ggacacttac	1260
caaccagta tgagggacgg tgtgcatatc	ccgcaagtgg actgataaaa cccatcgcg	1320
cgtaggtgaa aaccgcgtcac caaacctaa	cagtcaatgc ctccatagct gagtgggtggc	1380
caaggttacc ccctggagcc tggctctcctt	ctaacttaag ctacctcaat tgtgtcttgt	1440
caaaaaaggc ctggtactgt acgaacacca	ctaaccctta tgccgcatac ctccgcctaa	1500
gtgtactatg cgacaatcct aggaacacca	gctgacaatg gactgccact gacggattcc	1560
tgtggatatg gggaaaccag gcttactcac	agctacctta tcaactggcaa ggtacttgct	1620
tcctaggcac aattcaacct ggattctttt	tacttccgaa gcaggcgggc aacaccctca	1680
gagtccctgt gtatgataac cagagaaaaa	tgatccttgg aggtaggagg gagccaaaga	1740
ttgtgagagg acgagtggcc tctgcaacgg	atcattgaat actatgggtcc tgccacttgg	1800
gcagaggatg gttcatgggg ttatcgcaact	cccatatata tgccaaatag agcgattaga	1860
ctacaagctg ttctagagat aatcactaac	caaactgcct cagccctaga aatgctcgcg	1920
caacaacaaa accaaatgcg cgcggaatt	tatcaaaaca ggctggccct agactactta	1980
ttagcagaag aggggtgcggg ctgtggtaag	tttaacatct ccaattgctg tcttaacata	2040
ggcaataatg gagaagaggt tctggaaatc	gcttcaaaca tcagaaaagt agcccgtgta	2100
ccagtccaaa cctgggagggg atgggaccca	gcaaaccctc taggaggggtg gttctcta	2160
ttaggaggat ttaaaatgct ggtggggaca	gtcattttca tcaactgggt cctcctgttt	2220
ctcccctgtg gtatcccatt aaaactcttg	ttgaaactac agttaacctc ctgacaatcc	2280
agatgatgct cctgctacag cggcacgatg	gataccaacc cgtctctcaa gaatacccca	2340
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ttattgagaa agtcgtccct tttccctttt	ctataaccaa atagacagga atggaagatt	2460
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ggtacaaaact tgcaccagca gcaagatagc	agaggcagga agagagctgg ctggaagaca	2580
cgtacccccct gaagatcaag agggaggtcg	ccctggtact acatagcagt cacgttaggc	2640
tgggacaatt cctgtttaca gaggactata	aaaccctgc cccatcctca cttggggctg	2700
atgccatttt aggcctcagc ctgtctgcat	gcaggcgctc attaaaacag catgttgctc	2760
c		2761

<210> 14
 <211> 160
 <212> PRT
 <213> Homo sapiens

2015201738 07 Apr 2015

11/223

342-10PCT.txt

<400> 14

Met Ala Cys Ile Tyr Pro Thr Thr Phe Tyr Thr Ser Leu Pro Thr Lys
1 5 10 15

Ser Leu Asn Met Gly Ile Ser Leu Thr Thr Ile Leu Ile Leu Ser Val
20 25 30

Ala Val Leu Leu Ser Thr Ala Ala Pro Pro Ser Cys Arg Glu Cys Tyr
35 40 45

Gln Ser Leu His Tyr Arg Gly Glu Met Gln Gln Tyr Phe Thr Tyr His
50 55 60

Thr His Ile Glu Arg Ser Cys Tyr Gly Asn Leu Ile Glu Glu Cys Val
65 70 75 80

Glu Ser Gly Lys Ser Tyr Tyr Lys Val Lys Asn Leu Gly Val Cys Gly
85 90 95

Ser Arg Asn Gly Ala Ile Cys Pro Arg Gly Lys Gln Trp Leu Cys Phe
100 105 110

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

Lys Arg Glu Gln Ile Ile Ala Lys Ala Lys Ala Ser Lys Pro Thr Thr
130 135 140

Pro Pro Glu Asn Arg Pro Arg His Phe His Ser Phe Ile Gln Lys Leu
145 150 155 160

<210> 15

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 15

cctctagtcg cctctctgtg c

21

<210> 16

<211> 17

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 16

accctggtgc gatggat

17

<210> 17

<211> 1635

2015201738 07 Apr 2015

12/223

342-10PCT.txt

<212> DNA
<213> Homo sapiens

<400> 17

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gcctgtccct gccttaagtg cctactggat cccgggagcc tgggctggg cctgggcact    60
gcttcctcct tggccctca ggcccttga agcagagaga gaacctcttg cagatcccag    120
gctcgtcccc agcacagcag acaccaggaa ggtggccaga gcctcactga gccgaaccga    180
cggccgcccc cccaccagc ctggagccat ggataaattc cgcagtctct tccagcactt    240
ccagtcaagc tcggagtcgg tgatgaatgg catctgcctg ctgctggctg cggtcaccgt    300
caagctgtac tcctcctttg acttcaactg tccctgcctg gtgcactaca atgcactcta    360
cggcctgggc ctgctgctga cgcctcgct cgccctgttt ctctcgggcc tcctcgccaa    420
ccggcagctc gtggtgatgg tcgaggagtg gcgccggccc gcagggcacc ggaggaagga    480
cccaggcatc atcaggtaca tgtgctcctc tgtgctgcag agggcgctgg cgcctccctc    540
ggtctggatc ctgctggccc tccttgacgg gaagtgcttc gtgtgtgcct tcagcagctc    600
tgtggaccct gagaagtttc tggactttgc caacatgacc cccagccagg tacagctctt    660
cctggccaag gttccctgca aggaggatga gctggtcagg gatagccctg ctcggaaggc    720
agtgtctcgc tacctgcggt gcctgtcaca ggccatcggc tggagcgtca ccctgctgct    780
gatcatcgcg gccttccttg cccgctgcct gagggcctgc ttcgaccaga cagtcttctc    840
gcagcgcaga tactggagca actacgtgga cctggagcag aagctcttcg acgagacctg    900
ctgtgagcat gcgcgggact tcgcgcaccg ctgctgctg cacttctttg ccagcatgcg    960
gagtgagctg caggcgcggg ggctgcgccg gggcaatgca ggcaggagac tcgagctccc   1020
cgcagtgctt gagccccag aaggcctgga tagtggaagt ggggaaggccc acctgcgcgc   1080
aatctccagc cgggagcagg tggaccgcct cctaagcacg tgggtactcca gcaagccgcc   1140
gctggacctg gctgcatccc ccgggctctg cgggggtggc cttagccacc gcgcccctac   1200
cttggcactg ggcacgaggc tgtcacaaca caccgacgtg tagggctcctg gccaggcttg   1260
aagcggcagt gttcgcaggt gaaatgccgc gctgacaaag ttctggagtc tttccaggcc   1320
gtggggaccc cacggcaggc accctaagtc ttgttagcct cctttttaaa gtagcccaat   1380
ctctgcctag tttctgggtg tggcctccag cgcgcttcac aaactttaat gtggactcgg   1440
ttcaccgagg gccttggtta atacaggttc agacagtgtg gccaggaccg agtctgagat   1500
tctgcatttt aaacaagctc ctggaggctg atgtgctttt ggtcagtga ccaaactttg   1560
agtagcaaga atctaagtaa atctgccatg ggttctgggt tctagatgtc aattctaaat   1620
aataataatg acctt                                     1635
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<210> 18
<211> 344
<212> PRT
<213> Homo sapiens

<400> 18

2015201738 07 Apr 2015

13/223

342-10PCT.txt

Met Asp Lys Phe Arg Met Leu Phe Gln His Phe Gln Ser Ser Ser Glu
1 5 10 15

Ser Val Met Asn Gly Ile Cys Leu Leu Leu Ala Ala Val Thr Val Lys
20 25 30

Leu Tyr Ser Ser Phe Asp Phe Asn Cys Pro Cys Leu Val His Tyr Asn
35 40 45

Ala Leu Tyr Gly Leu Gly Leu Leu Leu Thr Pro Pro Leu Ala Leu Phe
50 55 60

Leu Cys Gly Leu Leu Ala Asn Arg Gln Ser Val Val Met Val Glu Glu
65 70 75 80

Trp Arg Arg Pro Ala Gly His Arg Arg Lys Asp Pro Gly Ile Ile Arg
85 90 95

Tyr Met Cys Ser Ser Val Leu Gln Arg Ala Leu Ala Ala Pro Leu Val
100 105 110

Trp Ile Leu Leu Ala Leu Leu Asp Gly Lys Cys Phe Val Cys Ala Phe
115 120 125

Ser Ser Ser Val Asp Pro Glu Lys Phe Leu Asp Phe Ala Asn Met Thr
130 135 140

Pro Ser Gln Val Gln Leu Phe Leu Ala Lys Val Pro Cys Lys Glu Asp
145 150 155 160

Glu Leu Val Arg Asp Ser Pro Ala Arg Lys Ala Val Ser Arg Tyr Leu
165 170 175

Arg Cys Leu Ser Gln Ala Ile Gly Trp Ser Val Thr Leu Leu Leu Ile
180 185 190

Ile Ala Ala Phe Leu Ala Arg Cys Leu Arg Pro Cys Phe Asp Gln Thr
195 200 205

Val Phe Leu Gln Arg Arg Tyr Trp Ser Asn Tyr Val Asp Leu Glu Gln
210 215 220

Lys Leu Phe Asp Glu Thr Cys Cys Glu His Ala Arg Asp Phe Ala His
225 230 235 240

Arg Cys Val Leu His Phe Phe Ala Ser Met Arg Ser Glu Leu Gln Ala
245 250 255

Arg Gly Leu Arg Arg Gly Asn Ala Gly Arg Arg Leu Glu Leu Pro Ala
260 265 270

2015201738 07 Apr 2015

14/223

342-10PCT.txt

Val Pro Glu Pro Pro Glu Gly Leu Asp Ser Gly Ser Gly Lys Ala His
275 280 285

Leu Arg Ala Ile Ser Ser Arg Glu Gln Val Asp Arg Leu Leu Ser Thr
290 295 300

Trp Tyr Ser Ser Lys Pro Pro Leu Asp Leu Ala Ala Ser Pro Gly Leu
305 310 315 320

Cys Gly Gly Gly Leu Ser His Arg Ala Pro Thr Leu Ala Leu Gly Thr
325 330 335

Arg Leu Ser Gln His Thr Asp Val
340

<210> 19
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 19
gaggaaggac ccaggcatca 20

<210> 20
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 20
gaaggcacac acgaagcact 20

<210> 21
<211> 4556
<212> DNA
<213> Homo sapiens

<400> 21
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ccgcccggga gtcgggagcc gcggggaacc gggcacctgc accgcctct gggagtgagt 120
ggttccagct ggtgcctggc ctgtgtctct tggatgccct gtggcttcag tccgtctcct 180
gttgcccacc acctcgtccc tgggcccgcct gataccccag cccaacagct aaggtgtgga 240
tggaacagtag ggggctggct tctctcactg gtcaggggtc ttctcccctg tctgcctccc 300
ggagctagga ctgcagaggg gcctatcatg gtgcttgag gccccctggc tgtctcgctg 360
ttgctgcca gcctcacact gctggtgtcc cacctctcca gctcccagga tgtctccagt 420
gagcccagca gtgagcagca gctgtgcgcc cttagcaagc accccaccgt ggcctttgaa 480
gacctgcagc cgtaggtctc taacttcacc taccctggag cccgggattt ctcccagctg 540

342-10PCT.txt

gcttttgacc	cctccgggaa	ccagctcatc	gtgggagcca	ggaactacct	cttcagactc	600
agccttgcca	atgtctctct	tcttcaggcc	acagagtggg	cctccagtga	ggacacgcgc	660
cgctcctgcc	aaagcaaagg	gaagactgag	gaggagtgtc	agaactacgt	gcgagtcctg	720
atcgtcgccg	gccggaaggt	gttcatgtgt	ggaaccaatg	ccttttcccc	catgtgcacc	780
agcagacagg	tggggaacct	cagccggact	attgagaaga	tcaatgggtg	ggcccgtgc	840
ccctatgacc	cacgccacaa	ctccacagct	gtcatctcct	cccaggggga	gctctatgca	900
gccacggtca	tcgacttctc	aggctgggac	cctgccatct	accgcagcct	gggcagtggg	960
ccaccgcttc	gcactgcccc	atataactcc	aagtggctta	atgagccaaa	cttcgtggca	1020
gcctatgata	ttgggctggt	tgcatacttc	ttcctgcggg	agaacgcagt	ggagcacgac	1080
tgtggacgca	ccgtgtactc	tcgctgggcc	cgctgttgca	agaatgacgt	ggggggccga	1140
ttcctgctgg	aggacacatg	gaccacattc	atgaaggccc	ggctcaactg	ctcccgcccg	1200
ggcgaggtcc	ccttctacta	taacgagctg	cagagtgcct	tccacttgcc	ggagcaggac	1260
ctcatctatg	gagttttcac	aaccaacgta	aacagcatcg	cggcttctgc	tgtctgcgcc	1320
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agggctgcct	ggctcccat	agccaacccc	atccccaatt	tccagtgtgg	caccctgcct	1440
gagaccggtc	ccaacgagaa	cctgacggag	cgcagcctgc	aggacgcgca	gcgctcttc	1500
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cgcttctcac	acctcgtggt	ggacctgggt	caggctaaag	acacgctcta	ccatgtactc	1620
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342-10PCT.txt

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07 Apr 2015
2015201738

17/223
342-10PCT.txt

<211> 1151
<212> PRT
<213> Homo sapiens
<400> 22

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Gly Pro Pro Asp Thr Pro Ala Gln Gln Leu Arg Cys Gly Trp Thr Val
20 25 30

Gly Gly Trp Leu Leu Ser Leu Val Arg Gly Leu Leu Pro Cys Leu Pro
35 40 45

Pro Gly Ala Arg Thr Ala Glu Gly Pro Ile Met Val Leu Ala Gly Pro
50 55 60

Leu Ala Val Ser Leu Leu Leu Pro Ser Leu Thr Leu Leu Val Ser His
65 70 75 80

Leu Ser Ser Ser Gln Asp Val Ser Ser Glu Pro Ser Ser Glu Gln Gln
85 90 95

Leu Cys Ala Leu Ser Lys His Pro Thr Val Ala Phe Glu Asp Leu Gln
100 105 110

Pro Trp Val Ser Asn Phe Thr Tyr Pro Gly Ala Arg Asp Phe Ser Gln
115 120 125

Leu Ala Leu Asp Pro Ser Gly Asn Gln Leu Ile Val Gly Ala Arg Asn
130 135 140

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

Glu Trp Ala Ser Ser Glu Asp Thr Arg Arg Ser Cys Gln Ser Lys Gly
165 170 175

Lys Thr Glu Glu Glu Cys Gln Asn Tyr Val Arg Val Leu Ile Val Ala
180 185 190

Gly Arg Lys Val Phe Met Cys Gly Thr Asn Ala Phe Ser Pro Met Cys
195 200 205

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

Gly Val Ala Arg Cys Pro Tyr Asp Pro Arg His Asn Ser Thr Ala Val
225 230 235 240

Ile Ser Ser Gln Gly Glu Leu Tyr Ala Ala Thr Val Ile Asp Phe Ser
245 250 255

2015201738 07 Apr 2015

18/223
342-10PCT.txt

Gly Arg Asp Pro Ala Ile Tyr Arg Ser Leu Gly Ser Gly Pro Pro Leu
260 265 270

Arg Thr Ala Gln Tyr Asn Ser Lys Trp Leu Asn Glu Pro Asn Phe Val
275 280 285

Ala Ala Tyr Asp Ile Gly Leu Phe Ala Tyr Phe Phe Leu Arg Glu Asn
290 295 300

Ala Val Glu His Asp Cys Gly Arg Thr Val Tyr Ser Arg Val Ala Arg
305 310 315 320

Val Cys Lys Asn Asp Val Gly Gly Arg Phe Leu Leu Glu Asp Thr Trp
325 330 335

Thr Thr Phe Met Lys Ala Arg Leu Asn Cys Ser Arg Pro Gly Glu Val
340 345 350

Pro Phe Tyr Tyr Asn Glu Leu Gln Ser Ala Phe His Leu Pro Glu Gln
355 360 365

Asp Leu Ile Tyr Gly Val Phe Thr Thr Asn Val Asn Ser Ile Ala Ala
370 375 380

Ser Ala Val Cys Ala Phe Asn Leu Ser Ala Ile Ser Gln Ala Phe Asn
385 390 395 400

Gly Pro Phe Arg Tyr Gln Glu Asn Pro Arg Ala Ala Trp Leu Pro Ile
405 410 415

Ala Asn Pro Ile Pro Asn Phe Gln Cys Gly Thr Leu Pro Glu Thr Gly
420 425 430

Pro Asn Glu Asn Leu Thr Glu Arg Ser Leu Gln Asp Ala Gln Arg Leu
435 440 445

Phe Leu Met Ser Glu Ala Val Gln Pro Val Thr Pro Glu Pro Cys Val
450 455 460

Thr Gln Asp Ser Val Arg Phe Ser His Leu Val Val Asp Leu Val Gln
465 470 475 480

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

Thr Ile Leu Lys Ala Leu Ser Thr Ala Ser Arg Ser Leu His Gly Cys
500 505 510

Tyr Leu Glu Glu Leu His Val Leu Pro Pro Gly Arg Arg Glu Pro Leu
515 520 525

2015201738 07 Apr 2015

19/223
342-10PCT.txt

Arg Ser Leu Arg Ile Leu His Ser Ala Arg Ala Leu Phe Val Gly Leu
530 535 540

Arg Asp Gly Val Leu Arg Val Pro Leu Glu Arg Cys Ala Ala Tyr Arg
545 550 555 560

Ser Gln Gly Ala Cys Leu Gly Ala Arg Asp Pro Tyr Cys Gly Trp Asp
565 570 575

Gly Lys Gln Gln Arg Cys Ser Thr Leu Glu Asp Ser Ser Asn Met Ser
580 585 590

Leu Trp Thr Gln Asn Ile Thr Ala Cys Pro Val Arg Asn Val Thr Arg
595 600 605

Asp Gly Gly Phe Gly Pro Trp Ser Pro Trp Gln Pro Cys Glu His Leu
610 615 620

Asp Gly Asp Asn Ser Gly Ser Cys Leu Cys Arg Ala Arg Ser Cys Asp
625 630 635 640

Ser Pro Arg Pro Arg Cys Gly Gly Leu Asp Cys Leu Gly Pro Ala Ile
645 650 655

His Ile Ala Asn Cys Ser Arg Asn Gly Ala Trp Thr Pro Trp Ser Ser
660 665 670

Trp Ala Leu Cys Ser Thr Ser Cys Gly Ile Gly Phe Gln Val Arg Gln
675 680 685

Arg Ser Cys Ser Asn Pro Ala Pro Arg His Gly Gly Arg Ile Cys Val
690 695 700

Gly Lys Ser Arg Glu Glu Arg Phe Cys Asn Glu Asn Thr Pro Cys Pro
705 710 715 720

Val Pro Ile Phe Trp Ala Ser Trp Gly Ser Trp Ser Lys Cys Ser Ser
725 730 735

Asn Cys Gly Gly Gly Met Gln Ser Arg Arg Arg Ala Cys Glu Asn Gly
740 745 750

Asn Ser Cys Leu Gly Cys Gly Val Glu Phe Lys Thr Cys Asn Pro Glu
755 760 765

Gly Cys Pro Glu Val Arg Arg Asn Thr Pro Trp Thr Pro Trp Leu Pro
770 775 780

Val Asn Val Thr Gln Gly Gly Ala Arg Gln Glu Gln Arg Phe Arg Phe
785 790 795 800

2015201738 07 Apr 2015

20/223
342-10PCT.txt

Thr Cys Arg Ala Pro Leu Ala Asp Pro His Gly Leu Gln Phe Gly Arg
805 810 815

Arg Arg Thr Glu Thr Arg Thr Cys Pro Ala Asp Gly Ser Gly Ser Cys
820 825 830

Asp Thr Asp Ala Leu Val Glu Val Leu Leu Arg Ser Gly Ser Thr Ser
835 840 845

Pro His Thr Val Ser Gly Gly Trp Ala Ala Trp Gly Pro Trp Ser Ser
850 855 860

Cys Ser Arg Asp Cys Glu Leu Gly Phe Arg Val Arg Lys Arg Thr Cys
865 870 875 880

Thr Asn Pro Glu Pro Arg Asn Gly Gly Leu Pro Cys Val Gly Asp Ala
885 890 895

Ala Glu Tyr Gln Asp Cys Asn Pro Gln Ala Cys Pro Val Arg Gly Ala
900 905 910

Trp Ser Cys Trp Thr Ser Trp Ser Pro Cys Ser Ala Ser Cys Gly Gly
915 920 925

Gly His Tyr Gln Arg Thr Arg Ser Cys Thr Ser Pro Ala Pro Ser Pro
930 935 940

Gly Glu Asp Ile Cys Leu Gly Leu His Thr Glu Glu Ala Leu Cys Ala
945 950 955 960

Thr Gln Ala Cys Pro Glu Gly Trp Ser Pro Trp Ser Glu Trp Ser Lys
965 970 975

Cys Thr Asp Asp Gly Ala Gln Ser Arg Ser Arg His Cys Glu Glu Leu
980 985 990

Leu Pro Gly Ser Ser Ala Cys Ala Gly Asn Ser Ser Gln Ser Arg Pro
995 1000 1005

Cys Pro Tyr Ser Glu Ile Pro Val Ile Leu Pro Ala Ser Ser Met
1010 1015 1020

Glu Glu Ala Thr Asp Cys Ala Gly Phe Asn Leu Ile His Leu Val
1025 1030 1035

Ala Thr Gly Ile Ser Cys Phe Leu Gly Ser Gly Leu Leu Thr Leu
1040 1045 1050

Ala Val Tyr Leu Ser Cys Gln His Cys Gln Arg Gln Ser Gln Glu
1055 1060 1065

2015201738 07 Apr 2015

21/223
342-10PCT.txt

Ser Thr Leu Val His Pro Ala Thr Pro Asn His Leu His Tyr Lys
1070 1075 1080

Gly Gly Gly Thr Pro Lys Asn Glu Lys Tyr Thr Pro Met Glu Phe
1085 1090 1095

Lys Thr Leu Asn Lys Asn Asn Leu Ile Pro Asp Asp Arg Ala Asn
1100 1105 1110

Phe Tyr Pro Leu Gln Gln Thr Asn Val Tyr Thr Thr Thr Tyr Tyr
1115 1120 1125

Pro Ser Pro Leu Asn Lys His Ser Phe Arg Pro Glu Ala Ser Pro
1130 1135 1140

Gly Gln Arg Cys Phe Pro Asn Ser
1145 1150

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<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 23
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<210> 24
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 24
gttcgacgtc ttgaactcca c 21

<210> 25
<211> 1299
<212> DNA
<213> Homo sapiens

<400> 25
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gggactcctg agtgggggtca acaagtactc cacagccttt gggcgcatct ggctgtctct 180
ggtcttcattc ttccgcgtgc tgggtgtacct ggtgacggcc gagcgtgtgt ggagtgatga 240
ccacaaggac ttcgactgca atactcgcca gcccggtgc tccaacgtct gctttgatga 300
gttcttccct gtgtcccatg tgcgcctctg ggcctgcag cttatcctgg tgacatgcc 360

22/223

342-10PCT.txt

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ctgggtggaca tatgtctgca gcctagtgtt caaggcgagc gtggacatcg cctttctcta 540
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<210> 26
<211> 273
<212> PRT
<213> Homo sapiens

<400> 26

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20 25 30

Val Leu Val Tyr Leu Val Thr Ala Glu Arg Val Trp Ser Asp Asp His
35 40 45

Lys Asp Phe Asp Cys Asn Thr Arg Gln Pro Gly Cys Ser Asn Val Cys
50 55 60

Phe Asp Glu Phe Phe Pro Val Ser His Val Arg Leu Trp Ala Leu Gln
65 70 75 80

Leu Ile Leu Val Thr Cys Pro Ser Leu Leu Val Val Met His Val Ala
85 90 95

Tyr Arg Glu Val Gln Glu Lys Arg His Arg Glu Ala His Gly Glu Asn
100 105 110

23/223
342-10PCT.txt

Ser Gly Arg Leu Tyr Leu Asn Pro Gly Lys Lys Arg Gly Gly Leu Trp
115 120 125

Trp Thr Tyr Val Cys Ser Leu Val Phe Lys Ala Ser Val Asp Ile Ala
130 135 140

Phe Leu Tyr Val Phe His Ser Phe Tyr Pro Lys Tyr Ile Leu Pro Pro
145 150 155 160

Val Val Lys Cys His Ala Asp Pro Cys Pro Asn Ile Val Asp Cys Phe
165 170 175

Ile Ser Lys Pro Ser Glu Lys Asn Ile Phe Thr Leu Phe Met Val Ala
180 185 190

Thr Ala Ala Ile Cys Ile Leu Leu Asn Leu Val Glu Leu Ile Tyr Leu
195 200 205

Val Ser Lys Arg Cys His Glu Cys Leu Ala Ala Arg Lys Ala Gln Ala
210 215 220

Met Cys Thr Gly His His Pro His Gly Thr Thr Ser Ser Cys Lys Gln
225 230 235 240

Asp Asp Leu Leu Ser Gly Asp Leu Ile Phe Leu Gly Ser Asp Ser His
245 250 255

Pro Pro Leu Leu Pro Asp Arg Pro Arg Asp His Val Lys Lys Thr Ile
260 265 270

Leu

<210> 27
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 27
ggagtagtca ctcagtagca gc

22

<210> 28
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 28
gaactcatca aagcagacg

19

2015201738 07 Apr 2015

24/223
342-10PCT.txt

<210> 29
<211> 1528
<212> DNA
<213> Homo sapiens

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gtccttgtgg ttcctctcta cctggggaaa taagggtcag cggccatggc tacagcaaga 300
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gtttatgaat ctgggcagca gatgttccag ggggtcaa atccatcccc cctggctac 720
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aaaaaaaaa aaaaaaaaaa aaaaaaaa 1528

<210> 30
<211> 293
<212> PRT
<213> Homo sapiens

<400> 30

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1 5 10 15

07 Apr 2015
2015201738

25/223
342-10PCT.txt

Thr Ala Leu Leu Leu Gly Val Thr Glu His Val Leu Ala Asn Asn Asp
20 25 30

Val Ser Cys Asp His Pro Ser Asn Thr Val Pro Ser Gly Ser Asn Gln
35 40 45

Asp Leu Gly Ala Gly Ala Gly Glu Asp Ala Arg Ser Asp Asp Ser Ser
50 55 60

Ser Arg Ile Ile Asn Gly Ser Asp Cys Asp Met His Thr Gln Pro Trp
65 70 75 80

Gln Ala Ala Leu Leu Leu Arg Pro Asn Gln Leu Tyr Cys Gly Ala Val
85 90 95

Leu Val His Pro Gln Trp Leu Leu Thr Ala Ala His Cys Arg Lys Lys
100 105 110

Val Phe Arg Val Arg Leu Gly His Tyr Ser Leu Ser Pro Val Tyr Glu
115 120 125

Ser Gly Gln Gln Met Phe Gln Gly Val Lys Ser Ile Pro His Pro Gly
130 135 140

Tyr Ser His Pro Gly His Ser Asn Asp Leu Met Leu Ile Lys Leu Asn
145 150 155 160

Arg Arg Ile Arg Pro Thr Lys Asp Val Arg Pro Ile Asn Val Ser Ser
165 170 175

His Cys Pro Ser Ala Gly Thr Lys Cys Leu Val Ser Gly Trp Gly Thr
180 185 190

Thr Lys Ser Pro Gln Val His Phe Pro Lys Val Leu Gln Cys Leu Asn
195 200 205

Ile Ser Val Leu Ser Gln Lys Arg Cys Glu Asp Ala Tyr Pro Arg Gln
210 215 220

Ile Asp Asp Thr Met Phe Cys Ala Gly Asp Lys Ala Gly Arg Asp Ser
225 230 235 240

Cys Gln Gly Asp Ser Gly Gly Pro Val Val Cys Asn Gly Ser Leu Gln
245 250 255

Gly Leu Val Ser Trp Gly Asp Tyr Pro Cys Ala Arg Pro Asn Arg Pro
260 265 270

Gly Val Tyr Thr Asn Leu Cys Lys Phe Thr Lys Trp Ile Gln Glu Thr
275 280 285

2015201738 07 Apr 2015

26/223
342-10PCT.txt

Ile Gln Ala Asn Ser
290

<210> 31
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 31
cagaaaaggt gcgaggatg 19

<210> 32
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 32
ctgggatgac tcaggagttg g 21

<210> 33
<211> 636
<212> DNA
<213> Homo sapiens

<400> 33
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gcgcagtctg gcctcgctcg gggccactcc tcgtag 636

<210> 34
<211> 211
<212> PRT
<213> Homo sapiens

<400> 34

Met Thr Glu Ala Ala Ser Leu Val Pro Lys Arg Pro Arg Arg Leu Arg
1 5 10 15

07 Apr 2015
2015201738

27/223
342-10PCT.txt

Gly Ser His Lys Leu Arg Val Leu Ala Trp Pro Val Val Val Val
20 25 30

Asn Phe Val Trp Gln Cys Asn Gly Ser Ile Ala His Thr Phe Leu Glu
35 40 45

Leu Ser Phe Ala Cys Pro Gly Gly Arg Tyr Ala Gly Ser Arg Pro Ala
50 55 60

Pro Val Ala Gly Met Asp Arg Asp Gln Gln Arg Ala Glu Ser Ala Cys
65 70 75 80

Val Pro His Ser Arg Ser Arg Gly Pro Asn Leu Pro Ser Ala Gln Ser
85 90 95

Pro Ala Gln Ser Leu Pro Gly Pro Glu Leu Ser Gln Thr Pro His Pro
100 105 110

His Ser Arg Leu Thr Pro Arg Ser Trp Ala Trp Ala Pro Leu Ala Arg
115 120 125

Val Gln Gly Gln Pro Ser Ser Pro Ser Ala Arg Pro Arg Pro Ser Phe
130 135 140

Leu Gly Ala Gly Pro Leu Arg Gly Pro Ser Gly Pro Glu Gln Ala Pro
145 150 155 160

Pro Pro Gly Gly Leu Arg Leu Ser Pro Arg Asp Leu Pro Arg Pro Thr
165 170 175

Val Gly Gly Ser Gln Ala Ala Thr Pro Gly Arg Arg Arg Pro Leu Ala
180 185 190

Glu Pro Pro Arg Ser Leu Pro Ser Ala Gln Ser Gly Leu Ala Arg Gly
195 200 205

His Ser Ser
210

<210> 35
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 35
tgctctcact gtggtcctca g

<210> 36
<211> 21

07 Apr 2015

2015201738

28/223
342-10PCT.txt

<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 36
tttgtaaagc tccagcgcta c

21

<210> 37
<211> 969
<212> DNA
<213> Homo sapiens

<400> 37
atgaaggact gtaggaacaa tggcaaggat tgtcaaagtg cccctgcaac acgtaggcac 60
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ctgggggggcc tcatggcggg gccattcatc ctggccaagg acctgtgcct gcagcaggac 180
cccctgacac agagctacct catcagcacc attttctttg ctccagcatc tgcattgctcc 240
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cccagatgc tccagacagg gattctccag ccggaccagg ttgttcagat gctgctgacc 900
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<210> 38
<211> 322
<212> PRT
<213> Homo sapiens

<400> 38

Met Lys Asp Cys Arg Asn Asn Gly Lys Asp Cys Gln Ser Ala Pro Ala
1 5 10 15

Thr Arg Arg His Leu Phe Ser Glu Ala Ala Leu Pro Pro Tyr Arg Leu
20 25 30

Ser Gln Gly His Phe Leu Thr Ala Leu Gly Gly Leu Met Ala val Pro
35 40 45

2015201738 07 Apr 2015

29/223

342-10PCT.txt

Phe Ile Leu Ala Lys Asp Leu Cys Leu Gln Gln Asp Pro Leu Thr Gln
50 55 60

Ser Tyr Leu Ile Ser Thr Ile Phe Phe Ala Pro Ala Ser Ala Cys Ser
65 70 75 80

Cys Lys Leu Pro Ile Pro Gln Gly Gly Thr Phe Ala Phe Val Val Ile
85 90 95

Ser Leu Ala Met Leu Ser Leu Pro Ser Trp Asn Cys Pro Glu Trp Thr
100 105 110

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

Trp Gln Lys Arg Ile Gln Glu Gly Ala Ile Met Val Thr Ser Cys Val
130 135 140

Arg Met Leu Val Gly Phe Ser Gly Leu Thr Gly Phe Leu Met Gly Phe
145 150 155 160

Ile Cys Ser Leu Ala Val Ala Pro Thr Asn Cys Leu Val Ala Leu Pro
165 170 175

Leu Leu Asp Ser Ala Gly Asn Asn Ala Gly Ile Gln Trp Gly Ile Ser
180 185 190

Ala Met Tyr Cys Phe Val Leu Arg Leu Arg Lys Asp Glu Leu Trp Pro
195 200 205

Phe Gly Ser Pro Arg Leu Arg Leu Pro Pro Ser Pro Pro Arg Asp Arg
210 215 220

Arg His Val Pro Thr Pro Val Ile Gly Gly Met Thr Leu Phe Gly Val
225 230 235 240

Ile Thr Ala Val Gly Ile Ser Asn Leu Gln Tyr Val Asp Met Asn Leu
245 250 255

Ser Arg Ser Leu Phe Ala Phe Gly Phe Ser Ile Tyr Cys Gly Leu Thr
260 265 270

Ile Pro Asn Arg Val Ser Lys Asn Pro Glu Met Leu Gln Thr Gly Ile
275 280 285

Leu Gln Pro Asp Gln Val Val Gln Met Leu Leu Thr Met Gly Met Phe
290 295 300

Ile Ser Gly Phe Leu Gly Phe Leu Leu Asp Asn Thr Ile Pro Glu Leu
305 310 315 320

2015201738 07 Apr 2015

30/223
342-10PCT.txt

Leu Gln

<210> 39
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 39
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<210> 40
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 40
caggaggga gggagagcat 20

<210> 41
<211> 1679
<212> DNA
<213> Homo sapiens

<400> 41
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gctggccccg tgccccacgg ccggcctggc cggcgccctg ggggtcacgg cgtgcgccgc 240
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ctgctggttc tgcaaccagg atacgtggt gccctatggg aaccgcaact gctgggactg 360
tccccactgc gagcagtaca acggcttcca ggagaacggc gactacaaca agccgatccc 420
cgcccagtagc ttggagcacc tgaaccacgt ggtgagcagc gcgccagcc tgcgcgaccc 480
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cctactgacc accgcgtgt atggggccag cggacacttc gcccaggca cactgtgccc 900
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2015201738 07 Apr 2015

31/223

342-10PCT.txt

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ctgctgccac ctctctggcc aatggccctt tctctggcct ggtgactgga atgtgggcag 1620
cgcccacaca ggctctggcc catggcttcc tactggcagc tccaggcacc cccctctca 1679

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<210> 42
 <211> 392
 <212> PRT
 <213> Homo sapiens

<400> 42

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Ala Gly Gly Leu Gly Val Thr Ala Cys Ala Ala Ala Gly Val Leu Leu
 20 25 30

Tyr Arg Ile Ala Arg Arg Met Lys Pro Thr His Thr Met Val Asn Cys
 35 40 45

Trp Phe Cys Asn Gln Asp Thr Leu Val Pro Tyr Gly Asn Arg Asn Cys
 50 55 60

Trp Asp Cys Pro His Cys Glu Gln Tyr Asn Gly Phe Gln Glu Asn Gly
 65 70 75 80

Asp Tyr Asn Lys Pro Ile Pro Ala Gln Tyr Leu Glu His Leu Asn His
 85 90 95

Val Val Ser Ser Ala Pro Ser Leu Arg Asp Pro Ser Gln Pro Gln Gln
 100 105 110

Trp Val Ser Ser Gln Val Leu Leu Cys Lys Arg Cys Asn His His Gln
 115 120 125

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

2015201738 07 Apr 2015

32/223

342-10PCT.txt

Arg Tyr Asp Glu Glu Val Glu Val Tyr Arg His His Leu Glu Gln Met
145 150 155 160

Tyr Lys Leu Cys Arg Pro Cys Gln Ala Ala Val Glu Tyr Tyr Ile Lys
165 170 175

His Gln Asn Arg Gln Leu Arg Ala Leu Leu Leu Ser His Gln Phe Lys
180 185 190

Arg Arg Glu Ala Asp Gln Thr His Ala Gln Asn Phe Ser Ser Ala Val
195 200 205

Lys Ser Pro Val Gln Val Ile Leu Leu Arg Ala Leu Ala Phe Leu Ala
210 215 220

Cys Ala Phe Leu Leu Thr Thr Ala Leu Tyr Gly Ala Ser Gly His Phe
225 230 235 240

Ala Pro Gly Thr Thr Val Pro Leu Ala Leu Pro Pro Gly Gly Asn Gly
245 250 255

Ser Ala Thr Pro Asp Asn Gly Thr Thr Pro Gly Ala Glu Gly Trp Arg
260 265 270

Gln Leu Leu Gly Leu Leu Pro Glu His Met Ala Glu Lys Leu Cys Glu
275 280 285

Ala Trp Ala Phe Gly Gln Ser His Gln Thr Gly Val Val Ala Leu Gly
290 295 300

Leu Leu Thr Cys Leu Leu Ala Met Leu Leu Ala Gly Arg Ile Arg Leu
305 310 315 320

Arg Arg Ile Asp Ala Phe Cys Thr Cys Leu Trp Ala Leu Leu Leu Gly
325 330 335

Leu His Leu Ala Glu Gln His Leu Gln Ala Ala Ser Pro Ser Trp Leu
340 345 350

Asp Thr Leu Lys Phe Ser Thr Thr Ser Leu Cys Cys Leu Val Gly Phe
355 360 365

Thr Ala Ala Val Ala Thr Arg Lys Ala Thr Gly Pro Arg Arg Phe Arg
370 375 380

Pro Arg Arg Ser Glu Lys Gln Pro
385 390

<210> 43

<211> 23

<212> DNA

<213> Artificial Sequence

2015201738 07 Apr 2015

33/223

342-10PCT.txt

<220>
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<400> 43
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<210> 44
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 44
ggacttcacg gcggaggag 19

<210> 45
<211> 727
<212> DNA
<213> Homo sapiens

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ggtgaaagga ctctggattg gttggcagtc tgcttttttt ttccaaggt gatcacttta 180
ctgtagaaga aatgaggtta acagaaaaga gtgaggggaga acaacaactc aagcccaaca 240
actctaattgc acccaatgaa gatcaagaag aagaaatcca acagtcagaa cagcatactc 300
cagcaaggca gcgaacacaa agagcagaca cacagccatc cagatgtcga ttgccttcac 360
gtaggacacc tacaacatcc agcgacagaa cgatcaacct tcttgaagtc cttccgtggc 420
ctactgagtg gatcttcaac ccctatcgat tgcttgcctt ttttgagctt tatcctgaat 480
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aaaagatcgg actgccatc atactccacc tcttcgcact ctccaccctc tacttctaca 600
agtttttcct tcctacaatt ctttcccttt ctttctttat tcttcttgta cttctgcttc 660
tgctttttat tattgtcttc attctgatct tcttctgatt cttttgtttc aataaacagc 720
aatgagc 727

<210> 46
<211> 168
<212> PRT
<213> Homo sapiens

<400> 46

Met Arg Leu Thr Glu Lys Ser Glu Gly Glu Gln Gln Leu Lys Pro Asn
1 5 10 15

Asn Ser Asn Ala Pro Asn Glu Asp Gln Glu Glu Glu Ile Gln Gln Ser
20 25 30

07 Apr 2015
2015201738

34/223

342-10PCT.txt

Glu Gln His Thr Pro Ala Arg Gln Arg Thr Gln Arg Ala Asp Thr Gln
35 40 45

Pro Ser Arg Cys Arg Leu Pro Ser Arg Arg Thr Pro Thr Thr Ser Ser
50 55 60

Asp Arg Thr Ile Asn Leu Leu Glu Val Leu Pro Trp Pro Thr Glu Trp
65 70 75 80

Ile Phe Asn Pro Tyr Arg Leu Pro Ala Leu Phe Glu Leu Tyr Pro Glu
85 90 95

Phe Leu Leu Val Phe Lys Glu Ala Phe His Asp Ile Ser His Cys Leu
100 105 110

Lys Ala Gln Met Glu Lys Ile Gly Leu Pro Ile Ile Leu His Leu Phe
115 120 125

Ala Leu Ser Thr Leu Tyr Phe Tyr Lys Phe Phe Leu Pro Thr Ile Leu
130 135 140

Ser Leu Ser Phe Phe Ile Leu Leu Val Leu Leu Leu Leu Phe Ile
145 150 155 160

Ile Val Phe Ile Leu Ile Phe Phe
165

<210> 47
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 47
gctggtgaaa ggactctgga 20

<210> 48
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 48
tcgctggatg ttgtaggtgt 20

<210> 49
<211> 950
<212> DNA
<213> Homo sapiens

<400> 49
gcgagcccga gcaggcagac gcgcggccgg cggctctgggg gcgcgccgcc tcccgggtccc 60

2015201738 07 Apr 2015

35/223

342-10PCT.txt

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caaaatgtga agcggggagg gcgagagacgc agagacggcc cggccgggcg ccctcgccgc 120
cctccggcag ccgcgccgct ccctccgctg cacgcccagg cctgagcagc gaggccaccg 180
ggccgcgcgc tcccagcttc gctcggacgc ggcttcggcc cgcagagggg tcgtggcccc 240
gacgcggcga gagctgggcc caggacggtg cgtccggcct cgcccgcggc tgctcgcacc 300
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acctgctgga gctgatggtg aagcgcatgg acgactggc caggctggag aacagcagtg 600
agctgcaccg ggccggcggc gacctgcact ttcccgcaga caggatgccc cctggggccg 660
gcctcatgga gcggatccag gctattgccc agaactgtc cgacatcgct gtgaagggtg 720
accagatcct gcgccacagt ctgctcctgc acagcaagg gtcagaaggc cggcgggacc 780
agtgtgaggc acccagtgac cccaagttcc ctgactgctc aggggaagg gacagtggatg 840
cgtgcccgtt ggacctctga cccctgctac gccttctttg ggggtggacg caccgagtgc 900
tccttctca tctacctcag tgaggtcgag tggttctgcc ccccgctgcc 950

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<210> 50
 <211> 181
 <212> PRT
 <213> Homo sapiens

<400> 50

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 1 5 10 15

Val Thr Leu Arg Pro Phe Arg Leu Phe Val Leu Gly Ile Gly Phe Phe
 20 25 30

Thr Leu Cys Phe Leu Met Thr Ser Leu Gly Gly Gln Phe Ser Ala Arg
 35 40 45

Arg Leu Gly Asp Ser Pro Phe Thr Ile Arg Thr Glu Val Met Gly Gly
 50 55 60

Pro Glu Ser Arg Gly Val Leu Arg Lys Met Ser Asp Leu Leu Glu Leu
 65 70 75 80

Met Val Lys Arg Met Asp Ala Leu Ala Arg Leu Glu Asn Ser Ser Glu
 85 90 95

Leu His Arg Ala Gly Gly Asp Leu His Phe Pro Ala Asp Arg Met Pro
 100 105 110

Pro Gly Ala Gly Leu Met Glu Arg Ile Gln Ala Ile Ala Gln Asn Val
 115 120 125

36/223

342-10PCT.txt

Ser Asp Ile Ala Val Lys Val Asp Gln Ile Leu Arg His Ser Leu Leu
 130 135 140

Leu His Ser Lys Val Ser Glu Gly Arg Arg Asp Gln Cys Glu Ala Pro
 145 150 155 160

Ser Asp Pro Lys Phe Pro Asp Cys Ser Gly Lys Val Ala Val Asp Ala
 165 170 175

Cys Pro Leu Asp Leu
 180

<210> 51
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide

<400> 51
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<210> 52
 <211> 20
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide

<400> 52
 ggccccccat cacttctgtg 20

<210> 53
 <211> 396
 <212> DNA
 <213> Homo sapiens

<400> 53
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 acctaccact atgaccacat gagctttcac tacacggctg tcctgatgtt ctcccagggtg 180
 atcagcatct gctgggctgc catgggggtca ctctatgctg agatgacaga aaacaatgct 240
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<210> 54
 <211> 99
 <212> PRT
 <213> Homo sapiens

2015201738 07 Apr 2015

37/223

342-10PCT.txt

<400> 54

Met Met Leu Thr Thr Ala Ala Leu Met Leu Phe Phe Leu His Leu Gly
1 5 10 15

Ile Phe Ile Arg Asp Val His Asn Phe Cys Ile Thr Tyr His Tyr Asp
20 25 30

His Met Ser Phe His Tyr Thr Val Val Leu Met Phe Ser Gln Val Ile
35 40 45

Ser Ile Cys Trp Ala Ala Met Gly Ser Leu Tyr Ala Glu Met Thr Glu
50 55 60

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

Ser Gly His Arg Val Pro Gly Gly Ala Pro Leu Arg Pro Gly Glu Ser
85 90 95

Glu Gln Gly

<210> 55

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 55

ccgttgagca ttgttttctg tc

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<210> 56

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 56

tgctcttctt cttacacctg gg

22

<210> 57

<211> 539

<212> DNA

<213> Homo sapiens

<400> 57

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catcggtatgc tcatgttcac cacaactgtc ctcacctgca ttgcttttgt tatgccgttt 180

atatacaggg gaggcaggag taggcatgca ggttaccacc catacctcgg ctgtatagtg 240

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gacttaaaac aatctggaaa atgtgggtgc atctctttta aggattggta gattacgcag 420
ccataaaaaa gaatgaagtc atgtcttttg tagcaacatg gatgctgctg gaagtgatta 480
tcctacatga attaatgcag aaacagaaaa tcacatacca catgttctca cttataaat 539

<210> 58
<211> 133
<212> PRT
<213> Homo sapiens

<400> 58

Met Phe Val Ala Trp Met Thr Thr Val Ser Ile Gly Val Leu Val Ala
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Arg Phe Phe Lys Pro Val Trp Ser Lys Ala Phe Leu Leu Gly Glu Ala
20 25 30

Ala Trp Phe Gln Val His Arg Met Leu Met Phe Thr Thr Thr Val Leu
35 40 45

Thr Cys Ile Ala Phe Val Met Pro Phe Ile Tyr Arg Gly Gly Trp Ser
50 55 60

Arg His Ala Gly Tyr His Pro Tyr Leu Gly Cys Ile Val Met Thr Leu
65 70 75 80

Ala Val Leu Gln Pro Leu Leu Ala Val Phe Arg Pro Pro Leu His Asp
85 90 95

Pro Arg Arg Gln Met Phe Asn Trp Thr His Trp Ser Met Gly Thr Ala
100 105 110

Ala Arg Ile Ile Ala Asp Leu Lys Gln Ser Gly Lys Cys Gly Cys Ile
115 120 125

Ser Phe Lys Asp Trp
130

<210> 59
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 59

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<210> 60
<211> 20

342-10PCT.txt

<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 60
catcactata cagccgaggt

20

<210> 61
<211> 3317
<212> DNA
<213> Homo sapiens

<400> 61
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gtgccctggg ctggtcacct ctgcattttg ctctgctggg agtttgctcc tggccctcca 180
acagcgctc ctctgtgagg aggaactcct gttcccgtag ctctgctggc tctggaggct 240
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cctctcgtcc tcctgggtag cctgggagga atggcagaag aaagcagtga agccaggtag 360
cagtagcccc gccacccac caggctctgc tgtaggctgg gctctcaagg cagctgctcc 420
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gacacaccag tcgcctgact cccggtcagg caaacgcaca catcaagttc ttgcaagcca 1560

2015201738 07 Apr 2015

40/223

342-10PCT.txt

gggctctgct ggcattctca agaggagggg	gggtcctggc cctgaccaca gggctccctt	1620
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 <213> Homo sapiens
 <400> 62

2015201738 07 Apr 2015

41/223

342-10PCT.txt

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His Gln Gly Ala Phe Arg Ala Gly Asn Val Ile Gly Gln Leu Ile Tyr
20 25 30

Leu Leu Thr Trp Ser Leu Phe Thr Ala Trp Leu Arg Pro Pro Thr Leu
35 40 45

Leu Gln Gly Pro Arg Thr Ser Pro Gln Gly Ser Pro Pro Arg Ser Pro
50 55 60

Trp Gly Asp Cys Ala Glu Pro Ser Cys Leu Cys Glu Met Lys Ile Arg
65 70 75 80

Arg Arg Arg His Glu Gly Pro Ala Trp Gly Gln Ser Gly Phe Leu Ala
85 90 95

Gly Gly Leu His Leu Val Pro Ser Ser Leu Ser Leu Ala Ala Cys Gly
100 105 110

Val Val Arg Met Lys Gly Leu Trp Gly Arg Gly Ala Gly Ile Arg Gly
115 120 125

Arg

<210> 63
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 63
ccccaaggct ccgaacaccc 20

<210> 64
<211> 20
<212> DNA
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<220>
<223> Oligonucleotide

<400> 64
cccgatcaca tttcctgccc 20

<210> 65
<211> 3338
<212> DNA
<213> Homo sapiens

<400> 65
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342-10PCT.txt

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ccaccacaga gtcatagagg tcaagtcctt ttcttgtgaa acctaataaaa tgcaaattcc	720
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2015201738 07 Apr 2015

43/223

342-10PCT.txt

ctaaattatg	ccaagagaga	acattctgat	atttctcctc	aattctaggc	atgacagcgt	2160
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taaaaaactg	ggtgtagttg	tgagtatagt	gaatgcacat	agtatgtgcc	tttggcatgt	2340
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aaatgaggta	aagagtttaa	accagggaag	gcatagctgt	ggcaccaaaa	caacctgtta	2520
aaggcgagct	gtaggcacca	aaaaacctat	tatggactga	attgtgttcc	tcaaattcat	2580
atgttgaagt	gctaacccca	agtacaaat	gtgactgtat	ttggggatag	ggccctgaa	2640
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<210> 66
 <211> 122
 <212> PRT
 <213> Homo sapiens

<400> 66

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			20					25					30		
Ser	Leu	Phe	His	Phe	Ile	Val	Phe	Ser	Pro	Ser	Phe	Leu	Ser	Phe	Ser
		35					40					45			
Leu	Leu	Leu	Ser	Phe	Ser	Ser	Leu	Leu	Phe	Pro	Leu	Val	Phe	Asn	Phe
	50					55					60				
Asn	Phe	Asn	Phe	Trp	Pro	Ser	Tyr	Thr	Ser	Ile	Cys	Leu	Ser	Arg	Lys
65					70					75					80

2015201738 07 Apr 2015

44/223
342-10PCT.txt

Leu Asn Ser Arg Gln Leu Ile Ile His Leu Ile Ser Ser Ala Lys Gln
85 90 95

Met Pro Ser Met Val Ser Phe Val Ile Arg Leu Leu Trp Asp Gln Asn
100 105 110

Val Ser Tyr Ser Ser Gly Lys Asn Glu Thr
115 120

<210> 67
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<212> DNA
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<220>
<223> Oligonucleotide

<400> 67
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19

<210> 68
<211> 17
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<220>
<223> Oligonucleotide

<400> 68
cgctcatctt ctctca

17

<210> 69
<211> 1119
<212> DNA
<213> Homo sapiens

<400> 69
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aagaaatgca gaccctgcgt gtggtttttg caaccctggg tgtgggagct gcttctcttg 180
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45/223

342-10PCT.txt

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cctagctgcc cctcagagga gctctgtgct ataggctctgt gctgaggaaa gcaaaacacc	960
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ctttgccttt ggtgtatcct catcccttcc acagtgacct catacatccc ctgagcctca	1080
ctagatcaca cagaccatct ctgccagcc tgtccagga	1119

<210> 70
 <211> 97
 <212> PRT
 <213> Homo sapiens
 <400> 70

Met Ile Phe Asn Asn Phe Ser Ser Val Ala Val Phe Thr Pro Arg Gly
 1 5 10 15

Arg Ala Thr Gly Ile Thr Gly Asn Phe Ala Asn Ile Gly Gly Ala Leu
 20 25 30

Ala Ser Leu Met Met Ile Leu Ser Ile Tyr Ser Arg Pro Leu Pro Trp
 35 40 45

Ile Ile Tyr Gly Val Phe Ala Ile Leu Ser Gly Leu Val Val Leu Leu
 50 55 60

Leu Pro Glu Thr Arg Asn Gln Pro Leu Leu Asp Ser Ile Gln Asp Val
 65 70 75 80

Glu Asn Glu Gly Val Asn Ser Leu Ala Ala Pro Gln Arg Ser Ser Val
 85 90 95

Leu

<210> 71
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide

<400> 71
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21

<210> 72
 <211> 21
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 <220>

2015201738 07 Apr 2015

46/223
342-10PCT.txt

<223> Oligonucleotide

<400> 72

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21

<210> 73

<211> 2837

<212> DNA

<213> Homo sapiens

<400> 73

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catgaggatt ggtgtgacct gttccatatt ccgtgggtcca ttatttggtg ctgaaagaga	300
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342-10PCT.txt

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<210> 74
 <211> 102
 <212> PRT
 <213> Homo sapiens

<400> 74

Met Cys His Gly Glu Thr Phe Phe Arg Trp Ile Leu Arg Leu His Cys
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Asn Thr Ser Phe Leu Leu Leu Leu Gln Gln Ile Ile Ile Ile Ile Ile
 20 25 30

Ile Ile Ile Ile Ile Ile Ile Phe Arg Trp Ser Leu Ala Leu Ser Leu
 35 40 45

Arg Leu Glu Cys Ser Gly Ala Ile Ser Ala Arg Cys Lys Leu Arg Leu
 50 55 60

Val Gly Ser Cys His Ser Arg Ala Ser Ala Ser Gln Val Ala Gly Thr
 65 70 75 80

48/223

342-10PCT.txt

Thr Gly Thr Arg His His Thr Trp Leu Met Phe Arg Ile Phe Ser Arg
 85 90 95

Gly Gly Val Ser Ser Cys
 100

<210> 75
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<220>
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<400> 75
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<210> 76
 <211> 21
 <212> DNA
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<220>
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<400> 76
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<210> 77
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 <212> DNA
 <213> Homo sapiens

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342-10PCT.txt

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342-10PCT.txt

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2015201738 07 Apr 2015

51/223

342-10PCT.txt

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<212> PRT
<213> Homo sapiens

<400> 78

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Pro Glu Ser Glu Ser Val Leu Val Leu Thr Val Leu Met Pro Thr Glu
35 40 45

Glu Ala Tyr Ala Leu Pro Leu Val Val Lys Val Val Asp Asn Trp Ala
50 55 60

Phe Gly Gln Gln Thr Val Thr Gly Gln Ala Asn Ile Asp Phe Leu Gln
65 70 75 80

Pro Tyr Phe Cys Asp Pro Trp Ala Gln Asp Tyr Met His Pro Lys Leu
85 90 95

Pro Thr Leu Ser Glu Lys Lys His Gln Asp Phe Leu Gly Tyr Leu Tyr
100 105 110

Arg Lys Phe Trp Phe Lys Ser Ser Lys Ala Glu Asp Glu Tyr Glu His
115 120 125

2015201738 07 Apr 2015

52/223

342-10PCT.txt

Glu Val Asp Trp Trp Ser Lys Leu Phe Trp Ala Thr Asp Glu His Lys
130 135 140

Ser Leu Lys Tyr Lys Tyr Lys Asp Tyr His Thr Leu Lys Val Tyr Glu
145 150 155 160

Cys Glu Leu Glu Ala Val Pro Ala Phe Gln Gly Leu Gln Asp Phe Cys
165 170 175

Gln Thr Phe Lys Leu Tyr Gln Glu Gln Pro Lys Leu Asp Ser Pro Val
180 185 190

Val Gly Glu Phe Lys Gly Leu Phe Arg Ile Tyr Pro Phe Pro Glu Asn
195 200 205

Pro Glu Ala Pro Lys Pro Pro Leu Gln Phe Leu Val Trp Pro Glu Arg
210 215 220

Glu Asp Phe Pro Gln Pro Cys Leu Val Arg Val Tyr Met Val Arg Ala
225 230 235 240

Ile Asn Leu Gln Pro Gln Asp Tyr Asn Gly Leu Cys Asp Pro Tyr Val
245 250 255

Ile Leu Lys Leu Gly Lys Thr Glu Leu Gly Asn Arg Asp Met Tyr Gln
260 265 270

Pro Asn Thr Leu Asp Pro Ile Phe Gly Met Met Phe Glu Leu Thr Cys
275 280 285

Asn Ile Pro Leu Glu Lys Asp Leu Glu Ile Gln Leu Tyr Asp Phe Asp
290 295 300

Leu Phe Ser Pro Asp Asp Lys Ile Gly Thr Thr Val Ile Asp Leu Glu
305 310 315 320

Asn Arg Leu Leu Ser Gly Phe Gly Ala His Cys Gly Leu Ser Lys Ser
325 330 335

Tyr Cys Gln Ser Gly Pro Phe Arg Trp Arg Asp Gln Met Pro Pro Ser
340 345 350

Tyr Leu Leu Glu Arg Tyr Ala Lys Arg Lys Gly Leu Pro Pro Pro Leu
355 360 365

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

Leu Gln Ser Phe Glu Pro Lys Thr Pro Thr Val His Gly Leu Gly Pro
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2015201738 07 Apr 2015

53/223

342-10PCT.txt

Lys Lys Glu Arg Leu₄₀₅ Ala Leu Tyr Leu₄₁₀ Leu His Thr Gln Gly Leu₄₁₅ Val
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Ile Asp Gln₄₃₅ Gly Lys Val Gln Met Trp Val Asp Ile Phe₄₄₅ Pro Lys Lys
Leu Gly₄₅₀ Pro Pro Gly Pro Gln₄₅₅ Val Asn Ile Asn₄₆₀ Pro Arg Lys Pro Lys
Arg Tyr Glu Leu Arg Cys₄₇₀ Ile Ile Trp Lys Thr₄₇₅ Ala Asn Val Asp₄₈₀ Leu
Val Asp Asp Asn₄₈₅ Leu Ser Arg Glu Lys Thr₄₉₀ Ser Asp Ile Tyr Ile₄₉₅ Lys
Gly Trp Leu Tyr₅₀₀ Gly Leu Glu Lys Asp₅₀₅ Met Gln Lys Thr Asp₅₁₀ Ile His
Tyr His Ser₅₁₅ Leu Thr Gly Glu Ala₅₂₀ Asp Phe Asn Trp Arg₅₂₅ Phe Ile Phe
Thr Met₅₃₀ Asp Tyr Leu Ala₅₃₅ Glu Arg Thr Cys₅₄₀ Val Gln Ser Gln Lys
Asp Tyr Ile Trp Ser Leu₅₅₀ Asp Ala Thr Ser Met₅₅₅ Lys Phe Pro Ala Arg₅₆₀
Leu Ile Ile Gln Val₅₆₅ Trp Asp Asn Asp Ile₅₇₀ Phe Ser Pro Asp Asp₅₇₅ Phe
Leu Gly Val₅₈₀ Leu Glu Leu Asp Leu Ser₅₈₅ Asp Met Pro Leu Pro₅₉₀ Ala Arg
His Ala Lys₅₉₅ Gln Cys Ser Ile Arg₆₀₀ Met Met Asp Ala₆₀₅ Asp Pro Lys Trp
Pro Tyr Phe Ile Gln Tyr Lys₆₁₅ His Phe Ser Leu Phe₆₂₀ Lys Lys Lys Thr
Val Thr Gly Trp Trp Pro₆₃₀ Cys Gln Val Leu Asp₆₃₅ Gly Gly Lys Trp Arg₆₄₀
Leu Ser Gly Lys Val₆₄₅ Lys Met Ser Leu Glu₆₅₀ Ile Leu Ser Glu Lys₆₅₅ Glu
Ala Leu Ile Lys₆₆₀ Pro Ala Gly Arg Gly₆₆₅ Gln Ser Glu Pro Asn₆₇₀ Gln Tyr

54/223

342-10PCT.txt

Pro Thr Leu His Pro Pro Leu Arg Thr Asn Thr Ser Phe Thr Trp Leu
675 680 685

Arg Ser Pro Val Gln Asn Phe Cys Tyr Ile Phe Trp Lys Arg Tyr Arg
690 695 700

Phe Lys Leu Ile Ala Phe Met Val Ile Ser Ile Ile Ala Leu Met Leu
705 710 715 720

Phe Asn Phe Ile Tyr Ser Ala Pro His Tyr Leu Ala Met Ser Trp Ile
725 730 735

Lys Pro Gln Leu Gln Leu Tyr Pro Pro Ile Lys Ile Phe Asn Ile Ile
740 745 750

Asn Ser Leu Asn Thr Ser Asn Ala Ser Ser Ser Ile Leu Pro Thr Gln
755 760 765

Asp Pro Asn Leu Lys Pro Thr Ile Asp His Glu Trp Lys Leu His Pro
770 775 780

Gly Pro Thr Asn His Leu Ser Asp Ile Phe Pro Glu Leu Pro Ala Pro
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Gly Asp

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21

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21

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342-10PCT.txt

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2015201738 07 Apr 2015

56/223

342-10PCT.txt

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Val	Glu	Ser	Ala	Ala	Phe	Asp	Ala	Phe	Leu	Ser	Thr	Val	Glu	Asp	Leu
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Asp	Leu	Ser	Tyr	Asn	Asn	Leu	Glu	Ala	Leu	Pro	Trp	Glu	Ala	Val	Gly
				85					90						95

57/223

342-10PCT.txt

Gln Met Val Asn₁₀₀ Leu Asn Thr Leu Thr₁₀₅ Leu Asp His Asn₁₁₀ Leu Ile Asp

His Ile Ala₁₁₅ Glu Gly Thr Phe Val₁₂₀ Gln Leu His Lys₁₂₅ Leu Val Arg Leu

Asp Met Thr Ser Asn Arg₁₃₅ Leu His Lys Leu Pro₁₄₀ Pro Asp Gly Leu Phe

Leu Arg Ser Gln Gly Thr₁₅₀ Gly Pro Lys Pro₁₅₅ Thr Pro Leu Thr Val₁₆₀

Ser Phe Gly Gly Asn₁₆₅ Pro Leu His Cys₁₇₀ Asn Cys Glu Leu Leu Trp₁₇₅ Leu

Arg Arg Leu Thr₁₈₀ Arg Glu Asp Asp₁₈₅ Leu Glu Thr Cys Ala Thr₁₉₀ Pro Glu

His Leu Thr₁₉₅ Asp Arg Tyr Phe Trp₂₀₀ Ser Ile Pro Glu₂₀₅ Glu Glu Phe Leu

Cys Glu₂₁₀ Pro Pro Leu Ile Thr₂₁₅ Arg Gln Ala Gly₂₂₀ Gly Arg Ala Leu Val

Val Glu Gly Gln Ala Val₂₃₀ Ser Leu Arg Cys₂₃₅ Arg Ala Val Gly Asp₂₄₀ Pro

Glu Pro Val Val₂₄₅ His Trp Val Ala Pro Asp₂₅₀ Gly Arg Leu Leu Gly₂₅₅ Asn

Ser Ser Arg Thr₂₆₀ Arg Val Arg Gly₂₆₅ Asp Gly Thr Leu Asp Val₂₇₀ Thr Ile

Thr Thr Leu Arg Asp Ser Gly₂₈₀ Thr Phe Thr Cys Ile₂₈₅ Ala Ser Asn Ala

Ala Gly₂₉₀ Glu Ala Thr Ala Pro₂₉₅ Val Glu Val Cys₃₀₀ Val Val Pro Leu Pro

Leu Met Ala Pro Pro₃₁₀ Ala Ala Pro Pro₃₁₅ Pro Leu Thr Glu Pro Gly₃₂₀

Ser Ser Asp Ile Ala₃₂₅ Thr Pro Gly Arg₃₃₀ Pro Gly Ala Asn Asp Ser₃₃₅ Ala

Ala Glu Arg Arg₃₄₀ Leu Val Ala Ala Glu₃₄₅ Leu Thr Ser Asn Ser₃₅₀ Val Leu

Ile Arg Trp₃₅₅ Pro Ala Gln Arg Pro₃₆₀ Val Pro Gly Ile Arg₃₆₅ Met Tyr Gln

2015201738 07 Apr 2015

58/223
342-10PCT.txt

Val Gln Tyr Asn Ser Ser Val Asp Asp Ser Leu Val Tyr Arg Met Ile
370 375 380

Pro Ser Thr Ser Gln Thr Phe Leu Val Asn Asp Leu Ala Ala Gly Arg
385 390 395 400

Ala Tyr Asp Leu Cys Val Leu Ala Val Tyr Asp Asp Gly Ala Thr Ala
405 410 415

Leu Pro Ala Thr Arg Val Val Gly Cys Val Gln Phe Thr Thr Ala Gly
420 425 430

Asp Pro Ala Pro Cys Arg Pro Leu Arg Ala His Phe Leu Gly Gly Thr
435 440 445

Met Ile Ile Ala Ile Gly Gly Val Ile Val Ala Ser Val Leu Val Phe
450 455 460

Ile Val Leu Leu Met Ile Arg Tyr Lys Val Tyr Gly Asp Gly Asp Ser
465 470 475 480

Arg Arg Val Lys Gly Ser Arg Ser Leu Pro Arg Val Ser His Val Cys
485 490 495

Ser Gln Thr Asn Gly Ala Gly Thr Gly Ala Ala Gln Ala Pro Ala Leu
500 505 510

Pro Ala Gln Asp His Tyr Glu Ala Leu Arg Glu Val Glu Ser Gln Ala
515 520 525

Ala Pro Ala Val Ala Val Glu Ala Lys Ala Met Glu Ala Glu Thr Ala
530 535 540

Ser Ala Glu Pro Glu Val Val Leu Gly Arg Ser Leu Gly Gly Ser Ala
545 550 555 560

Thr Ser Leu Cys Leu Leu Pro Ser Glu Glu Thr Ser Gly Glu Glu Ser
565 570 575

Arg Ala Ala Val Gly Pro Arg Arg Ser Arg Ser Gly Ala Leu Glu Pro
580 585 590

Pro Thr Ser Ala Pro Pro Thr Leu Ala Leu Val Pro Gly Gly Ala Ala
595 600 605

Ala Arg Pro Arg Pro Gln Gln Arg Tyr Ser Phe Asp Gly Asp Tyr Gly
610 615 620

Ala Leu Phe Gln Ser His Ser Tyr Pro Arg Arg Ala Arg Arg Thr Lys
625 630 635 640

342-10PCT.txt

Arg His Arg Ser Thr Pro His Leu Asp Gly Ala Gly Gly Gly Ala Ala
645 650 655

Gly Glu Asp Gly Asp Leu Gly Leu Gly Ser Ala Arg Ala Cys Leu Ala
660 665 670

Phe Thr Ser Thr Glu Trp Met Leu Glu Ser Thr Val
675 680

<210> 83
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 83
cgaactccgt gctcatc

17

<210> 84
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 84
cgacaagtc gtaggca

17

<210> 85
<211> 2206
<212> DNA
<213> Homo sapiens

<400> 85
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acaccgaaga cgacaccagc catccggcca atcccgcccc gccgcgcccc gcaggcccg 120
ccactcctcg cttctccact tcccttctcg aagtgtccgg tcgcttctcg caggcggcgc 180
gcttgctggg tcacagttag gcggctccgc gcaggcgag cggggcgggc gaggagcggg 240
gaagctgact cagggtgctg gccgggggtcc tgcggggtag gagcgcgagg ccggcctgag 300
ggaggaggcc tagcgacca tccggcgccct cccgccccgg gcacccgcc gcggccgcgc 360
atctgctggg cccagaggg cctccatctc aaaacaacgt gtttttagga tctcatccac 420
tatcacagtt tcagctttcc ccaaactgga atgtgtcttt gcagacgcc atccttatta 480
aagggcaaag acttctcata cacctaggat ggatcttata ttcttggcgg gactgcagag 540
aagggtgccgt gtcctgagtc ctcatgtcag ggcacaggct tccagccagt tctacctggg 600
ttatgtttat ctcaattccc tgggtggtatt ggtgtctgct gggttttgcc agaatgaaga 660
caccgtgttt tcatttgta gttgattcgt atttccagg aagacattct gagattacag 720

2015201738 07 Apr 2015

60/223

342-10PCT.txt

cattgtctta	gtcaaggtgc	tgcaagaagga	cagaactaat	aggatatatg	tacatatgaa	780
agaaagttta	tgaagaactg	gtcacacca	tcacaaggca	aagtcccatg	acaggccatc	840
tgcaagctga	ggagcgagga	agccagcagt	ggctcagccg	gagtccaaca	gcctcaaacg	900
gaatccaaca	gttcaggctt	cagtctgtgg	ccaaatgccc	agagaccccg	gaaagctact	960
gggtgttagtc	ccagagccgg	aaggccaaag	aacctggagt	gtgatgtcca	agggcaggag	1020
gaatggacag	aagcatccag	catggggtaa	agacgaaagc	cagaagactc	agcaagctag	1080
cttacctact	ttcttctgcc	tgcttgttc	tagccgcgct	ggcagccggt	tggaggggtgc	1140
ccaccccccac	tgaggggtgga	tcttctcttc	ctagtccact	gactcaaatt	tcagtctctc	1200
tgggagcacc	atcacaccag	aaacaatacc	agccatctag	ccacccttca	gttcaccatc	1260
acaaccattg	tcttattcat	gaaacttctg	cagaccacc	ttaacctcca	tcggtgactt	1320
ctacctgaag	ccctctgatt	gttgcccagt	gggtgctttt	aaaataattt	ccatagtttc	1380
ttctacacct	ttagttggca	ttctactgta	aaggagagat	tttattttct	tactcattta	1440
tttggttagtt	tatagtcacc	accatatgga	tgcaagttc	tgtctcattc	actgggaagt	1500
attctattgc	agtcattgatt	tattttgatg	ttcacatccc	agagttggtg	agtgagcgcc	1560
ccttcacgct	ggctcccag	tgctgacgtg	tccccgtcct	tctctgcact	tttccttacc	1620
tcctggcctc	agatattcca	gggtcatttg	ttctctccct	gctccaaccc	tgcaagtcagc	1680
catctcccta	gggacgttgg	ttcctttatg	gaagggtggca	tttagaagcc	aggatttggg	1740
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gctggaggcc	aagagtctga	gaccagcctg	gctaacatgg	tgaaaccctt	ccccgtctct	1860
actacaaata	aaaaattagc	tgggtgtggt	ggcacgtgcc	tgtaatccca	gttactcagg	1920
aggctgaagc	accagaatct	cttgaaccca	ggaggccgag	gttgcaagtga	gccaagattg	1980
caccactgca	ctacagcttg	ggtagacagc	cgagacaccg	tctcaaaaag	gataataatt	2040
taaaaaacag	caggatttgg	gtgagcagtg	cgctcattgc	ttctgggctc	tctcgggtgga	2100
cataggctag	gaatgtaaga	tgtatgtgcc	tgtgtatata	cacacgtctg	tagctatgtc	2160
tatgttgcat	acatgtgttt	ttccaaaaac	caaatccata	accatg		2206

<210> 86
 <211> 93
 <212> PRT
 <213> Homo sapiens
 <400> 86

Met Asp Arg Ser Ile Gln His Gly Val Lys Thr Lys Ala Arg Arg Leu
 1 5 10 15

Ser Lys Leu Ala Tyr Leu Leu Ser Ser Ala Cys Leu Val Leu Ala Ala
 20 25 30

Leu Ala Ala Gly Trp Arg Val Pro Thr Pro Thr Glu Gly Gly Ser Ser
 35 40 45

2015201738 07 Apr 2015

61/223

342-10PCT.txt

Ser Pro Ser Pro Leu Thr Gln Ile Ser Val Ser Leu Gly Ala Pro Ser
50 55 60

His Gln Lys Gln Tyr Gln Pro Ser Ser His Pro Ser Val His His His
65 70 75 80

Asn His Cys Leu Ile His Glu Thr Ser Ala Asp Pro Pro
85 90

<210> 87
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 87
aaactacgtg tggccaggat c 21

<210> 88
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 88
cgacatgagg actcaggaca c 21

<210> 89
<211> 455
<212> DNA
<213> Homo sapiens

<400> 89
gtgaagacag ggagctcaag tgacctcctc cagggatatat agctgtggtg tgggaagcat 60
catgagaaca cggctcttga tggggataat tactctgaat ctaccaggct gattaagcca 120
cagcagatca gcaggtgaga attcaactgt ccagatagaa aggtggacat ggaaaaattg 180
ggctttgcaa atggtcaccc aattcttgcc ttcttggtct ccagatcacc cttcctatac 240
cgccactctg gagaaagaag tacagaacgc taacaaggat ggcttggagt tgcagtggtc 300
acctcagatc ttaaggtcac tttggagatg gaaccctgt gactaggaat ggcagaagag 360
aaaggtagaa agagattgag tcctggggat gtggcagagc accatcctag ccccgtagtg 420
cgtacttctg gacttccttt aaattgagag aaaca 455

<210> 90
<211> 61
<212> PRT
<213> Homo sapiens

<400> 90

342-10PCT.txt

Cys Phe Ser Gln Phe Lys Gly Ser Pro Glu Val Arg Ser Thr Gly Leu
1 5 10 15

Gly Trp Cys Ser Ala Thr Ser Pro Gly Leu Asn Leu Phe Leu Pro Phe
20 25 30

Ser Ser Ala Ile Pro Ser His Arg Gly Ser Ile Ser Lys Val Thr Leu
35 40 45

Arg Ser Glu Val Thr Thr Ala Thr Pro Ser His Pro Cys
50 55 60

<210> 91
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 91
gaacacgggtc ttgatgggg

20

<210> 92
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 92
gccatccttg ttagcgttct g

21

<210> 93
<211> 1230
<212> DNA
<213> Homo sapiens

<400> 93
aggggcagag ggggtcttccc aaccctaccc ctatttttcgg tgatttttgt gtgagaatat 60
taatattaaa aataaacgga gaaaaaaaat cctgttttcgc taacggctgg tggtagcagg 120
ttgagtaccg ggagggctgc aagaccgtga ttgatgggga ggactgcgca gaccctggcg 180
aggggtgagcc cctccccgga ggcgcctgtg gaatgtccag ggctctggtc cgctcctcgg 240
gatgggggggt gcctaatcct agagccgcat tccaggataa ggggggtggg gagaggctgg 300
gccggggggag gggcaggaaa gagggctata agggcagcgg cccaggcggg cgggatccag 360
gcggggccatg gcggatgtcc ccggggcaca gcgagcgggt cctgggtgacg gcccagagcc 420
ccgggacccc ctggactgtt gggcctgcgc tgttcttgta acagcccaga atctgctggg 480
ggctgccttc aatcttctcc tgctgggtgct ggtgctaggg accatcttgc taccgctgt 540
caccatgctg ggcttcggct tcctctgcca ctctcagttc ctgcgctccc aggcacccc 600
ttgcaccgcg cacctgcggg accccggttt cacggcccta ctggtcaccg gattcctgct 660

2015201738 07 Apr 2015

63/223

342-10PCT.txt

cctcgtgccg ctgctcgtgc ttgctctggc cagctaccgc cgcctctgcc tgcgcctccg	720
cctagccgat tgcctcgtgc cctacagccg agccctttat cggcgtcggc gcgccccgca	780
gccgcggcaa atccgggcct caccagggtc ccaggccgtt cccacatcag gaaaggctctg	840
ggctctaataa ccctcgagtc aagaacaacc ctgacggctg ccctccctct tattcggccc	900
aaggacttga agccccggcat cttccgacct gccctgcccc caccctgcc tgagcggagt	960
cctagcatcc ccttgggagc agcagcgtca gtggaccag tgctgagaaa agccccaca	1020
tcccgaaaaa cccactttcc tttcacgacc cacatctcaa tcctgaacat ctaggctgga	1080
acctgcacac ctccccctca gctccgtcgt gaatgggaca acaatctcgt gccctcgttt	1140
tatgggtgcag cttctctagt atttctgggg ctggggggcg gggctggagg ggaaggagtg	1200
tccacgcatc aataaagatt taacgaactg	1230

<210> 94
 <211> 159
 <212> PRT
 <213> Homo sapiens

<400> 94

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

342-10PCT.txt

<210> 95
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 95
ttcctctgcc actctcagtt c

21

<210> 96
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 96
cgataaaggg ctcggctgta g

21

<210> 97
<211> 1020
<212> DNA
<213> Homo sapiens

<400> 97
atggaggagg aggaggagga tgatgactat gagaactcaa cacctcccta caaggacctt 60
cctcccaagc cagggaccat ggaggaggag gaggaggatg atgactatga gaactcaaca 120
cctccctaca aggaccttcc tcccaagcca gggaccatgg aggaggagga ggaggatgat 180
gactatgaga actcaacacc tccctacaag gaccttcctc ccaagccagg ttcaagtgtc 240
ccaccaagac ctccaagggc agcaaaggaa acagagaaac cccacttcc ttgcaagccc 300
cggaacatga caggcctgga cctcgccgct gtcacctgtc cacctcctca actggctgtg 360
aatcttgagc cttctccatt gcagccatcc ctggccgcaa ctccagtccc ctggctcaat 420
cagaggtctg gaggtcctgg ctgctgccag aagaggtgga tgggtgtacct gtgtctgctg 480
gtggtgactt cctgttcctt gggctgcctt ggtctcactg tgaccctgat taagttgact 540
ggcatggcag ggctagctgg cctgaagcat gacattgccc gtgtaagagc tgacaccaac 600
cagtccctgg tggaactttg gggcttatta gactgccgcc gaattacctg tcctgaaggc 660
tggctgccct ttgagggcaa gtgttactac ttctcccaa gcaccaagtc atgggatgag 720
gcccggatgt tctgccagga gaattactct cacttgggtca tcatcaatag ctttgctgag 780
cacaattttg tggccaaggc ccatggctct ccacgggtgt actggctggg gctgaatgac 840
agggcccagg aaggggactg gaggtggctg gatgggtctc ctgtgacatt aaggcaacca 900
gaggaacca ataacatcca cgatgaggac tgtgctacca tgaacaaagg tggcacctgg 960
aatgatctct cttgctacaa aactacgtat tggattttgtg agcggaaatg ttcctgttga 1020

<210> 98
<211> 339
<212> PRT

2015201738 07 Apr 2015

65/223

342-10PCT.txt

<213> Homo sapiens

<400> 98

Met Glu Glu Glu Glu Glu Asp Asp Asp Tyr Glu Asn Ser Thr Pro Pro
1 5 10 15

Tyr Lys Asp Leu Pro Pro Lys Pro Gly Thr Met Glu Glu Glu Glu Glu
20 25 30

Asp Asp Asp Tyr Glu Asn Ser Thr Pro Pro Tyr Lys Asp Leu Pro Pro
35 40 45

Lys Pro Gly Thr Met Glu Glu Glu Glu Glu Asp Asp Asp Tyr Glu Asn
50 55 60

Ser Thr Pro Pro Tyr Lys Asp Leu Pro Pro Lys Pro Gly Ser Ser Ala
65 70 75 80

Pro Pro Arg Pro Pro Arg Ala Ala Lys Glu Thr Glu Lys Pro Pro Leu
85 90 95

Pro Cys Lys Pro Arg Asn Met Thr Gly Leu Asp Leu Ala Ala Val Thr
100 105 110

Cys Pro Pro Pro Gln Leu Ala Val Asn Leu Glu Pro Ser Pro Leu Gln
115 120 125

Pro Ser Leu Ala Ala Thr Pro Val Pro Trp Leu Asn Gln Arg Ser Gly
130 135 140

Gly Pro Gly Cys Cys Gln Lys Arg Trp Met Val Tyr Leu Cys Leu Leu
145 150 155 160

Val Val Thr Ser Leu Phe Leu Gly Cys Leu Gly Leu Thr Val Thr Leu
165 170 175

Ile Lys Leu Thr Gly Met Ala Gly Leu Ala Gly Leu Lys His Asp Ile
180 185 190

Ala Arg Val Arg Ala Asp Thr Asn Gln Ser Leu Val Glu Leu Trp Gly
195 200 205

Leu Leu Asp Cys Arg Arg Ile Thr Cys Pro Glu Gly Trp Leu Pro Phe
210 215 220

Glu Gly Lys Cys Tyr Tyr Phe Ser Pro Ser Thr Lys Ser Trp Asp Glu
225 230 235 240

Ala Arg Met Phe Cys Gln Glu Asn Tyr Ser His Leu Val Ile Ile Asn
245 250 255

342-10PCT.txt
 Ser Phe Ala Glu His Asn Phe Val Ala Lys Ala His Gly Ser Pro Arg
 260 265 270
 Val Tyr Trp Leu Gly Leu Asn Asp Arg Ala Gln Glu Gly Asp Trp Arg
 275 280 285
 Trp Leu Asp Gly Ser Pro Val Thr Leu Arg Gln Pro Glu Glu Pro Asn
 290 295 300
 Asn Ile His Asp Glu Asp Cys Ala Thr Met Asn Lys Gly Gly Thr Trp
 305 310 315 320
 Asn Asp Leu Ser Cys Tyr Lys Thr Thr Tyr Trp Ile Cys Glu Arg Lys
 325 330 335
 Cys Ser Cys

<210> 99
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide

<400> 99
 atagctttgc tgagcacctt c

21

<210> 100
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide

<400> 100
 aagagacact cagatatgga c

21

<210> 101
 <211> 1680
 <212> DNA
 <213> Homo sapiens

<400> 101
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 ctgcggattt tatatggtgt gctcttcta ctgatttacc tggcagccct aatgagtaac 120
 cttctcatca ttacttcat taccctggac gtaaagctcc aaacacccat gtacttcttc 180
 ctgaagaact tatccttttt ggatgtcttc ctgggtctcg ttccaatccc aaaattcatt 240
 gtcaacaacc taaccacaa caattccatt tccattctag gatgtgcctt ccagctactt 300
 ttaatgactt ctttctcagc aggagagata tttatcctca ctgccatgtc ctatgaccgc 360
 tatgtagcca tctgctgtcc cctgaactac gaggtaatca tgaatactgg agtctgtgtg 420

342-10PCT.txt

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acattttcca tgcctttctg tggctccagt gtgattccac agtttttctg tgatgttcct 540
tcattactaa ggatttcctg ttctgaaaca ctaatggtaa tttatgcagg tattggagtt 600
gggtgatgtt taagcatttc ttgtttcatc tgtattgtga tctcttacat ttatatcttc 660
tccactgtac tgaagatccc taccactaaa ggactgtgtg attgggttaa agggctcagt 720
gcggggactc tgttttctgg tttcagtacc acaatggaca caggcaacaa aactctgccc 780
caggactttc tcttactggg ctttcctggg tctcaaactc ttcagctctc tctctttatg 840
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agcacctccc atcagttgca taccctcatg tacttctttc tgagcaacct ctccttcctg 960
gagatttggg ataccacagc agcagtggcc aaagcactgg ccatcctact ggggagaagt 1020
cagaccatat catttacaag ctgtcttttg cagatgtact ttgttttctc attaggctgc 1080
acagagtact tcctcctggc agccatggct tatgaccgct gtcttgccat ctgctatcct 1140
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gtgtgtgggt tcgtggccat tgcagtggcc acagccctca tcagtggcct gtccttctgt 1260
ggccccctg ccatcaacca cttcttctgt gacattgcac cctggattgc cctggcctgc 1320
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atttggtatg ggtccacagt tttccttcac gtccgcacct ctatcaaaga tgccttggat 1560
ctgatcaaag ctgtccacgt cctgaacct gtggtgactc cagttttaaa ccccttcac 1620
tatacgcttc gtaataagga agtaagagag actctgctga agaaatggaa gggaaaataa 1680

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<210> 102
 <211> 559
 <212> PRT
 <213> Homo sapiens

<400> 102

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

Asn Ile Gln Lys Leu Arg Ile Leu Tyr Gly Val Leu Phe Leu Leu Ile
 20 25 30

Tyr Leu Ala Ala Leu Met Ser Asn Leu Leu Ile Ile Thr Leu Ile Thr
 35 40 45

Leu Asp Val Lys Leu Gln Thr Pro Met Tyr Phe Phe Leu Lys Asn Leu
 50 55 60

Ser Phe Leu Asp Val Phe Leu Val Ser Val Pro Ile Pro Lys Phe Ile
 65 70 75 80

2015201738 07 Apr 2015

68/223

342-10PCT.txt

Val Asn Asn Leu Thr His Asn Asn Ser Ile Ser Ile Leu Gly Cys Ala
85 90 95

Phe Gln Leu Leu Leu Met Thr Ser Phe Ser Ala Gly Glu Ile Phe Ile
100 105 110

Leu Thr Ala Met Ser Tyr Asp Arg Tyr Val Ala Ile Cys Cys Pro Leu
115 120 125

Asn Tyr Glu Val Ile Met Asn Thr Gly Val Cys Val Leu Met Ala Ser
130 135 140

Val Ser Trp Ala Ile Gly Gly Leu Phe Gly Thr Ala Tyr Thr Ala Gly
145 150 155 160

Thr Phe Ser Met Pro Phe Cys Gly Ser Ser Val Ile Pro Gln Phe Phe
165 170 175

Cys Asp Val Pro Ser Leu Leu Arg Ile Ser Cys Ser Glu Thr Leu Met
180 185 190

Val Ile Tyr Ala Gly Ile Gly Val Gly Ala Cys Leu Ser Ile Ser Cys
195 200 205

Phe Ile Cys Ile Val Ile Ser Tyr Ile Tyr Ile Phe Ser Thr Val Leu
210 215 220

Lys Ile Pro Thr Thr Lys Gly Leu Cys Asp Trp Val Lys Gly Leu Ser
225 230 235 240

Ala Gly Thr Leu Phe Ser Gly Phe Ser Thr Thr Met Asp Thr Gly Asn
245 250 255

Lys Thr Leu Pro Gln Asp Phe Leu Leu Leu Gly Phe Pro Gly Ser Gln
260 265 270

Thr Leu Gln Leu Ser Leu Phe Met Leu Phe Leu Val Met Tyr Ile Leu
275 280 285

Thr Val Ser Gly Asn Val Ala Ile Leu Met Leu Val Ser Thr Ser His
290 295 300

Gln Leu His Thr Pro Met Tyr Phe Phe Leu Ser Asn Leu Ser Phe Leu
305 310 315 320

Glu Ile Trp Tyr Thr Thr Ala Ala Val Pro Lys Ala Leu Ala Ile Leu
325 330 335

Leu Gly Arg Ser Gln Thr Ile Ser Phe Thr Ser Cys Leu Leu Gln Met
340 345 350

2015201738 07 Apr 2015

69/223

342-10PCT.txt

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

<210> 103
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 103
catttcttgt ttcattctgta ttgtg

<210> 104
<211> 20

2015201738 07 Apr 2015

70/223

342-10PCT.txt

<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 104
tgttgcctgt gtccattgtg 20

<210> 105
<211> 499
<212> DNA
<213> Homo sapiens

<400> 105
acaccacat ggtcggcgtg caggatattt cgctggaccc tagaaaagcc accacgacct 60
gtgggccatg atgctacccc aatggctgct gctgctgttc cttctcttct tctttctctt 120
cctcctcacc aggggctcac tttctccaac aaaatacaac cttttggagc tcaaggagtc 180
ttgcatccgg aaccaggact gcgagactgg ctgctgccaa cgtgctccag acaattgcga 240
gtcgactgc gcggagaagg ggtccgaggg cagtctgtgt caaacgcagg tggtctttgg 300
ccaatataga gcgtgtccct gcctgcggaa cctgacttgt atatattcaa agaatgagaa 360
atggcttagc atcgctatg gccgttgtca gaaaattgga aggcagaagt tggctaagaa 420
aatgttcttc tagtgctccc tccttcttgc tgccctctcc tcctccacct gctctcctcc 480
ctaccagag ctctgtgtt 499

<210> 106
<211> 121
<212> PRT
<213> Homo sapiens

<400> 106

Met Met Leu Pro Gln Trp Leu Leu Leu Leu Phe Leu Leu Phe Phe Phe
1 5 10 15

Leu Phe Leu Leu Thr Arg Gly Ser Leu Ser Pro Thr Lys Tyr Asn Leu
20 25 30

Leu Glu Leu Lys Glu Ser Cys Ile Arg Asn Gln Asp Cys Glu Thr Gly
35 40 45

Cys Cys Gln Arg Ala Pro Asp Asn Cys Glu Ser His Cys Ala Glu Lys
50 55 60

Gly Ser Glu Gly Ser Leu Cys Gln Thr Gln Val Phe Phe Gly Gln Tyr
65 70 75 80

Arg Ala Cys Pro Cys Leu Arg Asn Leu Thr Cys Ile Tyr Ser Lys Asn
85 90 95

Glu Lys Trp Leu Ser Ile Ala Tyr Gly Arg Cys Gln Lys Ile Gly Arg
100 105 110

2015201738 07 Apr 2015

71/223
342-10PCT.txt

Gln Lys Leu Ala Lys Lys Met Phe Phe
115 120

<210> 107
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 107
tgtgtcaaac gcaggtg 17

<210> 108
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 108
ggagggagca ctagaagaac 20

<210> 109
<211> 659
<212> DNA
<213> Homo sapiens

<400> 109
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gaaagtctgg tgagttgaag tccaagaccc caggaaacaa ctagccctgc tgggctgccc 120
ctccttcgga gtgggactat atgatcctca tcaggccaat ccacgtcaca gaatgggtcta 180
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cttgatttca tcttacaatc tgattccatg tgtctcccat attttaagga ttctttatta 420
tttctggctt acagagaaca aacattattt ttgctttcc tggctctgtc tagattttca 480
aaaataactc tgtcacttct gttatatggg atcattgctt gtaattatct atttacttat 540
ctgtctctgg actggactct ttacagacag gcaataacta attatctgtc tgtctggcat 600
ttggtagtca ctcataaatc gtttattgca ttactaacta aataaaaaag ttgaccttg 659

<210> 110
<211> 144
<212> PRT
<213> Homo sapiens

<400> 110
Met Lys Val Ile Ala Glu Thr Phe Tyr Trp Leu Pro Gly Cys Arg His
1 5 10 15

2015201738 07 Apr 2015

72/223

342-10PCT.txt

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

<210> 111
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 111
atcctggcga atgaaacaag agaat

25

<210> 112
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 112
gcaaccagta aaatgtctca gcaatg

26

<210> 113
<211> 831
<212> DNA
<213> Homo sapiens

<400> 113
atgcgaagaa agaacctcac agaggtaaca gagtttggtt tcctgggatt ctccagattc 60
cacaacatc acatcactct ctttgtgggt tttctcatcc tgtacacatt aactgtggct 120

2015201738 07 Apr 2015

73/223

342-10PCT.txt

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ggcaatgcc a tcatcatgac catcatctgc attgaccgtc acctccacac tcccatgtac 180
ttcttcctga gcatgctggc tagctcaaag acagtgtaca cactgttcat cattccacag 240
atgctctcca gcttcgtaac ccagaccag ccaatctccc tagcagggtg taccacccaa 300
acgtttcttct ttgttacctt ggccatcaac aattgcttct tgctcacagt gatgggctat 360
gaccactata tggccatctg caatcccttg agatacaggg tcattacgag caagaagggtg 420
tgtgtccagc tgggtgtgtgg agccttttagc attggcctgg ccatggcagc tgtccaggta 480
acatccatat ttaccttacc tttttgtcac acggtggttg gtcatttctt ctgtgacatc 540
ctccctgtca tgaaactctc ctgtattaat accactatca atgagataat caattttgtt 600
gtcagggttat ttgtcatcct ggtcccatg ggtctggtct tcatctccta tgcctcatc 660
atctccactg tcctcaagat tgcctcagct gagggttgga agaagacctt tgccacctgt 720
gccttcacc tcaactgtggc cattgtccat tatggctgtg cttccattgc ctacctcatg 780
cccaagtcag aaaactctat agaacaagac ctcttctct cagtgccta a 831

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<210> 114
 <211> 276
 <212> PRT
 <213> Homo sapiens

<400> 114

Met Arg Arg Lys Asn Leu Thr Glu Val Thr Glu Phe Val Phe Leu Gly
 1 5 10 15

Phe Ser Arg Phe His Lys His His Ile Thr Leu Phe Val Val Phe Leu
 20 25 30

Ile Leu Tyr Thr Leu Thr Val Ala Gly Asn Ala Ile Ile Met Thr Ile
 35 40 45

Ile Cys Ile Asp Arg His Leu His Thr Pro Met Tyr Phe Phe Leu Ser
 50 55 60

Met Leu Ala Ser Ser Lys Thr Val Tyr Thr Leu Phe Ile Ile Pro Gln
 65 70 75 80

Met Leu Ser Ser Phe Val Thr Gln Thr Gln Pro Ile Ser Leu Ala Gly
 85 90 95

Cys Thr Thr Gln Thr Phe Phe Phe Val Thr Leu Ala Ile Asn Asn Cys
 100 105 110

Phe Leu Leu Thr Val Met Gly Tyr Asp His Tyr Met Ala Ile Cys Asn
 115 120 125

Pro Leu Arg Tyr Arg Val Ile Thr Ser Lys Lys Val Cys Val Gln Leu
 130 135 140

2015201738 07 Apr 2015

74/223

342-10PCT.txt

Val Cys Gly Ala Phe Ser Ile Gly Leu Ala Met Ala Ala Val Gln Val
145 150 155 160

Thr Ser Ile Phe Thr Leu Pro Phe Cys His Thr Val Val Gly His Phe
165 170 175

Phe Cys Asp Ile Leu Pro Val Met Lys Leu Ser Cys Ile Asn Thr Thr
180 185 190

Ile Asn Glu Ile Ile Asn Phe Val Val Arg Leu Phe Val Ile Leu Val
195 200 205

Pro Met Gly Leu Val Phe Ile Ser Tyr Val Leu Ile Ile Ser Thr Val
210 215 220

Leu Lys Ile Ala Ser Ala Glu Gly Trp Lys Lys Thr Phe Ala Thr Cys
225 230 235 240

Ala Phe His Leu Thr Val Val Ile Val His Tyr Gly Cys Ala Ser Ile
245 250 255

Ala Tyr Leu Met Pro Lys Ser Glu Asn Ser Ile Glu Gln Asp Leu Leu
260 265 270

Leu Ser Val Thr
275

<210> 115
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 115
cttcgtaacc cagacca

18

<210> 116
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 116
cttgctcgta atgaccct

18

<210> 117
<211> 1233
<212> DNA
<213> Homo sapiens

<400> 117
gaagcagcca ccaccatctt gggagctctg ggagcaagga cccctgtaac acattcatcc

60

07 Apr 2015
2015201738

75/223

342-10PCT.txt

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ttgaatgaca aaatgtctgg tccagcatgg tattataaca taaacatgaa gaggaagaga 120
catgagagat acgcacagtg aagagaccaa gctgggacac agtacgaagg tggcatctgc 180
acgccaagca gagggacctc agaagaaact gagccagcca gcaccccacc ttcgtctttg 240
acctccagcc tccagaacta aggatagagc tcttcatctc tgttagaaac gaccatcaaa 300
aagatacatc aattcattag aatcaaaagg acatgagtta tcagaattct ttctcctgaa 360
agaaagtgga gatcaaaggt aaaacttcta gagaatgaga tgaaggcaga tgaaagaagt 420
taacaagaca ttacatgact tgataatatt gcatgtatgc aaaaacctta tgaaatcaac 480
tgtgttctag cgaccacttg tttttctttt tgtcataata ctttttattc tcttgcaatg 540
atattgattc atctgcacct gacatcaact ctgcatttgt agaagggtgat aagaatacag 600
ggaaatggaa taagtggcct tgacctgcaat cccgcagcag cagaaatgtc catttcctct 660
ctcctgaata atactacatt ctccactggg ttccacaagt ttcgaggtaa aagcatgaac 720
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cttttaatac gcaaacttcc tccaaggcct cctgaagtca cccagaaatg catttcccca 840
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ctcttgaggt cttgctgact gcatgttcca ggctccacat ttaagctcca gtgactgctg 960
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jaattctgaa tgctggaatt ggcaatattt caggttcttt ccaactggaa ataccatgc 1080
aataatattt agtaagtcaa tagccataga aacctactga caaatgagt attttaacag 1140
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jccttctatg tgtaaaaata aatacacaga cac 1233

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<210> 118
 <211> 90
 <212> PRT
 <213> Homo sapiens

<400> 118

Met Ser Ile Ser Ser Leu Leu Asn Asn Thr Thr Phe Ser Thr Gly Phe
1 5 10 15

His Lys Phe Arg Gly Lys Ser Met Asn Ile His Glu Val Thr Ile Thr
20 25 30

Thr Leu Thr Thr Thr Thr Ile Ile Ser Thr Ile Phe Thr Leu Leu Ile
35 40 45

Arg Lys Leu Pro Pro Arg Leu Pro Glu Val Thr Gln Lys Cys Ile Ser
50 55 60

Pro Arg Val Ser Cys Ala Asn Ile Val Ser Tyr Gly Thr Leu Gly Ser
65 70 75 80

2015201738 07 Apr 2015

76/223

342-10PCT.txt

Tyr Pro Asp Pro Gln Leu Leu Glu Ser Cys
85 90

<210> 119
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 119
cacccacct tcgtctttg

19

<210> 120
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 120
gttttacctt tgatctccac tttc

24

<210> 121
<211> 4209
<212> DNA
<213> Homo sapiens

<400> 121
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ccttggtgtt tgccctgggg ttcttcttcc tattactccc ctacttatct tacttccatt 180
gtgatgaccc accctcacca tcgcctggga agagaaagtg tccagtaggg cggaggcgga 240
ggcccagagg caggatgaaa aaccacagtc tgagagctgg tagagagtgc ccgagaggcc 300
tggaggagac ttcggacctt ctttcacaac tgcagagcct cctggggcca caccttgaca 360
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cgtagcttc cccggtcct caagccaagc atcctcagga tctggcctcc accccatcac 540
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gcgcctttta ctcacagtc cagcaagatc ctctttcccg ccaccacca gagacctgtc 960
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342-10PCT.txt

aagtcacaga	aacagccaag	gtcaacattt	gggaagaaaa	agaaaatggt	ggatcattta	1080
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agctgcccgg	acctcagaag	tgctcagatc	ctaggctctt	gcaggaaagt	ttttggaaga	1260
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aggatgtgca	tggtttcgag	gctccagggg	ccagcaaaaag	ctctctacac	cctagagtgt	3000
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2015201738 07 Apr 2015

78/223

342-10PCT.txt
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cagatgggca agcatctgtt gtgccccacg cttcagagaa tttggtttct caagtgcccc 3180
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ttttttatt 4209

<210> 122
<211> 1343
<212> PRT
<213> Homo sapiens

<400> 122

Met Glu Asn Leu Pro Phe Pro Leu Lys Leu Leu Ser Ala Ser Ser Leu
1 5 10 15

Asn Ala Pro Ser Ser Thr Pro Trp Val Leu Asp Ile Phe Leu Thr Leu
20 25 30

Val Phe Ala Leu Gly Phe Phe Phe Leu Leu Leu Pro Tyr Leu Ser Tyr
35 40 45

Phe His Cys Asp Asp Pro Pro Ser Pro Ser Pro Gly Lys Arg Lys Cys
50 55 60

Pro Val Gly Arg Arg Arg Arg Pro Arg Gly Arg Met Lys Asn His Ser
65 70 75 80

07 Apr 2015
2015201738

79/223

342-10PCT.txt

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

Leu Leu Ser Gln Leu Gln Ser Leu Leu Gly Pro His Leu Asp Lys Gly
100 105 110

Asp Phe Gly Gln Leu Ser Gly Pro Asp Pro Pro Gly Glu Val Gly Glu
115 120 125

Arg Ala Pro Asp Gly Ala Ser Gln Ser Ser His Glu Pro Met Glu Asp
130 135 140

Ala Ala Pro Ile Leu Ser Pro Leu Ala Ser Pro Asp Pro Gln Ala Lys
145 150 155 160

His Pro Gln Asp Leu Ala Ser Thr Pro Ser Pro Gly Pro Met Thr Thr
165 170 175

Ser Val Ser Ser Leu Ser Ala Ser Gln Pro Pro Glu Pro Ser Leu Pro
180 185 190

Leu Glu His Pro Ser Pro Glu Pro Pro Ala Leu Phe Pro His Pro Pro
195 200 205

His Thr Pro Asp Pro Leu Ala Cys Ser Pro Pro Pro Pro Lys Gly Phe
210 215 220

Thr Ala Pro Pro Leu Arg Asp Ser Thr Leu Ile Thr Pro Ser His Cys
225 230 235 240

Asp Ser Val Ala Leu Pro Leu Gly Thr Val Pro Gln Ser Leu Ser Pro
245 250 255

His Glu Asp Leu Val Ala Ser Val Pro Ala Ile Ser Gly Leu Gly Gly
260 265 270

Ser Asn Ser His Val Ser Ala Ser Ser Arg Trp Gln Glu Thr Ala Arg
275 280 285

Thr Ser Cys Ala Phe Asn Ser Ser Val Gln Gln Asp Pro Leu Ser Arg
290 295 300

His Pro Pro Glu Thr Cys Gln Met Glu Ala Gly Ser Leu Phe Leu Leu
305 310 315 320

Ser Ser Asp Gly Gln Asn Val Val Gly Ile Gln Val Thr Glu Thr Ala
325 330 335

Lys Val Asn Ile Trp Glu Glu Lys Glu Asn Val Gly Ser Phe Thr Asn
340 345 350

2015201738 07 Apr 2015

80/223

342-10PCT.txt

Gln Met Thr Pro Glu Lys His Leu Asn Ser Leu Gly Asn Leu Ala Lys
355 360 365

Ser Leu Asp Ala Glu Gln Asp Thr Thr Asn Pro Lys Pro Phe Trp Asn
370 375 380

Met Gly Glu Asn Ser Lys Gln Leu Pro Gly Pro Gln Lys Cys Ser Asp
385 390 395 400

Pro Arg Leu Leu Gln Glu Ser Phe Trp Lys Asn Tyr Ser Gln Leu Phe
405 410 415

Trp Gly Leu Pro Ser Leu His Ser Glu Ser Leu Val Ala Asn Ala Trp
420 425 430

Val Thr Asp Arg Ser Tyr Thr Leu Gln Ser Pro Pro Phe Leu Phe Asn
435 440 445

Glu Met Ser Asn Val Cys Pro Ile Gln Arg Glu Thr Thr Met Ser Pro
450 455 460

Leu Leu Phe Gln Ala Gln Pro Leu Ser His Arg Gln Pro Phe Ile Ser
465 470 475 480

Ser Thr Pro Gln Phe Leu Pro Thr Pro Met Ala Gln Ala Glu Ala Gln
485 490 495

Ala His Leu Gln Ser Ser Phe Pro Val Leu Ser Pro Ala Phe Pro Ser
500 505 510

Leu Ile Lys Asn Thr Gly Val Ala Cys Pro Ala Ser Gln Asn Lys Val
515 520 525

Gln Ala Leu Ser Leu Pro Glu Thr Gln His Pro Glu Trp Pro Leu Leu
530 535 540

Arg Lys Gln Leu Glu Gly Arg Leu Ala Leu Pro Ser Arg Val Gln Lys
545 550 555 560

Ser Gln Asp Val Phe Ser Val Ser Thr Pro Asn Leu Pro Gln Glu Ser
565 570 575

Leu Thr Ser Ile Leu Pro Glu Asn Phe Pro Val Ser Pro Glu Leu Arg
580 585 590

Arg Gln Leu Glu Gln His Ile Lys Lys Trp Ile Ile Gln His Trp Gly
595 600 605

Asn Leu Gly Arg Ile Gln Glu Ser Leu Asp Leu Met Gln Leu Arg Asp
610 615 620

2015201738 07 Apr 2015

81/223

342-10PCT.txt

Glu Ser Pro Gly Thr Ser Gln Ala Lys Gly Lys Pro Ser Pro Trp Gln
625 630 635 640

Ser Ser Thr Ser Thr Gly Glu Ser Ser Lys Glu Ala Gln Lys Val Lys
645 650 655

Phe Gln Leu Glu Arg Asp Leu Cys Pro His Leu Gly Gln Ile Leu Gly
660 665 670

Glu Thr Pro Gln Asn Leu Ser Arg Asp Met Lys Ser Phe Pro Arg Lys
675 680 685

Val Leu Gly Val Thr Ser Glu Glu Ser Glu Arg Asn Leu Arg Lys Pro
690 695 700

Leu Arg Ser Asp Ser Gly Ser Asp Leu Leu Arg Cys Thr Glu Arg Thr
705 710 715 720

His Ile Glu Asn Ile Leu Lys Ala His Met Gly Arg Asn Leu Gly Gln
725 730 735

Thr Asn Glu Gly Leu Ile Pro Val Arg Val Arg Arg Ser Trp Leu Ala
740 745 750

Val Asn Gln Ala Leu Pro Val Ser Asn Thr His Val Lys Thr Ser Asn
755 760 765

Leu Ala Ala Pro Lys Ser Gly Lys Ala Cys Val Asn Thr Ala Gln Val
770 775 780

Leu Ser Phe Leu Glu Pro Cys Thr Gln Gln Gly Leu Gly Ala His Ile
785 790 795 800

Val Arg Phe Trp Ala Lys His Arg Trp Gly Leu Pro Leu Arg Val Leu
805 810 815

Lys Pro Ile Gln Cys Phe Lys Leu Glu Lys Val Ser Ser Leu Ser Leu
820 825 830

Thr Gln Leu Ala Gly Pro Ser Ser Ala Thr Cys Glu Ser Gly Ala Gly
835 840 845

Ser Glu Val Glu Val Asp Met Phe Leu Arg Lys Pro Pro Met Ala Ser
850 855 860

Leu Arg Lys Gln Val Leu Thr Lys Ala Ser Asp His Met Pro Glu Ser
865 870 875 880

Leu Leu Ala Ser Ser Pro Ala Trp Lys Gln Phe Gln Arg Ala Pro Arg
885 890 895

07 Apr 2015
2015201738

82/223

342-10PCT.txt

Gly Ile Pro Ser Trp Asn Asp His Gly Pro Leu Lys Pro Pro Pro Ala
900 905 910

Gly Gln Glu Gly Arg Trp Pro Ser Lys Pro Leu Thr Tyr Ser Leu Thr
915 920 925

Gly Ser Thr Gln Gln Ser Arg Ser Leu Gly Ala Gln Ser Ser Lys Ala
930 935 940

Gly Glu Thr Arg Glu Ala Val Pro Gln Cys Arg Val Pro Leu Glu Thr
945 950 955 960

Cys Met Leu Ala Asn Leu Gln Ala Thr Ser Glu Asp Val His Gly Phe
965 970 975

Glu Ala Pro Gly Thr Ser Lys Ser Ser Leu His Pro Arg Val Ser Val
980 985 990

Ser Gln Asp Pro Arg Lys Leu Cys Leu Met Glu Glu Val Val Ser Glu
995 1000 1005

Phe Glu Pro Gly Met Ala Thr Lys Ser Glu Thr Gln Pro Gln Val
1010 1015 1020

Cys Ala Ala Val Val Leu Leu Pro Asp Gly Gln Ala Ser Val Val
1025 1030 1035

Pro His Ala Ser Glu Asn Leu Val Ser Gln Val Pro Gln Gly His
1040 1045 1050

Leu Gln Ser Met Pro Thr Gly Asn Met Arg Ala Ser Gln Glu Leu
1055 1060 1065

His Asp Leu Met Ala Ala Arg Arg Ser Lys Leu Val Gln Glu Glu
1070 1075 1080

Pro Arg Asn Pro Asn Cys Gln Gly Ser Cys Lys Ser Gln Arg Pro
1085 1090 1095

Met Phe Pro Pro Ile His Lys Ser Glu Lys Ser Arg Lys Pro Asn
1100 1105 1110

Leu Glu Lys His Glu Glu Arg Leu Glu Gly Leu Arg Thr Pro Gln
1115 1120 1125

Leu Thr Pro Val Arg Lys Thr Glu Asp Thr His Gln Asp Glu Gly
1130 1135 1140

Val Gln Leu Leu Pro Ser Lys Lys Gln Pro Pro Ser Val Ser His
1145 1150 1155

83/223

342-10PCT.txt

Phe Gly Glu Asn Ile Lys Gln Phe Phe Gln Trp Ile Phe Ser Lys
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 Lys Lys Ser Lys Pro Ala Pro Val Thr Ala Glu Ser Gln Lys Thr
 1175 1180 1185
 Val Lys Asn Arg Ser Cys Val Tyr Ser Ser Ser Ala Glu Ala Gln
 1190 1195 1200
 Gly Leu Met Thr Ala Val Gly Gln Met Leu Asp Lys Lys Met Ser
 1205 1210 1215
 Leu Cys His Ala His His Ala Ser Lys Val Asn Gln His Lys Gln
 1220 1225 1230
 Lys Phe Gln Ala Pro Val Cys Gly Phe Pro Cys Asn His Arg His
 1235 1240 1245
 Leu Phe Tyr Ser Glu His Gly Arg Ile Leu Ser Tyr Ala Ala Ser
 1250 1255 1260
 Ser Gln Gln Ala Thr Leu Lys Ser Gln Gly Cys Pro Asn Arg Asp
 1265 1270 1275
 Arg Gln Ile Arg Asn Gln Gln Pro Leu Lys Ser Val Arg Cys Asn
 1280 1285 1290
 Asn Glu Gln Trp Gly Leu Arg His Pro Gln Ile Leu His Pro Lys
 1295 1300 1305
 Lys Ala Val Ser Pro Val Ser Pro Pro Gln His Trp Pro Lys Thr
 1310 1315 1320
 Ser Gly Ala Ser Ser His His His His Cys Pro Arg His Cys Leu
 1325 1330 1335
 Leu Trp Glu Gly Ile
 1340

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 <223> Oligonucleotide
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<210> 124
 <211> 18
 <212> DNA
 <213> Artificial Sequence

07 Apr 2015

2015201738

84/223

342-10PCT.txt

<220>
<223> Oligonucleotide

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18

<210> 125
<211> 3136
<212> DNA
<213> Homo sapiens

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gccgcgcgtg cctctgtcct ccgcgcgctg ctcagctgaa ggcgcacagg attcaattac 120
tggacttgtc aactctgccg gtgtacgtgc ctttctctt ccactatgag aggaccgatt 180
gtattgcaca tttgtctggc tttctgtagc cttctgctt tcagcgttgc cacacaatgt 240
ctggccttcc ccaaaataga aaggaggagg gagatagcac atgttcatgc ggaaaaagg 300
cagtccgata agatgaacac cgatgaccta gaaaatagct ctgttacctc aaagcagact 360
ccccaactgg tggctcttga agatccaatg atgatgtcag cagtaccatc ggcaacatca 420
ttaaataaag cattctcgat taacaaagaa acccagcctg gacaagctgg gctcatgcaa 480
acagaacgcc ctggtgtttc cacacctact gagtcagggtg tcccctcagc tgaagaagta 540
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agcactaact tttagcccat tgtagaagag atcacagaaa ccacaaaagg ttttctgaag 720
tatatggata atcaatcatt tgcaactgaa agtcaggaag gagttgggtt gggacattca 780
ccttcctcct atgtgaatac taaggaaatg ctaaccacca atccaaagac tgagaaat 840
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gagcctggaa gcctcaccgc tgataaggag aagccttcgc agatgacagc tgataacacc 960
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gaggcagacc aactgttggg aaatacaatg aaagacatca tctactcaaga gatgacaaca 1560
gctgttcaag agccagatgc cactttatcc atggtgacac aagagcaggt tgctaccctc 1620

2015201738 07 Apr 2015

85/223

342-10PCT.txt

gagccttatca gagacagtgg caagactgag gaagaaaagg aggaccctc tcctgtgtct	1680
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actacagtcg tccctttgtc ttttgaagtt actcccactg tggaagaaca aatggacaca	1800
gtcacagggc caaatgagga gttcacacca gttctgggat ctccagtgaac acctcctgga	1860
ataatggtgg gggaaaccag catttcccct gcacttctctg ctttggaggc atcctctgag	1920
agaagaactg ttgttccatc tattactcgt gttaatacag ctgcctcata tggcctggac	1980
caacttgaat ctgaagaggg acaagaagat gaggatgaag aggatgaaga agatgaagat	2040
gaagaagagg aagatgagga agaagatgag gaagataaag atgcagactc gctggatgag	2100
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gtactgagca gaaatggcat gttgtatact aaacgtatca tgcagtattt ggttttattc	2700
tgtagtgaat tttccacaac cgtgggctac aactcataaa tatgcaacat atatgttttt	2760
cagtaggagt tgctacatta ggcagagtaa atattttgta gttttccaca gtgtcttttc	2820
cttggtttga attacctgca ttgagaataa tgattgttgc caccaaggca tgcttgactc	2880
tgagatataa atcttaacaa agaataactt ctcaagatat actctaccta cttgaaacca	2940
cagggttgtg ggccatggta catactgcat ttgcatcaaa ctagcagtaa ctcagaatga	3000
aatcattttc attagaagc tctctcagca tattaggatt atatgtagat ttgtatgtat	3060
tttgcattat gtacttcagt ctccctagttt tattattctc accttccggt ttattcttgg	3120
cgaggaaaaa aatgca	3136

<210> 126
 <211> 774
 <212> PRT
 <213> Homo sapiens

<400> 126

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

2015201738 07 Apr 2015

86/223

342-10PCT.txt

Arg Arg Arg Glu Ile Ala His Val His Ala Glu Lys Gly Gln Ser Asp
35 40 45

Lys Met Asn Thr Asp Asp Leu Glu Asn Ser Ser Val Thr Ser Lys Gln
50 55 60

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

Pro Ser Ala Thr Ser Leu Asn Lys Ala Phe Ser Ile Asn Lys Glu Thr
85 90 95

Gln Pro Gly Gln Ala Gly Leu Met Gln Thr Glu Arg Pro Gly Val Ser
100 105 110

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

Ser Gln Pro Glu Arg Ile Ser Pro Glu Ser Gly Leu Ala Lys Ala Met
130 135 140

Leu Thr Ile Ala Ile Thr Ala Thr Pro Ser Leu Thr Val Asp Glu Lys
145 150 155 160

Glu Glu Leu Leu Thr Ser Thr Asn Phe Gln Pro Ile Val Glu Glu Ile
165 170 175

Thr Glu Thr Thr Lys Gly Phe Leu Lys Tyr Met Asp Asn Gln Ser Phe
180 185 190

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

Tyr Val Asn Thr Lys Glu Met Leu Thr Thr Asn Pro Lys Thr Glu Lys
210 215 220

Phe Glu Ala Asp Thr Asp His Arg Thr Thr Ser Phe Pro Gly Ala Glu
225 230 235 240

Ser Thr Ala Gly Ser Glu Pro Gly Ser Leu Thr Pro Asp Lys Glu Lys
245 250 255

Pro Ser Gln Met Thr Ala Asp Asn Thr Gln Ala Ala Ala Thr Lys Gln
260 265 270

Pro Leu Glu Thr Ser Glu Tyr Thr Leu Ser Val Glu Pro Glu Thr Asp
275 280 285

Ser Leu Leu Gly Ala Pro Glu Val Thr Val Ser Val Ser Thr Ala Val
290 295 300

2015201738 07 Apr 2015

87/223

342-10PCT.txt

Pro Ala Ala Ser Ala Leu Ser Asp Glu Trp Asp Asp Thr Lys Leu Glu
305 310 315 320

Ser Val Ser Arg Ile Arg Thr Pro Lys Leu Gly Asp Asn Glu Glu Thr
325 330 335

Gln Val Arg Thr Glu Met Ser Gln Thr Ala Gln Val Ser His Glu Gly
340 345 350

Met Glu Gly Gly Gln Pro Trp Thr Glu Ala Ala Gln Val Ala Leu Gly
355 360 365

Leu Pro Glu Gly Glu Thr His Thr Gly Thr Ala Leu Leu Ile Ala His
370 375 380

Gly Asn Glu Arg Ser Pro Ala Phe Thr Asp Gln Ser Ser Phe Thr Pro
385 390 395 400

Thr Ser Leu Met Glu Asp Met Lys Val Ser Ile Val Asn Leu Leu Gln
405 410 415

Ser Thr Gly Asp Phe Thr Glu Ser Thr Lys Glu Asn Asp Ala Leu Phe
420 425 430

Phe Leu Glu Thr Thr Val Ser Val Ser Val Tyr Glu Ser Glu Ala Asp
435 440 445

Gln Leu Leu Gly Asn Thr Met Lys Asp Ile Ile Thr Gln Glu Met Thr
450 455 460

Thr Ala Val Gln Glu Pro Asp Ala Thr Leu Ser Met Val Thr Gln Glu
465 470 475 480

Gln Val Ala Thr Leu Glu Leu Ile Arg Asp Ser Gly Lys Thr Glu Glu
485 490 495

Ile Lys Glu Asp Pro Ser Pro Val Ser Asp Val Pro Gly Val Thr Gln
500 505 510

Leu Ser Arg Arg Trp Glu Pro Leu Ala Thr Thr Ile Ser Thr Thr Val
515 520 525

Ala Pro Leu Ser Phe Glu Val Thr Pro Thr Val Glu Glu Gln Met Asp
530 535 540

Thr Val Thr Gly Pro Asn Glu Glu Phe Thr Pro Val Leu Gly Ser Pro
45 550 555 560

Ala Thr Pro Pro Gly Ile Met Val Gly Glu Pro Ser Ile Ser Pro Ala
565 570 575

88/223

342-10PCT.txt

Leu Pro Ala Leu Glu Ala Ser Ser Glu Arg Arg Thr Val Val Pro Ser
580 585 590

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

Ser Glu Glu Gly Gln Glu Asp Glu Asp Glu Glu Asp Glu Glu Asp Glu
610 615 620

Asp Glu Glu Glu Glu Asp Glu Glu Glu Asp Glu Glu Asp Lys Asp Ala
625 630 635 640

Asp Ser Leu Asp Glu Gly Leu Asp Gly Asp Thr Glu Leu Pro Gly Phe
645 650 655

Thr Leu Pro Gly Ile Thr Ser Gln Glu Pro Gly Leu Glu Glu Gly Asn
660 665 670

Met Asp Leu Leu Glu Gly Ala Thr Tyr Gln Val Pro Asp Ala Leu Glu
675 680 685

Trp Glu Gln Gln Asn Gln Gly Leu Val Arg Ser Trp Met Glu Lys Leu
690 695 700

Lys Asp Lys Ala Gly Tyr Met Ser Gly Met Leu Val Pro Val Gly Val
705 710 715 720

Gly Ile Ala Gly Ala Leu Phe Ile Leu Gly Ala Leu Tyr Ser Ile Lys
725 730 735

Val Met Asn Arg Arg Arg Arg Asn Gly Phe Lys Arg His Lys Arg Lys
740 745 750

Gln Arg Glu Phe Asn Ser Met Gln Asp Arg Val Met Leu Leu Ala Asp
755 760 765

Ser Ser Glu Asp Glu Phe
770

<210> 127
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<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 127
ccctccctgg tatcacat

<210> 128
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<212> DNA
<213> Artificial Sequence

<220>
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<400> 128
caccagcatc ccagacat

18

<210> 129
<211> 3627
<212> DNA
<213> Homo sapiens

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2015201738 07 Apr 2015

90/223

342-10PCT.txt

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2015201738 07 Apr 2015

91/223

342-10PCT.txt

<210> 130
<211> 1029
<212> PRT
<213> Homo sapiens
<400> 130

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

Arg Glu Lys Gln Lys Arg Asn Met Glu Glu Leu Lys Lys Glu Val Val
35 40 45

Met Asp Asp His Lys Leu Thr Leu Glu Glu Leu Ser Thr Lys Tyr Ser
50 55 60

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

Thr Arg Gly Gly Pro Asn Thr Val Thr Pro Pro Pro Thr Thr Pro Glu
85 90 95

Trp Val Lys Phe Cys Lys Gln Leu Phe Gly Gly Phe Ser Leu Leu Leu
100 105 110

Trp Thr Gly Ala Ile Leu Cys Phe Val Ala Tyr Ser Ile Gln Ile Tyr
115 120 125

Phe Asn Glu Glu Pro Thr Lys Asp Asn Leu Tyr Leu Ser Ile Val Leu
130 135 140

Ser Val Val Val Ile Val Thr Gly Cys Phe Ser Tyr Tyr Gln Glu Ala
145 150 155 160

Lys Ser Ser Lys Ile Met Glu Ser Phe Lys Asn Met Val Pro Gln Gln
165 170 175

Ala Leu Val Ile Arg Gly Gly Glu Lys Met Gln Ile Asn Val Gln Glu
180 185 190

Val Val Leu Gly Asp Leu Val Glu Ile Lys Gly Gly Asp Arg Val Pro
195 200 205

Ala Asp Leu Arg Leu Ile Ser Ala Gln Gly Cys Lys Val Asp Asn Ser
210 215 220

Ser Leu Thr Gly Glu Ser Glu Pro Gln Ser Arg Ser Pro Asp Phe Thr
225 230 235 240

2015201738 07 Apr 2015

92/223

342-10PCT.txt

His Glu Asn Pro Leu Glu Thr Arg Asn Ile Cys Phe Phe Ser Thr Asn
245 250 255

Cys Val Glu Gly Thr Ala Arg Gly Ile Val Ile Ala Thr Gly Asp Ser
260 265 270

Thr Val Met Gly Arg Ile Ala Ser Leu Thr Ser Gly Leu Ala Val Gly
275 280 285

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

Val Val Ala Val Phe Leu Gly Val Thr Phe Phe Ala Leu Ser Leu Leu
305 310 315 320

Leu Gly Tyr Gly Trp Leu Glu Ala Ile Ile Phe Leu Ile Gly Ile Ile
325 330 335

Val Ala Asn Val Pro Glu Gly Leu Leu Ala Thr Val Thr Val Cys Leu
340 345 350

Thr Leu Thr Ala Lys Arg Met Ala Arg Lys Asn Cys Leu Val Lys Asn
355 360 365

Leu Glu Ala Val Glu Thr Leu Gly Ser Thr Ser Thr Ile Cys Ser Asp
370 375 380

Lys Thr Gly Thr Leu Thr Gln Asn Arg Met Thr Val Ala His Met Trp
385 390 395 400

Phe Asp Met Thr Val Tyr Glu Ala Asp Thr Thr Glu Glu Gln Thr Gly
405 410 415

Lys Thr Phe Thr Lys Ser Ser Asp Thr Trp Phe Met Leu Ala Arg Ile
420 425 430

Ala Gly Leu Cys Asn Arg Ala Asp Phe Lys Ala Asn Gln Glu Ile Leu
435 440 445

Pro Ile Ala Lys Arg Ala Thr Thr Gly Asp Ala Ser Glu Ser Ala Leu
450 455 460

Leu Lys Phe Ile Glu Gln Ser Tyr Ser Ser Val Ala Glu Met Arg Glu
465 470 475 480

Lys Asn Pro Lys Val Ala Glu Ile Pro Phe Asn Ser Thr Asn Lys Tyr
485 490 495

Gln Met Ser Ile His Leu Arg Glu Asp Ser Ser Gln Thr His Val Leu
500 505 510

2015201738 07 Apr 2015

93/223

342-10PCT.txt

Met Met Lys Gly Ala Pro Glu Arg Ile Leu Glu Phe Cys Ser Thr Phe
515 520 525

Leu Leu Asn Gly Gln Glu Tyr Ser Met Asn Asp Glu Met Lys Glu Ala
530 535 540

Phe Gln Asn Ala Tyr Leu Glu Leu Gly Gly Leu Gly Glu Arg Val Leu
545 550 555 560

Gly Phe Cys Phe Leu Asn Leu Pro Ser Ser Phe Ser Lys Gly Phe Pro
565 570 575

Phe Asn Thr Asp Glu Ile Asn Phe Pro Met Asp Asn Leu Cys Phe Val
580 585 590

Gly Leu Ile Ser Met Ile Asp Pro Pro Arg Ala Ala Val Pro Asp Ala
595 600 605

Val Ser Lys Cys Arg Ser Ala Gly Ile Lys Val Ile Met Val Thr Gly
610 615 620

Asp His Pro Ile Thr Ala Lys Ala Ile Ala Lys Gly Val Gly Ile Ile
625 630 635 640

Ser Glu Gly Thr Glu Thr Ala Glu Glu Val Ala Ala Arg Leu Lys Ile
645 650 655

Pro Ile Ser Lys Val Asp Ala Ser Ala Ala Lys Ala Ile Val Val His
660 665 670

Gly Ala Glu Leu Lys Asp Ile Gln Ser Lys Gln Leu Asp Gln Ile Leu
675 680 685

Gln Asn His Pro Glu Ile Val Phe Ala Arg Thr Ser Pro Gln Gln Lys
690 695 700

Leu Ile Ile Val Glu Gly Cys Gln Arg Leu Gly Ala Val Val Ala Val
705 710 715 720

Thr Gly Asp Gly Val Asn Asp Ser Pro Ala Leu Lys Lys Ala Asp Ile
725 730 735

Gly Ile Ala Met Gly Ile Ser Gly Ser Asp Val Ser Lys Gln Ala Ala
740 745 750

Asp Met Ile Leu Leu Asp Asp Asn Phe Ala Ser Ile Val Thr Gly Val
755 760 765

Glu Glu Gly Arg Leu Ile Phe Asp Asn Leu Lys Lys Ser Ile Met Tyr
770 775 780

2015201738 07 Apr 2015

94/223

342-10PCT.txt

Thr Leu Thr Ser Asn Ile Pro Glu Ile Thr Pro Phe Leu Met Phe Ile
785 790 795 800

Ile Leu Gly Ile Pro Leu Pro Leu Gly Thr Ile Thr Ile Leu Cys Ile
805 810 815

Asp Leu Gly Thr Asp Met Val Pro Ala Ile Ser Leu Ala Tyr Glu Ser
820 825 830

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

Asn Leu Val Asn His Arg Leu Ile Gly Met Ala Tyr Gly Gln Ile Gly
850 855 860

Met Ile Gln Ala Leu Ala Gly Phe Phe Thr Tyr Phe Val Ile Leu Ala
865 870 875 880

Glu Asn Gly Phe Arg Pro Val Asp Leu Leu Gly Ile Arg Leu His Trp
885 890 895

Glu Asp Lys Tyr Leu Asn Asp Leu Glu Asp Ser Tyr Gly Gln Gln Trp
900 905 910

Thr Tyr Glu Gln Arg Lys Val Val Glu Phe Thr Cys Gln Thr Ala Phe
915 920 925

Phe Val Thr Ile Val Val Val Gln Trp Ala Asp Leu Ile Ile Ser Lys
930 935 940

Thr Arg Arg Asn Ser Leu Phe Gln Gln Gly Met Arg Asn Lys Val Leu
945 950 955 960

Ile Phe Gly Ile Leu Glu Glu Thr Leu Leu Ala Ala Phe Leu Ser Tyr
965 970 975

Thr Pro Gly Met Asp Val Ala Leu Arg Met Tyr Pro Leu Lys Ile Thr
980 985 990

Trp Trp Leu Cys Ala Ile Pro Tyr Ser Ile Leu Ile Phe Val Tyr Asp
995 1000 1005

Glu Ile Arg Lys Leu Leu Ile Arg Gln His Pro Asp Gly Trp Val
1010 1015 1020

Glu Arg Glu Thr Tyr Tyr
1025

<210> 131
<211> 21
<212> DNA
<213> Artificial Sequence

07 Apr 2015
2015201738

95/223

342-10PCT.txt

<220>
<223> Oligonucleotide

<400> 131
tgtaatcctg gctgagaatg g 21

<210> 132
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 132
aagtgagttg cggcgagt 18

<210> 133
<211> 279
<212> DNA
<213> Homo sapiens

<400> 133
atgtatgtaa aaattgcaaa acatctcaat gatgtttatg cccccagaa ggtactgtgt 60
cacgggatct catatattct ggctgtcatt gtcataataa gccactcttg gtcatatgga 120
aaagcattca gctgctccct gcctttgctc acagcgtgtg gtactctctt agaagctatt 180
cctgtcctat ttaggcagtt attcctgctt cttgtgttgg acctgaagtc aacagggcca 240
gcaatagaga agaaagatga tgtgaaggag agcaactga 279

<210> 134
<211> 92
<212> PRT
<213> Homo sapiens

<400> 134
Met Tyr Val Lys Ile Ala Lys His Leu Asn Asp Val Tyr Ala Pro Gln
1 5 10 15

Lys Val Leu Cys His Gly Ile Ser Tyr Ile Leu Ala Val Ile Val Ile
20 25 30

Ile Ser His Ser Trp Ser Tyr Gly Lys Ala Phe Ser Cys Ser Leu Pro
35 40 45

Leu Leu Thr Ala Cys Gly Thr Leu Leu Glu Ala Ile Pro Val Leu Phe
50 55 60

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

Ala Ile Glu Lys Lys Asp Asp Val Lys Glu Ser Asn
85 90

<210> 135
 <211> 20
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide

<400> 135
 tgctccctgc ctttgctcac

20

<210> 136
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide

<400> 136
 ggtacttggg ctcgaacgat gatc

24

<210> 137
 <211> 1569
 <212> DNA
 <213> Homo sapiens

<400> 137
 atgcctgtag ggggtggccc tgagagtgtg ggcaggtgca atggctgtca atgccacata 60
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 atcaggaaga agaagcagca aaattctgac ccacagccca agaggggtcg gggcagcaga 180
 acctcagcca cagccaatca cagcgggggc cttcggggag gggcgtggcc tgacaacttc 240
 ggcgacgcgg ctggaccaat ccggacggag gagagcgaag ctctctgtca ctgggcccag 300
 gtgcgctcct cagcgtctcc ggggtggcggg gcgcgcggga tggaggagtc ttgggaggct 360
 gcgcccggag gccaagccgg ggcagagctc ccaatggagc ccgtgggaag cctggtcccc 420
 acgctggagc agccgcaggt gcccgcgaag gtgcgacaac ctgaaggctc cgaaagcagc 480
 ccaagtccgg ccggggccgt ggagaaggcg gcgggcgcag gcctggagcc ctcgagcaag 540
 aaaaagccgc cttcgcctcg ccccgggtcc ccgcgcgtgc cgccgctcag cctgggctac 600
 ggggtctgcc ccgagccgcc gtcaccgggc cctgccttgg tcaagctgcc ccggaatggc 660
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 gtgcgcgtga agcccgtggg cgcggccggt ggcagcagca cgccatcgcc caggccctcc 780
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2015201738 07 Apr 2015

97/223

342-10PCT.txt

atggctgtgc tcctggcagt ctctgggggtt gtcattgtgg tcctggcctc aagagcagga 1200
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tgggtggggg cctggcgagg cccccagggc tggcactgga tcgacgaggc cccactcccg 1440
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gaaggcacgc tgggtggctgc aaactgcagc actccaagac cctgggtctg tgccaagggg 1560
accagtgga 1569

<210> 138
<211> 522
<212> PRT
<213> Homo sapiens

<400> 138

Met Pro Val Gly Gly Gly Pro Glu Ser Val Gly Arg Cys Asn Gly Cys
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Gln Cys His Ile Lys Gly Lys Gly Ile Tyr Ile Leu Asn Ser Glu Arg
20 25 30

Pro Val Pro Gly Asp Tyr Ile Tyr Ile Arg Lys Lys Lys Gln Gln Asn
35 40 45

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

Ala Asn His Ser Gly Val Leu Arg Gly Gly Ala Trp Pro Asp Asn Phe
65 70 75 80

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

His Trp Ala Gln Val Arg Ser Ser Ala Ser Pro Gly Gly Gly Ala Arg
100 105 110

Gly Met Glu Glu Ser Trp Glu Ala Ala Pro Gly Gly Gln Ala Gly Ala
115 120 125

Glu Leu Pro Met Glu Pro Val Gly Ser Leu Val Pro Thr Leu Glu Gln
130 135 140

Pro Gln Val Pro Ala Lys Val Arg Gln Pro Glu Gly Pro Glu Ser Ser
145 150 155 160

Pro Ser Pro Ala Gly Ala Val Glu Lys Ala Ala Gly Ala Gly Leu Glu
165 170 175

2015201738 07 Apr 2015

98/223

342-10PCT.txt

Pro Ser Ser Lys Lys Lys Pro Pro Ser Pro Arg Pro Gly Ser Pro Arg
180 185 190

Val Pro Pro Leu Ser Leu Gly Tyr Gly Val Cys Pro Glu Pro Pro Ser
195 200 205

Pro Gly Pro Ala Leu Val Lys Leu Pro Arg Asn Gly Glu Ala Pro Gly
210 215 220

Ala Glu Pro Ala Pro Ser Ala Trp Ala Pro Met Glu Leu Gln Val Asp
225 230 235 240

Val Arg Val Lys Pro Val Gly Ala Ala Gly Gly Ser Ser Thr Pro Ser
245 250 255

Pro Arg Pro Ser Thr Arg Phe Leu Lys Val Pro Val Pro Glu Ser Pro
260 265 270

Ala Phe Ser Arg His Ala Asp Pro Ala His Gln Leu Leu Arg Ala
275 280 285

Pro Ser Gln Gly Gly Thr Trp Gly Arg Arg Ser Pro Leu Ala Ala Ala
290 295 300

Arg Thr Glu Ser Gly Cys Asp Ala Glu Gly Arg Ala Ser Pro Ala Glu
305 310 315 320

Gly Ser Ala Gly Ser Pro Gly Ser Pro Thr Cys Cys Arg Cys Lys Glu
325 330 335

Leu Gly Leu Glu Lys Glu Asp Ala Ala Leu Leu Pro Arg Ala Gly Leu
340 345 350

Asp Gly Asp Glu Lys Leu Pro Arg Ala Val Thr Leu Thr Gly Leu Pro
355 360 365

Met Tyr Val Lys Ser Leu Tyr Trp Ala Leu Ala Phe Met Ala Val Leu
370 375 380

Leu Ala Val Ser Gly Val Val Ile Val Val Leu Ala Ser Arg Ala Gly
385 390 395 400

Ala Arg Cys Gln Gln Cys Pro Pro Gly Trp Val Leu Ser Glu Glu His
405 410 415

Cys Tyr Tyr Phe Ser Ala Glu Ala Gln Ala Trp Glu Ala Ser Gln Ala
420 425 430

Phe Cys Ser Ala Tyr His Ala Thr Leu Pro Leu Leu Ser His Thr Gln
435 440 445

342-10PCT.txt
 Asp Phe Leu Gly Arg Tyr Pro Val Ser Arg His Ser Trp Val Gly Ala
 450 455 460

Trp Arg Gly Pro Gln Gly Trp His Trp Ile Asp Glu Ala Pro Leu Pro
 465 470 475 480

Pro Gln Leu Leu Pro Glu Asp Gly Glu Asp Asn Leu Asp Ile Asn Cys
 485 490 495

Gly Ala Leu Glu Glu Gly Thr Leu Val Ala Ala Asn Cys Ser Thr Pro
 500 505 510

Arg Pro Trp Val Cys Ala Lys Gly Thr Gln
 515 520

<210> 139
 <211> 18
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide

<400> 139
 gagaaggagg atgcggcg 18

<210> 140
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide

<400> 140
 ggaccacaat gacaaccca g 21

<210> 141
 <211> 2217
 <212> DNA
 <213> Homo sapiens

<400> 141
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 ttccagactt atcgggcccc taaaataaaa gccaaaagaa gcatagccac tcctgaaaac 120
 ctgaagaaat tattgccacg tgttcccaaa aacagtgtccc tgagtgatga aatgacaaag 180
 cttcaciaaag gagctaagcc atgcaaatca aatacatttg gatgttttcc tattcatcag 240
 gctgtacttt caggttccaa agaatgcatg gaaataatat tgaagtttgg tgaagagcac 300
 ggggtacagca gacagtgtca catcaacttt gtggataacg ggaaagccag ccctctccat 360
 ctggctgtgc aaaatggtga cttggaaatg atgaaaatgt gcctggacaa tgggtgtacaa 420
 atagacctag tggagatgca acagatcaaa gagctggtaa tggatgaaga caacgatggg 480
 tgtactcttc tacattatgc atgtagacag gggggccctg gttctgtaaa taacctactt 540

342-10PCT.txt

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ggctttaatg tgtccattca ttccaaaagc aaagataaga aatcacctct gcattttgca 600
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cttctgaatg aaggggacct tcatggaatg actcctctcc atctggcagc aaagaatgga 720
catgataaag tagttcagct tcttctgaaa aaagggtgcat tgtttctcag atgggatgaa 780
tgtcttaagg ttttttagtca ttattctcca aacaataaat gtccaatttt ggaaatgatac 840
gaatacctcc ctgaatgcat gaagaaagt ctacccttct tttctaattgt tcacgtaaga 900
cctgctccaa accagaatca aataaaccat ggagaacaca ggttggttta cggatttata 960
gcccataatga taaatctagg attttactgt cttggtctca taccaatgac ctttcttggt 1020
gtcagaataa aaccaggaat ggctttcaac tctgctggaa tcatcaataa aactagtgtat 1080
cattcagaaa tactagataa catgaattca agtctaataa caatttgat gattttagtt 1140
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tgttgcatat gcaaagtgga tcggaaatcc accgccgtat gtccaacaa acccagatgt 1680
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aaattggctg ctccatacat cactcaccag atcaagccat tcttgcgagc agctgggttt 2040
tgcacagtga aggtggcca gagagatgac atctctgtgt ggagtgtgga tttcaggtgg 2100
ctcaatgcat gggaagcagc gattcgaaag cagtctctca gacaatctga gatggaggaa 2160
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<210> 142
 <211> 738
 <212> PRT
 <213> Homo sapiens
 <400> 142

Met Val Cys Thr Phe Asp Ser Glu Leu Leu Asn Cys Gln Arg Lys Asp

1

5

10

15

2015201738 07 Apr 2015

101/223

342-10PCT.txt

Glu Tyr Asn Gln Phe Gln Thr Tyr Arg Ala His Lys Ile Lys Ala Lys
20 25 30

Arg Ser Ile Ala Thr Pro Glu Asn Leu Lys Lys Leu Leu Pro Arg Val
35 40 45

Pro Lys Asn Ser Ala Leu Ser Asp Glu Met Thr Lys Leu His Lys Gly
50 55 60

Ala Lys Pro Cys Lys Ser Asn Thr Phe Gly Cys Phe Pro Ile His Gln
65 70 75 80

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

Gly Glu Glu His Gly Tyr Ser Arg Gln Cys His Ile Asn Phe Val Asp
100 105 110

Asn Gly Lys Ala Ser Pro Leu His Leu Ala Val Gln Asn Gly Asp Leu
115 120 125

Glu Met Met Lys Met Cys Leu Asp Asn Gly Val Gln Ile Asp Leu Val
130 135 140

Glu Met Gln Gln Ile Lys Glu Leu Val Met Asp Glu Asp Asn Asp Gly
145 150 155 160

Cys Thr Pro Leu His Tyr Ala Cys Arg Gln Gly Gly Pro Gly Ser Val
165 170 175

Asn Asn Leu Leu Gly Phe Asn Val Ser Ile His Ser Lys Ser Lys Asp
180 185 190

Lys Lys Ser Pro Leu His Phe Ala Ala Ser Tyr Gly Arg Ile Asn Thr
195 200 205

Cys Gln Arg Leu Leu Gln Asp Ile Ser Asp Thr Arg Leu Leu Asn Glu
210 215 220

Gly Asp Leu His Gly Met Thr Pro Leu His Leu Ala Ala Lys Asn Gly
225 230 235 240

His Asp Lys Val Val Gln Leu Leu Leu Lys Lys Gly Ala Leu Phe Leu
245 250 255

Arg Trp Asp Glu Cys Leu Lys Val Phe Ser His Tyr Ser Pro Asn Asn
260 265 270

Lys Cys Pro Ile Leu Glu Met Ile Glu Tyr Leu Pro Glu Cys Met Lys
275 280 285

2015201738 07 Apr 2015

102/223

342-10PCT.txt

Lys Val Leu Pro Phe Phe Ser Asn Val His Val Arg Pro Ala Pro Asn
290 295 300

Gln Asn Gln Ile Asn His Gly Glu His Arg Leu Ala Tyr Gly Phe Ile
305 310 315 320

Ala His Met Ile Asn Leu Gly Phe Tyr Cys Leu Gly Leu Ile Pro Met
325 330 335

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

Gly Ile Ile Asn Lys Thr Ser Asp His Ser Glu Ile Leu Asp Asn Met
355 360 365

Asn Ser Ser Leu Ile Thr Ile Cys Met Ile Leu Val Phe Cys Ser Ser
370 375 380

Ile Leu Gly Tyr Val Lys Glu Val Val Gln Ile Phe Gln Gln Lys Arg
385 390 395 400

Asn Tyr Phe Met Asp Ile Ser Ser Ser Thr Glu Trp Ile Ile Asn Thr
405 410 415

Met Gly Pro Ile Leu Val Leu Pro Leu Phe Thr Glu Ile Ala Ala His
420 425 430

Leu Gln Phe Glu Asn Cys Gly Ile Phe Ile Val Ile Leu Glu Val Ile
435 440 445

Phe Lys Thr Leu Leu Arg Ser Ala Val Val Phe Phe Phe Leu Leu Leu
450 455 460

Ala Phe Gly Leu Ser Phe Tyr Val Leu Leu Asn Leu Gln Ser Phe Leu
465 470 475 480

Glu Pro Phe Leu Lys Asn Lys Leu Ala His Pro Val Leu Ser Phe Ala
485 490 495

Gln Leu Ile Ser Phe Thr Val Phe Ala Pro Ile Val Leu Met Asn Leu
500 505 510

Leu Ile Gly Leu Ala Val Gly Asp Ile Ala Glu Val Gln Lys His Ala
515 520 525

Ser Leu Lys Arg Ile Ala Met Gln Lys Leu Pro Cys Cys Cys Ile Arg
530 535 540

Lys Val Asp Arg Lys Ser Thr Ala Val Cys Pro Asn Lys Pro Arg Cys
545 550 555 560

103/223

342-10PCT.txt

Asp Gly Thr Leu Phe Gln Val Leu Leu Ala Leu Gly Pro Leu Pro Leu
565 570 575

Glu Glu Asn Arg Asn Ile Lys Ser Phe Leu Pro Thr Glu Ile Thr Val
580 585 590

Lys Arg Thr His Glu His Leu Pro Ser Ala Gly Phe Gly His His Gly
595 600 605

Lys His Thr Leu Ser Leu Leu Leu Val Glu Glu Trp Leu Pro Leu Asn
610 615 620

Val Val His Ser Ser Cys Ser Ala Phe Arg Val Val Gly Gln Ile Phe
625 630 635 640

Pro Ile Arg His Phe Gln Trp Ile His Val Asn Glu Pro His Thr Gly
645 650 655

Asn Leu Lys Glu Lys Leu Ala Ala Pro Tyr Ile Thr His Gln Ile Lys
660 665 670

Pro Phe Leu Arg Ala Ala Gly Phe Cys Thr Val Lys Val Val Gln Arg
675 680 685

Asp Asp Ile Ser Val Trp Ser Val Asp Phe Arg Trp Leu Asn Ala Trp
690 695 700

Glu Ala Ala Ile Arg Lys Gln Ser Leu Arg Gln Ser Glu Met Glu Glu
705 710 715 720

Leu Ser Cys Ser Leu Leu Leu Arg Val Thr Asp Val His Thr Arg Ser
725 730 735

Leu Tyr

<210> 143
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 143
ttccttactc tccgctttcc

<210> 144
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

2015201738 07 Apr 2015

104/223

342-10PCT.txt

<400> 144
aactttgtgg ataacgggaa

20

<210> 145
<211> 1155
<212> DNA
<213> Homo sapiens

<400> 145
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cgtgcgggcg ctttgggggg ccacggttgg ggagcccaa cttcggggag gacgcggaat 180
ccggacgcgg gactgaacct gaggattcac ggagcccggt gctcccctat ggggcacggg 240
aagcggcaga tgcgcgtgca gagagggtccg tcccaccac cccctgggcg ccttgggtcc 300
aaggcgcata ggcgctcccg cctgtggccg ccaccggtgc agcagaacgc gggctctcgg 360
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cactttggga attttggaga agaaagaata aaggcagaaa tgaggatata gaaagcatgt 660
cacttgaaga tcaagaagtc aagcttggat gccaatggta aagtggatga tggtaggat 720
gatgatggtg aggatgatga tggtaggat gatgatggtg atgatgatgg tgaggatgat 780
gatggtgagg atgatgatgg tgaggatgat gatggtgagg atgatggtga ggatgatgat 840
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gatgatggtg aggatgatga tggtagcagt gaggatgatg gtgaggatgg tgatgatgat 960
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cgatacaaat tttga 1155

<210> 146
<211> 384
<212> PRT
<213> Homo sapiens

<400> 146

Met Gln Ser Leu Ile Ser Pro Val Thr Lys Ala Ile Leu Val Ala Leu
1 5 10 15

Phe Ile Phe Ala Ile Leu Leu Ile Leu Tyr Val Ile Leu Trp Asp Ala
20 25 30

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

2015201738 07 Apr 2015

105/223

342-10PCT.txt

Gly Trp Gly Ala Pro Thr Ser Gly Arg Thr Arg Asn Pro Asp Ala Gly
50 55 60

Leu Asn Pro Arg Ile His Gly Ala Arg Gly Ser Pro Met Gly His Gly
65 70 75 80

Lys Arg Gln Met Arg Val Gln Arg Gly Pro Ser His Pro Pro Pro Gly
85 90 95

Arg Leu Gly Ser Lys Ala His Arg Arg Ser Arg Leu Trp Pro Pro Pro
100 105 110

Val Gln Gln Asn Ala Gly Ser Arg Val Gly Pro Met Arg Tyr Gly Thr
115 120 125

Pro Gly Ala Ile Gly Ser Leu Ala Leu Cys Ser Gly Gly Gly Asp Pro
130 135 140

Ala Leu Lys Phe Pro Ile Thr Ser Met Asp Lys His Gly Lys Ile Met
145 150 155 160

Ser Trp Lys Asn Ser Ile Ala Leu Gln Ile Gln Thr Arg His Phe Ala
165 170 175

His Glu Thr Arg Val Pro Glu Ile Ser Arg Ser Lys Ser Arg Ile Arg
180 185 190

Asp Arg Gln Thr Tyr Gly Met Tyr His Phe Gly Asn Phe Gly Glu Glu
195 200 205

Arg Ile Lys Ala Glu Met Arg Ile Gln Lys Ala Cys His Leu Lys Ile
210 215 220

Lys Lys Ser Ser Leu Asp Ala Asn Gly Lys Val Asp Asp Gly Glu Asp
225 230 235 240

Asp Asp Gly Glu Asp Asp Asp Gly Glu Asp Asp Asp Gly Asp Asp Asp
245 250 255

Gly Glu Asp Asp Asp Gly Glu Asp Asp Gly Glu Asp Asp Asp Gly
260 265 270

Glu Asp Asp Gly Glu Asp Asp Asp Gly Asp Asp Asp Gly Glu Asp Asp
275 280 285

Asp Gly Asp Asp Asp Gly Asp Asp Asp Gly Glu Asp Asp Asp Gly Glu
290 295 300

Asp Asp Asp Gly Asp Ser Glu Asp Asp Gly Glu Asp Gly Asp Asp Asp
305 310 315 320

07 Apr 2015
2015201738

106/223

342-10PCT.txt

Gly Glu Asp Asp Asp Gly Asp Ser Glu Asp Asp Gly Asp Asp Gly Asp
325 330 335

Asp Asp Gly Glu Asp Asp Asp His Gly Asp Asp Val Arg Met Met Met
340 345 350

Met Met Val Met Thr Val Thr Met Met Lys Asn Val Val Gly Asn Tyr
355 360 365

Arg Leu Pro Glu Leu Pro Thr Trp Thr Ser Val Gln Arg Tyr Lys Phe
370 375 380

<210> 147
<211> 21
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2015201738 07 Apr 2015

107/223

342-10PCT.txt

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2015201738 07 Apr 2015

108/223

342-10PCT.txt
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2015201738 07 Apr 2015

109/223

342-10PCT.txt

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35 40 45

Leu Lys Asn Cys Glu Val Ile Val Leu Thr Ile Leu Ser Leu Ser Gly
50 55 60

Phe Val Ile Gly His Met Ala Tyr Asn Ser Val Glu Val His Gln Ile
65 70 75 80

Val Tyr Pro Leu Leu Arg Thr Ser Ser Phe Ser Leu Tyr Ser Tyr Phe
85 90 95

Ser Pro Leu Ile Ile Phe Met Val Ala Leu Asp Val Glu Phe Tyr Thr
100 105 110

Leu Lys Lys Met Phe Trp Gln Val Leu Leu Thr Gly Leu Ile Ser Phe
115 120 125

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

Asp Ser Trp Asp Leu Gln Ser Cys Leu Leu Phe Ser Ile Thr Leu Gly
145 150 155 160

Ile Ile Asp Pro Leu Arg Ser Val Asn Ser Leu Lys Thr Ile Gly Ile
165 170 175

Ser Lys Ile Tyr Ile Asp Leu Ile Arg Gly Glu Ser Leu Ile Ile Cys
180 185 190

Ser Ile Ala Ser Ile Phe Phe Gly Asn Phe Arg Gly Asn Arg Ile His
195 200 205

Phe Ser Ile Phe Arg Asp Leu His Val Gly Ile Glu Leu Ser Tyr Asp
210 215 220

Ile Leu Gly Ser Ile Ile Phe Gly Tyr Trp Cys Ala Lys Ile Ile Gln
225 230 235 240

Cys Ile Leu Ala Asp Val Phe Ser Asn Met Leu Thr Asn Ile Ile Leu
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Cys Phe Ser Met Val Tyr Met Thr Phe Tyr Ile Val Glu Phe Leu Gly
260 265 270

2015201738 07 Apr 2015

110/223

342-10PCT.txt

Met Ser Gly Thr Leu Ala Leu Ala Ala Val Gly Leu Asn Leu Asp Ser
275 280 285

Leu Thr Phe Lys Pro Lys Ile Glu Leu Val Ile Thr Lys Phe Leu Arg
290 295 300

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305 310 315 320

Val Ile Gly Cys Gly Glu Leu Ser His Tyr Glu Phe His Thr Ile Pro
325 330 335

Phe Ile Phe Ile Leu Phe Thr Thr Val Asn Leu Val Arg Leu Leu Thr
340 345 350

Ile Leu Leu Val Ser Pro Ile Leu Met His Ser Asn Tyr Glu Tyr Asn
355 360 365

Trp Arg Trp Gly Val Val Ile Thr Trp Ser Gly Ile Lys Gly Val Phe
370 375 380

Asn Leu Leu Trp Ala Pro Asp Val Tyr Asn Leu Ala Glu Arg Lys Val
385 390 395 400

Glu Val Pro Gln Met Phe Ile Leu Tyr Val Gln Val Ile Ser Leu Leu
405 410 415

Thr Met Gly Ile Asn Ser Tyr Val Met Thr Gln Ser Ala Arg Lys Leu
420 425 430

Asp Leu Cys Val Leu Ser Leu Pro Arg Gln Met Ile Leu Gln Asn Ala
435 440 445

Thr Gln His Ile Gln Glu Ile Val Gln Asn Thr Ile Thr Leu Phe Lys
450 455 460

Thr Glu Lys Ile Leu Thr Asn Val Asn Trp Thr Leu Val Glu Asp Lys
465 470 475 480

Thr Arg Ile Glu Tyr Ile Pro Phe Ser His Val Ser His Asn Asp Met
485 490 495

Lys Thr Glu Ser Thr Thr Asp Glu Ala Leu Met Glu Glu Ala Arg Leu
500 505 510

His Val Ala Ala Ile Gln Met Ser Ser Phe Glu Lys Gln Arg Asn Asn
515 520 525

Gly Ile Leu Glu Ile Glu Ala Ala Arg Ile Leu Ile Gly Ala Ala Lys
530 535 540

2015201738 07 Apr 2015

111/223

342-10PCT.txt

Cys Tyr Tyr Ser Ile Gln Gly Lys Phe Met Ser Ile Tyr Asp Val Ser
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Thr Tyr Met Arg Thr Arg Ser Trp Leu Ile Lys Phe Lys Asn Val Leu
565 570 575

Thr Phe Leu Glu Tyr Cys Ile Glu Lys Ile His Phe Ile Pro Pro Glu
580 585 590

Ser Asn Thr Phe Leu Thr Phe Ile Phe His Ile Val Phe Ser Glu Glu
595 600 605

Phe Glu Tyr Thr Gly Gln Ile Ile Asn Leu Ile Tyr Ile Tyr Pro Met
610 615 620

Ile Ile His Leu Trp Pro Met Ala Arg Gly Leu Asn Val Ser Ala Leu
625 630 635 640

Ile Ser Ile Asn Tyr Tyr Phe Met Phe Leu Tyr Val Leu Glu Ser Thr
645 650 655

Leu Lys Ile Ile Ile Leu Lys Arg Lys Tyr Phe Gln Gln Cys Trp Asn
660 665 670

Thr Leu Glu Phe Phe Ile Leu Val Ile Gly Ile Ile Asp Ile Phe Cys
675 680 685

Val Tyr Phe Val Lys Leu Arg Pro Asp Asn Leu Ala Leu Ile Gln Leu
690 695 700

Thr Val Ile Met Gly Tyr Leu Arg Ile Ile Arg Phe Leu Pro Leu Phe
705 710 715 720

Lys Ile Ile Val Pro Ile Leu Ile Arg Ile Ala Asp Val Gln Ile Lys
725 730 735

Lys Arg Leu Ser Leu Met Tyr Ser Ile Thr Lys Gly Tyr Ile Lys Ser
740 745 750

Gln Glu Asp Ala Lys Leu Leu Ile Lys Gln Ile Ala Val Cys Glu Ser
755 760 765

Ile Tyr Gln Lys Leu Cys Glu Ile Leu Glu Thr Asn Lys Gln Asp Ala
770 775 780

Val Lys Glu Leu Val Leu Met Glu His Glu Gly Arg Asp Val Val Ile
785 790 795 800

Ala Leu Lys Thr Lys Gln Ala Ile Arg Asn Val Ile Ala Lys Ala Leu
805 810 815

2015201738 07 Apr 2015

112/223

342-10PCT.txt

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820 825 830

Val Ile Glu Ile Asn Lys Val Leu Leu Lys Lys Leu Lys Ala Leu Asn
835 840 845

Asn Phe Pro Lys Ala Ile Pro Pro Pro Thr Pro Asp Ile Tyr Leu His
850 855 860

Asn Ile Ile Trp Leu Glu Gly Lys Asp Val Leu Ile Asp Phe Phe Lys
865 870 875 880

Glu Arg Ala Lys Leu Ala Cys Phe Asp Ser Gly Asp Thr Ile Cys Lys
885 890 895

Gly Gly Glu Met Pro Gln Gly Ile Tyr Leu Ile Ile Ser Gly Met Ala
900 905 910

Ile Leu His Ser Leu Ser Pro Thr Phe Gly Ile Glu Ser Asn Gln Arg
915 920 925

Cys Asp Arg Gly Ser Arg Asp Met Phe Thr Glu Phe Cys Thr Thr Gly
930 935 940

Asp Ile Ile Gly Glu Leu Ser Cys Leu Leu Lys Arg Glu Ile Glu Tyr
945 950 955 960

Thr Val Ile Cys Glu Thr Ser Leu Gln Ala Cys Phe Ile Ser Leu Glu
965 970 975

Asp Leu Tyr Glu Gly Phe Asp Ala Phe Trp Pro Ser Leu Glu Tyr Lys
980 985 990

Ile Trp Leu Lys Leu Ala Leu Ser Thr Ala Tyr Gln Tyr Phe Glu Ser
995 1000 1005

Ser Leu Ile Asp Glu Asp Leu Arg Phe Gln Asn Cys Val Met Phe
1010 1015 1020

Asn Gln Ala Tyr Val Glu Thr Leu Ser Ser Tyr Ser Asp Met Ile
1025 1030 1035

Ile Asp Asn Met Thr Met Lys Phe Val Ile Ile Val Tyr Gly Ser
1040 1045 1050

Val Ile Asp Thr Lys Thr Glu Glu Pro Tyr Phe Ala Pro Cys Ile
1055 1060 1065

Ile Pro Thr Thr Cys Glu Gln Val Gln Gly Thr Ser Asp Leu Ser
1070 1075 1080

07 Apr 2015 2015201738

113/223

342-10PCT.txt

Lys Leu Leu Ile Ile Gln Ala Ser Glu Leu Thr Gln Arg Asn Ser
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Asn Thr Asn Val Met Ala Ser Val Asn Thr Val Phe Glu Gln Pro
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<400> 152
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<210> 153
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<213> Homo sapiens

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2015201738 07 Apr 2015

114/223

342-10PCT.txt

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<212> PRT
<213> Homo sapiens

<400> 154

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20 25 30

Glu Phe Pro Ser Pro Cys Leu Asp Ser Lys Thr Lys Val Val Met Lys
35 40 45

Gly Gln Asn Val Ser Met Phe Cys Ser His Lys Asn Lys Ser Leu Gln
50 55 60

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

Gly Lys Gly Glu Pro Ala Ile Phe Asn Leu Ser Ile Thr Glu Ala His
85 90 95

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

Tyr Ser Arg Asp Phe Ser Phe Thr Ile Val Asp Pro Val Thr Ser Pro
115 120 125

Val Leu Asn Ile Met Val Ile Gln Thr Glu Thr Asp Arg His Ile Thr
130 135 140

Leu His Cys Leu Ser Val Asn Gly Ser Leu Pro Ile Asn Tyr Thr Phe
145 150 155 160

Phe Glu Asn His Val Ala Ile Ser Pro Ala Ile Ser Lys Tyr Asp Arg
165 170 175

Glu Pro Ala Glu Phe Asn Leu Thr Lys Lys Asn Pro Gly Glu Glu Glu
180 185 190

2015201738 07 Apr 2015

115/223

342-10PCT.txt

Glu Tyr Arg Cys Glu Ala Lys Asn Arg Leu Pro Asn Tyr Ala Thr Tyr
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Ser His Pro Val Thr Met Pro Ser Thr Gly Gly Asp Ser Cys Pro Phe
210 215 220
Cys Leu Lys Leu Leu Leu Pro Gly Leu Leu Leu Leu Leu Val Val Ile
225 230 235 240
Ile Leu Ile Leu Ala Phe Trp Val Leu Pro Lys Tyr Lys Thr Arg Lys
245 250 255
Ala Met Arg Asn Asn Val Pro Arg Asp Arg Gly Asp Thr Ala Met Glu
260 265 270
Val Gly Ile Tyr Ala Asn Ile Leu Glu Lys Gln Ala Lys Glu Glu Ser
275 280 285
Val Pro Glu Val Gly Ser Arg Pro Cys Val Ser Thr Ala Gln Asp Glu
290 295 300
Ala Lys His Ser Gln Glu Leu Gln Tyr Ala Thr Pro Val Phe Gln Glu
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325 330 335
Val Tyr Ser Glu Ser
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<220>
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21

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<210> 157
<211> 2713

2015201738 07 Apr 2015

116/223

342-10PCT.txt

<212> DNA
<213> Homo sapiens

<400> 157

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2015201738 07 Apr 2015

117/223

342-10PCT.txt

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 <213> Homo sapiens

<400> 158

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

Trp Pro Pro Gly Ser Pro Gln Ala Leu Arg Gln Pro Gly Arg Ala Arg
 35 40 45

Val Ala Met Ala Ala Leu Val Trp Leu Leu Ala Gly Ala Ser Met Ser
 50 55 60

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

Leu Leu Ser Ala Leu His Met Leu Val Ala Ala Leu Ala Cys His Arg
 85 90 95

Gly Ala Arg Arg Pro Met Pro Gly Gly Thr Arg Cys Arg Val Leu Leu
 100 105 110

Leu Ser Leu Thr Phe Gly Thr Ser Met Ala Cys Gly Asn Val Gly Leu
 115 120 125

2015201738 07 Apr 2015

118/223
342-10PCT.txt

Arg Ala Val Pro Leu Asp Leu Ala Gln Leu Val Thr Thr Thr Thr Pro
130 135 140

Leu Phe Thr Leu Ala Leu Ser Ala Leu Leu Leu Gly Arg Arg His His
145 150 155 160

Pro Leu Gln Leu Ala Ala Met Gly Pro Leu Cys Leu Gly Ala Ala Cys
165 170 175

Ser Leu Ala Gly Glu Phe Arg Thr Pro Pro Thr Gly Cys Gly Phe Leu
180 185 190

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

Leu Leu Gln Glu Glu Arg Leu Asp Ala Val Thr Leu Leu Tyr Ala Thr
210 215 220

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

Ala Gly Val Ala Pro Pro Pro Thr Ala Gly Asp Ser Arg Leu Trp Ala
245 250 255

Cys Ile Leu Leu Ser Cys Leu Leu Ser Val Leu Tyr Asn Leu Ala Ser
260 265 270

Phe Ser Leu Leu Ala Leu Thr Ser Ala Leu Thr Val His Val Leu Gly
275 280 285

Asn Leu Thr Val Val Gly Asn Leu Ile Leu Ser Arg Leu Leu Phe Gly
290 295 300

Ser Arg Leu Ser Ala Leu Ser Tyr Val Gly Ile Ala Leu Thr Leu Ser
305 310 315 320

Gly Met Phe Leu Tyr His Asn Cys Glu Phe Val Ala Ser Trp Ala Ala
325 330 335

Arg Arg Gly Leu Trp Arg Arg Asp Gln Pro Ser Lys Gly Leu
340 345 350

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<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 159
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2015201738 07 Apr 2015

119/223
342-10PCT.txt

<210> 160
<211> 21
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<220>
<223> Oligonucleotide

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21

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<212> DNA
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tag 963

<210> 162
<211> 305
<212> PRT
<213> Homo sapiens

<400> 162

Met Asn Ile Ile Leu Glu Ile Leu Leu Leu Ile Thr Ile Ile Tyr
1 5 10 15

Ser Tyr Leu Glu Ser Leu Val Lys Phe Phe Ile Pro Gln Arg Arg Lys
20 25 30

2015201738 07 Apr 2015

120/223

342-10PCT.txt

Ser Val Ala Gly Glu Ile Val Leu Ile Thr Gly Ala Gly His Gly Ile
35 40 45

Gly Arg Gln Thr Thr Tyr Glu Phe Ala Lys Arg Gln Ser Ile Leu Val
50 55 60

Leu Trp Asp Ile Asn Lys Arg Gly Val Glu Glu Thr Ala Ala Glu Cys
65 70 75 80

Arg Lys Leu Gly Val Thr Ala His Ala Tyr Val Val Asp Cys Ser Asn
85 90 95

Arg Glu Glu Ile Tyr Arg Ser Leu Asn Gln Val Lys Lys Glu Val Gly
100 105 110

Asp Val Thr Ile Val Val Asn Asn Ala Gly Thr Val Tyr Pro Ala Asp
115 120 125

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

Ile Leu Gly His Phe Trp Ile Thr Lys Ala Leu Leu Pro Ser Met Met
145 150 155 160

Glu Arg Asn His Gly His Ile Val Thr Val Ala Ser Val Cys Gly His
165 170 175

Glu Gly Ile Pro Tyr Leu Ile Pro Tyr Cys Ser Ser Lys Phe Ala Ala
180 185 190

Val Gly Phe His Arg Gly Leu Thr Ser Glu Leu Gln Ala Leu Gly Lys
195 200 205

Thr Gly Ile Lys Thr Ser Cys Leu Cys Pro Val Phe Val Asn Thr Gly
210 215 220

Phe Thr Lys Asn Pro Ser Thr Arg Leu Trp Pro Val Leu Glu Thr Asp
225 230 235 240

Glu Val Val Arg Ser Leu Ile Asp Gly Ile Leu Thr Asn Lys Lys Met
245 250 255

Ile Phe Val Pro Ser Tyr Ile Asn Ile Phe Leu Arg Leu Gln Asn Pro
260 265 270

Asp Asn Ile Lys Asn Ile Gly Leu Ala Leu Ala Ala Val Lys Arg Thr
275 280 285

Arg Leu Ile Thr Cys Leu Pro Val Ser Gln Glu Tyr Leu Arg Ser Phe
290 295 300

2015201738 07 Apr 2015

121/223
342-10PCT.txt

Ser
305

<210> 163
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<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 163
ggtctgacat cagaacttca g

21

<210> 164
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 164
tgcatacatc tctggctgga g

21

<210> 165
<211> 6014
<212> DNA
<213> Homo sapiens

<400> 165
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gctggtcctg gagacgtaca atgtcccgga gctgtcagct ggcgtcaact gcacctttga 180
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cctgcccgtg gagttgacag tcgtgtggaa tgggcacttc aacattgaca acccagctca 780
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342-10PCT.txt

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342-10PCT.txt

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342-10PCT.txt

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<210> 166
 <211> 817
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 <213> Homo sapiens

<400> 166

Met Lys Gln Cys Val Arg Leu Thr Val His Pro Asn Asn Ile Ser Val
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Ser Gln Tyr Asn Val Leu Leu Val Leu Glu Thr Tyr Asn Val Pro Glu
 20 25 30

Leu Ser Ala Gly Val Asn Cys Thr Phe Glu Asp Leu Ser Glu Met Asp
 35 40 45

Gly Leu Val Val Gly Asn Gln Ile Gln Cys Tyr Ser Pro Ala Ala Lys
 50 55 60

Glu Val Pro Arg Ile Ile Thr Glu Asn Gly Asp His His Val Val Gln
 65 70 75 80

Leu Gln Leu Lys Ser Lys Glu Thr Gly Met Thr Phe Ala Ser Thr Ser
 85 90 95

Phe Val Phe Tyr Asn Cys Ser Val His Asn Ser Cys Leu Ser Cys Val
 100 105 110

2015201738 07 Apr 2015

125/223

342-10PCT.txt

Glu Ser Pro Tyr Arg Cys His Trp Cys Lys Tyr Arg His Val Cys Thr
115 120 125

His Asp Pro Lys Thr Cys Ser Phe Gln Glu Gly Arg Val Lys Leu Pro
130 135 140

Glu Asp Cys Pro Gln Leu Leu Arg Val Asp Lys Ile Leu Val Pro Val
145 150 155 160

Glu Val Ile Lys Pro Ile Thr Leu Lys Ala Lys Asn Leu Pro Gln Pro
165 170 175

Gln Ser Gly Gln Arg Gly Tyr Glu Cys Ile Leu Asn Ile Gln Gly Ser
180 185 190

Glu Gln Arg Val Pro Ala Leu Arg Phe Asn Ser Ser Ser Val Gln Cys
195 200 205

Gln Asn Thr Ser Tyr Ser Tyr Glu Gly Met Glu Ile Asn Asn Leu Pro
210 215 220

Val Glu Leu Thr Val Val Trp Asn Gly His Phe Asn Ile Asp Asn Pro
225 230 235 240

Ala Gln Asn Lys Val His Leu Tyr Lys Cys Gly Ala Met Arg Glu Ser
245 250 255

Cys Gly Leu Cys Leu Lys Ala Asp Pro Asp Phe Ala Cys Gly Trp Cys
260 265 270

Gln Gly Pro Gly Gln Cys Thr Leu Arg Gln His Cys Pro Ala Gln Glu
275 280 285

Ser Gln Trp Leu Glu Leu Ser Gly Ala Lys Ser Lys Cys Thr Asn Pro
290 295 300

Arg Ile Thr Glu Ile Ile Pro Val Thr Gly Pro Arg Glu Gly Gly Thr
305 310 315 320

Lys Val Thr Ile Arg Gly Glu Asn Leu Gly Leu Glu Phe Arg Asp Ile
325 330 335

Ala Ser His Val Lys Val Ala Gly Val Glu Cys Ser Pro Leu Val Asp
340 345 350

Gly Tyr Ile Pro Ala Glu Gln Ile Val Cys Glu Met Gly Glu Ala Lys
355 360 365

Pro Ser Gln His Ala Gly Phe Val Glu Ile Cys Val Ala Val Cys Arg
370 375 380

2015201738 07 Apr 2015

126/223

342-10PCT.txt

Pro Glu Phe Met Ala Arg Ser Ser Gln Leu Tyr Tyr Phe Met Thr Leu
385 390 395 400

Thr Leu Ser Asp Leu Lys Pro Ser Arg Gly Pro Met Ser Gly Gly Thr
405 410 415

Gln Val Thr Ile Thr Gly Thr Asn Leu Asn Ala Gly Ser Asn Val Val
420 425 430

Val Met Phe Gly Lys Gln Pro Cys Leu Phe His Arg Arg Ser Pro Ser
435 440 445

Tyr Ile Val Cys Asn Thr Thr Ser Ser Asp Glu Val Leu Glu Met Lys
450 455 460

Val Ser Val Gln Val Asp Arg Ala Lys Ile His Gln Asp Leu Val Phe
465 470 475 480

Gln Tyr Val Glu Asp Pro Thr Ile Val Arg Ile Glu Pro Glu Trp Ser
485 490 495

Ile Val Ser Gly Asn Thr Pro Ile Ala Val Trp Gly Thr His Leu Asp
500 505 510

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

Ile Asn Ile Cys Glu Val Leu Asn Ala Thr Glu Met Thr Cys Gln Ala
530 535 540

Pro Ala Leu Ala Leu Gly Pro Asp His Gln Ser Asp Leu Thr Glu Arg
545 550 555 560

Pro Glu Glu Phe Gly Phe Ile Leu Asp Asn Val Gln Ser Leu Leu Ile
565 570 575

Leu Asn Lys Thr Asn Phe Thr Tyr Tyr Pro Asn Pro Val Phe Glu Ala
580 585 590

Phe Gly Pro Ser Gly Ile Leu Glu Leu Lys Pro Gly Thr Pro Ile Ile
595 600 605

Leu Lys Gly Lys Asn Leu Ile Pro Pro Val Ala Gly Gly Asn Val Lys
610 615 620

Leu Asn Tyr Thr Val Leu Val Gly Glu Lys Pro Cys Thr Val Thr Val
625 630 635 640

Ser Asp Val Gln Leu Leu Cys Glu Ser Pro Asn Leu Ile Gly Arg His
645 650 655

127/223

342-10PCT.txt

Lys Val Met Ala Arg Val Gly Gly Met Glu Tyr Ser Pro Gly Met Val
660 665 670

Tyr Ile Ala Pro Asp Ser Pro Leu Ser Leu Pro Ala Ile Val Ser Ile
675 680 685

Ala Val Ala Gly Gly Leu Leu Ile Ile Phe Ile Val Ala Val Leu Ile
690 695 700

Ala Tyr Lys Arg Lys Ser Arg Glu Ser Asp Leu Thr Leu Lys Arg Leu
705 710 715 720

Gln Met Gln Met Asp Asn Leu Glu Ser Arg Val Ala Leu Glu Cys Lys
725 730 735

Glu Gly Thr Glu Trp Pro His Ala Gly Gly His Val Cys Val Arg Val
740 745 750

Cys Ile Cys Val Cys Met His Ile Cys Val Cys Val Cys Ile Cys Phe
755 760 765

Ile Tyr Lys Gln Ala Gly Trp Ala Ala Val Gly Ser Ala Gly Gly Trp
770 775 780

Arg Cys Val Cys Leu Cys Glu Cys Val Cys Val His Val Cys Val Cys
785 790 795 800

Thr Ser Val Cys Ile Tyr Val Ser Tyr Thr Ser Lys Gln Ala Gly Gln
805 810 815

Gln

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<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 167
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21

<210> 168
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 168
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21

2015201738 07 Apr 2015

128/223

342-10PCT.txt

<210> 169
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<213> Homo sapiens

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2015201738 07 Apr 2015

129/223

342-10PCT.txt

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 <212> PRT
 <213> Homo sapiens

<400> 170

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Phe Thr Arg Phe Asp Asn Pro Ala Ala Val Ser Pro Thr Pro Thr Arg
 35 40 45

Gln Leu Thr Phe Asn Tyr Leu Leu Pro Val Asn Ala Trp Leu Leu Leu
 50 55 60

Asn Pro Ser Glu Leu Cys Cys Asp Trp Thr Met Gly Thr Ile Pro Leu
 65 70 75 80

Ile Glu Ser Leu Leu Asp Ile Arg Asn Leu Ala Thr Phe Thr Phe Phe
 85 90 95

Cys Phe Leu Gly Met Leu Gly Val Phe Ser Ile Arg Tyr Ser Gly Asp
 100 105 110

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

Lys Phe Glu Lys Ser Ser Glu Asp Ser Lys Gln Ser Arg Arg Val Glu
 130 135 140

2015201738 07 Apr 2015

130/223

342-10PCT.txt

Gly Thr Phe Gln Arg Asn Leu Glu Ile Pro Asn Ser Leu Lys Asp Lys
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Phe Glu Leu Gly Ala His Ala Phe Met Thr Val Leu Ile Cys Ser Ala
165 170 175

Leu Gly Leu Ser Leu Ala Val Arg Cys His Ser Val Gly Phe Val Val
180 185 190

Ala Glu Arg Val Leu Tyr Val Pro Ser Met Gly Phe Cys Ile Leu Val
195 200 205

Ala His Gly Trp Gln Lys Ile Ser Thr Lys Ser Val Phe Lys Lys Leu
210 215 220

Ser Trp Ile Cys Leu Ser Met Val Ile Leu Thr His Ser Leu Lys Thr
225 230 235 240

Phe His Arg Asn Trp Asp Trp Glu Ser Glu Tyr Thr Leu Phe Met Ser
245 250 255

Ala Leu Lys Val Asn Lys Asn Asn Ala Lys Leu Trp Asn Asn Val Gly
260 265 270

His Ala Leu Glu Asn Glu Lys Asn Phe Glu Arg Ala Leu Lys Tyr Phe
275 280 285

Leu Gln Ala Thr His Val Gln Pro Asp Asp Ile Gly Ala His Met Asn
290 295 300

Val Gly Arg Thr Tyr Lys Asn Leu Asn Arg Thr Lys Glu Ala Glu Glu
305 310 315 320

Ser Tyr Met Met Ala Lys Ser Leu Met Pro Gln Ile Ile Pro Gly Lys
325 330 335

Lys Tyr Ala Ala Arg Ile Ala Pro Asn His Leu Asn Val Tyr Ile Asn
340 345 350

Leu Ala Asn Leu Ile Arg Ala Asn Glu Ser Arg Leu Glu Glu Ala Asp
355 360 365

Gln Leu Tyr Arg Gln Ala Ile Ser Met Arg Pro Asp Phe Lys Gln Ala
370 375 380

Tyr Ile Ser Arg Gly Glu Leu Leu Leu Lys Met Asn Lys Pro Leu Lys
385 390 395 400

Ala Lys Glu Ala Tyr Leu Lys Ala Leu Glu Leu Asp Arg Asn Asn Ala
405 410 415

2015201738 07 Apr 2015

131/223

342-10PCT.txt

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

132/223

342-10PCT.txt

Ser Asn Lys Gln Leu Gly Lys Asn Gly Asp Glu Glu Thr Pro His Lys
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Thr Thr Lys Asp Ile Lys Glu Ile Glu Lys Lys Arg Val Ala Ala Leu
705 710 715 720

Lys Arg Leu Glu Glu Ile Glu Arg Ile Leu Asn Gly Glu
725 730

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<210> 172
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<220>
<223> Oligonucleotide

<400> 172
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<210> 173
<211> 3296
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<213> Homo sapiens

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2015201738 07 Apr 2015

133/223

342-10PCT.txt

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2015201738 07 Apr 2015

134/223

342-10PCT.txt

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<212> PRT
<213> Homo sapiens

<400> 174

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Val Asp Arg Ala Glu Val Pro Pro Leu Phe Trp Lys Pro Tyr Ile Tyr
35 40 45

Ala Gly Tyr Arg Pro Leu His Gln Thr Trp Arg Phe Tyr Phe Arg Thr
50 55 60

Leu Phe Gln Gln His Asn Glu Ala Val Asn Val Trp Thr His Leu Leu
65 70 75 80

Ala Ala Leu Val Leu Leu Leu Arg Leu Ala Leu Phe Val Glu Thr Val
85 90 95

Asp Phe Trp Gly Asp Pro His Ala Leu Pro Leu Phe Ile Ile Val Leu
100 105 110

Ala Ser Phe Thr Tyr Leu Ser Phe Ser Ala Leu Ala His Leu Leu Gln
115 120 125

Ala Lys Ser Glu Phe Trp His Tyr Ser Phe Phe Phe Leu Asp Tyr Val
130 135 140

Gly Val Ala Val Tyr Gln Phe Gly Ser Ala Leu Ala His Phe Tyr Tyr
145 150 155 160

Ala Ile Glu Pro Ala Trp His Ala Gln Val Gln Ala Val Phe Leu Pro
165 170 175

2015201738 07 Apr 2015

135/223
342-10PCT.txt

Met Ala Ala Phe Leu Ala Trp Leu Ser Cys Ile Gly Ser Cys Tyr Asn
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Lys Tyr Ile Gln Lys Pro Gly Leu Leu Gly Arg Thr Cys Gln Glu Val
195 200 205

Pro Ser Val Leu Ala Tyr Ala Leu Asp Ile Ser Pro Val Val His Arg
210 215 220

Ile Phe Val Ser Ser Asp Pro Thr Thr Asp Asp Pro Ala Leu Leu Tyr
225 230 235 240

His Lys Cys Gln Val Val Phe Phe Leu Leu Ala Ala Ala Phe Phe Ser
245 250 255

Thr Phe Met Pro Glu Arg Trp Phe Pro Gly Ser Cys His Val Phe Gly
260 265 270

Gln Gly His Gln Leu Phe His Ile Phe Leu Val Leu Cys Thr Leu Ala
275 280 285

Gln Leu Glu Ala Val Ala Leu Asp Tyr Glu Ala Arg Arg Pro Ile Tyr
290 295 300

Glu Pro Leu His Thr His Trp Pro His Asn Phe Ser Gly Leu Phe Leu
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2015201738 07 Apr 2015

137/223

342-10PCT.txt

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Arg Asp Ser Trp Phe Arg Gly Leu Ile Leu Leu Leu Thr Phe Leu Ile
 20 25 30

Tyr Ala Cys Tyr His Met Ser Arg Lys Pro Ile Ser Ile Val Lys Ser
 35 40 45

Arg Leu His Gln Asn Cys Ser Glu Gln Ile Lys Pro Ile Asn Asp Thr
 50 55 60

His Ser Leu Asn Asp Thr Met Trp Cys Ser Trp Ala Pro Phe Asp Lys
 65 70 75 80

Asp Asn Tyr Lys Glu Leu Leu Gly Gly Val Asp Asn Ala Phe Leu Ile
 85 90 95

Ala Tyr Ala Ile Gly Met Phe Ile Ser Gly Val Phe Gly Glu Arg Leu
 100 105 110

Pro Leu Arg Tyr Tyr Leu Ser Ala Gly Met Leu Leu Ser Gly Leu Phe
 115 120 125

Thr Ser Leu Phe Gly Leu Gly Tyr Phe Trp Asn Ile His Glu Leu Trp
 130 135 140

Tyr Phe Val Val Ile Gln Val Cys Asn Gly Leu Val Gln Thr Thr Gly
 145 150 155 160

Trp Pro Ser Val Val Thr Cys Val Gly Asn Trp Phe Gly Lys Gly Lys
 165 170 175

Arg Gly Phe Ile Met Gly Ile Trp Asn Ser His Thr Ser Val Gly Asn
 180 185 190

Ile Leu Gly Ser Leu Ile Ala Gly Ile Trp Val Asn Gly Gln Trp Gly
 195 200 205

2015201738 07 Apr 2015

138/223

342-10PCT.txt

Leu Ser Phe Ile Val Pro Gly Ile Ile Thr Ala Val Met Gly Val Ile
210 215 220

Thr Phe Leu Phe Leu Ile Glu His Pro Glu Asp Val Asp Cys Ala Pro
225 230 235 240

Pro Gln His His Gly Glu Pro Ala Glu Asn Gln Asp Asn Pro Glu Asp
245 250 255

Pro Gly Asn Ser Pro Cys Ser Ile Arg Glu Ser Gly Leu Glu Thr Val
260 265 270

Ala Lys Cys Ser Lys Gly Pro Cys Glu Glu Pro Ala Ala Ile Ser Phe
275 280 285

Phe Gly Ala Leu Arg Ile Pro Gly Val Val Glu Phe Ser Leu Cys Leu
290 295 300

Leu Phe Ala Lys Leu Val Ser Tyr Thr Phe Leu Tyr Trp Leu Pro Leu
305 310 315 320

Tyr Ile Ala Asn Val Ala His Phe Ser Ala Lys Glu Ala Gly Asp Leu
325 330 335

Ser Thr Leu Phe Asp Val Gly Gly Ile Ile Gly Gly Ile Val Ala Gly
340 345 350

Leu Val Ser Asp Tyr Thr Asn Gly Arg Ala Thr Thr Cys Cys Val Met
355 360 365

Leu Ile Leu Ala Ala Pro Met Met Phe Leu Tyr Asn Tyr Ile Gly Gln
370 375 380

Asp Gly Ile Ala Ser Ser Ile Val Met Leu Ile Ile Cys Gly Gly Leu
385 390 395 400

Val Asn Gly Pro Tyr Ala Leu Ile Thr Thr Ala Val Ser Ala Asp Leu
405 410 415

Gly Thr His Lys Ser Leu Lys Gly Asn Ala Lys Ala Leu Ser Thr Val
420 425 430

Thr Ala Ile Ile Asp Gly Thr Gly Ser Ile Gly Ala Ala Leu Gly Pro
435 440 445

Leu Leu Ala Gly Leu Ile Ser Pro Thr Gly Trp Asn Asn Val Phe Tyr
450 455 460

Met Leu Ile Ser Ala Asp Val Leu Ala Cys Leu Leu Leu Cys Arg Leu
465 470 475 480

2015201738 07 Apr 2015

139/223

342-10PCT.txt

Val Tyr Lys Glu Ile Leu Ala Trp Lys Val Ser Leu Ser Arg Gly Ser
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Gly Tyr Lys Glu Ile
500

<210> 177
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<212> DNA
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21

<210> 178
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21

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cttcttggca caggtaggaa aggatgatat tacaagggtc aaaatggggg taaacagaag 180
aggctgctcc tgcagaaggc ttcctgcaga agcccttgca cttggagggc tgggaagacc 240
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ggagataaat accagagaca tagaagggtg aagaatttgc ctctaggaag caggaattta 780
aatttgggga agacaggggtg gagcaagggg tataaatcta gtccattttt cttttctttt 840

2015201738 07 Apr 2015

140/223

342-10PCT.txt

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342-10PCT.txt

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2015201738 07 Apr 2015

142/223
342-10PCT.txt

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<211> 95
<212> PRT
<213> Homo sapiens

<400> 180

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20 25 30

Ala Ile Phe Cys Ser Ser Leu Leu Asp Ser Val Pro Gln Lys Val Glu
35 40 45

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

Gln Trp Val Thr Pro Ser Val Asp Trp Arg Met Glu Lys Glu Lys Arg
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<210> 182
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<400> 182
atgtggcctt caaag 15

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gccctctga ggtgtgactc cactcctcct gaggggtgctg taggagacat ctgcaaaaaa 180

143/223

342-10PCT.txt

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gtcccattag tacagggtatc tccgaatgct ccaactcttcc attacattga gtcaattgct 420
catgaccttg ggcctccaat tggggctatt ttcctgctat ccatctcctg gtctatagta 480
aaagagccaa tgagcagata a 501

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<211> 166
<212> PRT
<213> Homo sapiens
<400> 184

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20          25          30

```

```

Ile Asp Val Arg Val Val Gln Ala Ala Pro Leu Arg Cys Asp Ser Thr
35          40          45

```

```

Pro Pro Glu Gly Ala Val Gly Asp Ile Cys Lys Lys Glu Asp Ala Gly
50          55          60

```

```

Asn Met Pro Ser Thr Ser Glu Gly Ser Ile Tyr Pro Glu Met Ala His
65          70          75          80

```

```

Phe Leu Arg Asn Lys Leu Ala Gly Ser Ser Val Arg Lys Pro Asp Ser
85          90          95

```

```

Gly Phe Leu Trp Glu Gly Ala Leu Arg Ala Trp Leu Phe Leu Ile Leu
100          105          110

```

```

Ile Val Leu Thr His Ile Met Trp Val Pro Leu Val Gln Val Ser Pro
115          120          125

```

```

Asn Ala Pro Leu Phe His Tyr Ile Glu Ser Ile Ala His Asp Leu Gly
130          135          140

```

```

Pro Pro Ile Gly Ala Ile Phe Leu Leu Ser Ile Ser Trp Ser Ile Val
145          150          155          160

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Lys Glu Pro Met Ser Arg
165

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<210> 185
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342-10PCT.txt

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2015201738 07 Apr 2015

146/223

342-10PCT.txt

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catatatact ttttgcaaaa tttccttgat ttaaaatatt tgttatttta aatatacaaa 3840
acattttaga aaatcttaga gtaaatttta gtcttaaagc cagaaaataa gtttatagcc 3900
atctagatat tttgcatatt gctcttacag caataatggg ttgggttact ttatgaaaaa 3960
taaaatgtat taaaatat 3978

<210> 188
<211> 1129
<212> PRT
<213> Homo sapiens
<400> 188

Met Ala Gly Ile Phe Lys Glu Phe Phe Phe Ser Thr Glu Asp Leu Pro
1 5 10 15

Glu Val Ile Leu Thr Leu Ser Leu Ile Ser Ser Ile Gly Ala Phe Leu
20 25 30

Asn Arg His Leu Glu Asp Phe Pro Ile Pro Val Pro Val Ile Leu Phe
35 40 45

Leu Leu Gly Cys Ser Phe Glu Val Leu Ser Phe Thr Ser Ser Gln Val
50 55 60

Gln Arg Tyr Ala Asn Ala Ile Gln Trp Met Ser Pro Asp Leu Phe Phe
65 70 75 80

Arg Ile Phe Thr Pro Val Val Phe Phe Thr Thr Ala Phe Asp Met Asp
85 90 95

Thr Tyr Met Leu Gln Lys Leu Phe Trp Gln Ile Leu Leu Ile Ser Ile
100 105 110

Pro Gly Phe Leu Val Asn Tyr Ile Leu Val Leu Trp His Leu Ala Ser
115 120 125

Val Asn Gln Leu Leu Leu Lys Pro Thr Gln Trp Leu Leu Phe Ser Ala
130 135 140

2015201738 07 Apr 2015

147/223

342-10PCT.txt

Ile Leu Val Ser Ser Asp Pro Met Leu Thr Ala Ala Ala Ile Arg Asp
145 150 155 160

Leu Gly Leu Ser Arg Ser Leu Ile Ser Leu Ile Asn Gly Glu Ser Leu
165 170 175

Met Thr Ser Val Ile Ser Leu Ile Thr Phe Thr Ser Ile Met Asp Phe
180 185 190

Asp Gln Arg Leu Gln Ser Lys Arg Asn His Thr Leu Ala Glu Glu Ile
195 200 205

Val Gly Gly Ile Cys Ser Tyr Ile Ile Ala Ser Phe Leu Phe Gly Ile
210 215 220

Leu Ser Ser Lys Leu Ile Gln Phe Trp Met Ser Thr Val Phe Gly Asp
225 230 235 240

Asp Val Asn His Ile Ser Leu Ile Phe Ser Ile Leu Tyr Leu Ile Phe
245 250 255

Tyr Ile Cys Glu Leu Val Gly Met Ser Gly Ile Phe Thr Leu Ala Ile
260 265 270

Val Gly Leu Leu Leu Asn Ser Thr Ser Phe Lys Ala Ala Ile Glu Glu
275 280 285

Thr Leu Leu Leu Glu Phe Leu Thr Leu Leu Leu Ile Ser Pro Val Leu
290 295 300

Ser Arg Val Gly His Glu Phe Ser Trp Arg Trp Ile Phe Ile Met Val
305 310 315 320

Cys Ser Glu Met Lys Gly Met Pro Asn Ile Asn Met Ala Leu Leu Leu
325 330 335

Ala Tyr Ser Asp Leu Tyr Phe Gly Ser Asp Lys Glu Lys Ser Gln Ile
340 345 350

Leu Phe His Gly Val Leu Val Cys Leu Ile Thr Leu Val Val Asn Arg
355 360 365

Phe Ile Leu Pro Val Ala Val Thr Ile Leu Gly Leu Arg Asp Ala Thr
370 375 380

Ser Thr Lys Tyr Lys Ser Val Cys Cys Thr Phe Gln His Phe Gln Glu
385 390 395 400

Leu Thr Lys Ser Ala Ala Ser Ala Leu Lys Phe Asp Lys Asp Leu Ala
405 410 415

2015201738 07 Apr 2015

148/223

342-10PCT.txt

Asn Ala Asp Trp Asn Met Ile Glu Lys Ala Ile Thr Leu Glu Asn Pro
420 425 430

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

Pro His Cys Asn Lys Glu Ile Asp Glu Ile Phe Asn Thr Glu Ala Met
450 455 460

Glu Leu Ala Asn Arg Arg Leu Leu Ser Ala Gln Ile Ala Ser Tyr Gln
465 470 475 480

Arg Gln Tyr Arg Asn Glu Ile Leu Ser Gln Ser Ala Val Gln Val Leu
485 490 495

Val Gly Ala Ala Glu Ser Phe Gly Glu Lys Lys Gly Lys Cys Met Ser
500 505 510

Leu Asp Thr Ile Lys Asn Tyr Ser Glu Ser Gln Lys Thr Val Thr Phe
515 520 525

Ala Arg Lys Leu Leu Leu Asn Trp Val Tyr Asn Thr Arg Lys Glu Lys
530 535 540

Glu Gly Pro Ser Lys Tyr Phe Phe Phe Arg Ile Cys His Thr Ile Val
545 550 555 560

Phe Thr Glu Glu Phe Glu His Val Gly Tyr Leu Val Ile Leu Met Asn
565 570 575

Ile Phe Pro Phe Ile Ile Ser Trp Ile Ser Gln Leu Asn Val Ile Tyr
580 585 590

His Ser Glu Leu Lys His Thr Asn Tyr Cys Phe Leu Thr Leu Tyr Ile
595 600 605

Leu Glu Ala Leu Leu Lys Ile Ala Ala Met Arg Lys Asp Phe Phe Ser
610 615 620

His Ala Trp Asn Ile Phe Glu Leu Ala Ile Thr Leu Ile Gly Ile Leu
625 630 635 640

His Val Ile Leu Ile Glu Ile Asp Thr Ile Lys Tyr Ile Phe Asn Glu
645 650 655

Thr Glu Val Ile Val Phe Ile Lys Val Val Gln Phe Phe Arg Ile Leu
660 665 670

Arg Ile Phe Lys Leu Ile Ala Pro Lys Leu Leu Gln Ile Ile Asp Lys
675 680 685

2015201738 07 Apr 2015

149/223

342-10PCT.txt

Arg Met Ser His Gln Lys Thr Phe Trp Tyr Gly Ile Leu Lys Gly Tyr
690 695 700

Val Gln Gly Glu Ala Asp Ile Met Thr Ile Ile Asp Gln Ile Thr Ser
705 710 715 720

Ser Lys Gln Ile Lys Gln Met Leu Leu Lys Gln Val Ile Arg Asn Met
725 730 735

Glu His Ala Ile Lys Glu Leu Gly Tyr Leu Glu Tyr Asp His Pro Glu
740 745 750

Ile Ala Val Thr Val Lys Thr Lys Glu Glu Ile Asn Val Met Leu Asn
755 760 765

Met Ala Thr Glu Ile Leu Lys Ala Phe Gly Leu Lys Gly Ile Ile Ser
770 775 780

Lys Thr Glu Gly Ala Gly Ile Asn Lys Leu Ile Met Ala Lys Lys Lys
785 790 795 800

Glu Val Leu Asp Ser Gln Ser Ile Ile Arg Pro Leu Thr Val Glu Glu
805 810 815

Val Leu Tyr His Ile Pro Trp Leu Asp Lys Asn Lys Asp Tyr Ile Asn
820 825 830

Phe Ile Gln Glu Lys Ala Lys Val Val Thr Phe Asp Cys Gly Asn Asp
835 840 845

Ile Phe Glu Glu Gly Asp Glu Pro Lys Gly Ile Tyr Ile Ile Ile Ser
850 855 860

Gly Met Val Lys Leu Glu Lys Ser Lys Pro Gly Leu Gly Ile Asp Gln
865 870 875 880

Met Val Glu Ser Lys Glu Lys Asp Phe Pro Ile Ile Asp Thr Asp Tyr
885 890 895

Met Leu Ser Gly Glu Ile Ile Gly Glu Ile Asn Cys Leu Thr Asn Glu
900 905 910

Pro Met Lys Tyr Ser Ala Thr Cys Lys Thr Val Val Glu Thr Cys Phe
915 920 925

Ile Pro Lys Thr His Leu Tyr Asp Ala Phe Glu Gln Cys Ser Pro Leu
930 935 940

Ile Lys Gln Lys Met Trp Leu Lys Leu Gly Leu Ala Ile Thr Ala Arg
945 950 955 960

150/223

342-10PCT.txt

Lys Ile Arg Glu His Leu Ser Tyr Glu Asp Trp Asn Tyr Asn Met Gln
965 970 975

Leu Lys Leu Ser Asn Ile Tyr Val Val Asp Ile Pro Met Ser Thr Lys
980 985 990

Thr Asp Ile Tyr Asp Glu Asn Leu Ile Tyr Val Ile Leu Ile His Gly
995 1000 1005

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

Leu Ile Pro Ile Thr Cys His Gln Ile Gln Ser Ile Glu Asp Phe
1025 1030 1035

Thr Lys Val Val Ile Ile Gln Thr Pro Ile Asn Met Lys Thr Phe
1040 1045 1050

Arg Arg Asn Ile Arg Lys Phe Val Pro Lys His Lys Ser Tyr Leu
1055 1060 1065

Thr Pro Gly Leu Ile Gly Ser Val Gly Thr Leu Glu Glu Gly Ile
1070 1075 1080

Gln Glu Glu Arg Asn Val Lys Glu Asp Gly Ala His Ser Ala Ala
1085 1090 1095

Thr Ala Arg Ser Pro Gln Pro Cys Ser Leu Leu Gly Thr Lys Phe
1100 1105 1110

Asn Cys Lys Glu Ser Pro Arg Ile Asn Leu Arg Lys Val Arg Lys
1115 1120 1125

Glu

<210> 189
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 189
tttgaaccgg cacttgg

17

<210> 190
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

2015201738 07 Apr 2015

151/223

342-10PCT.txt

<400> 190
tcaaattgcag tagtaaagaa aac

23

<210> 191
<211> 2898
<212> DNA
<213> Homo sapiens

<400> 191
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ccgtctgtgg tgcgtgaccg cgtgtgtgtt gtgggggcgg ggaaaattca taaaaagaa 120
aaaaatatag cacatctctt ggaaatgaaa tacttcaagt ttaatatctc tcttgctaata 180
gcagaattta tcagccaaga cagctggctg gcctgggtgg ggtttgtaa agttgtcaag 240
tataaggcct actgtaagag ataccaagtg acttttagaa gacagtgtga gggtaaaact 300
gattactatg cttggaaaca cttagtggta caggataaaa ataagtctaa cacacacaaa 360
tacagaatga ttatttgtgt gataaataca gataccattt gtgagatggc ttatgcccat 420
atagaatggg acatgatagt ctgtgcagct tatgcacacg aacttccaaa atacgggtgta 480
aaggttggcc tgacaaatga tgctgcagca tgtgtactg gcctgctgct ggcattgcagg 540
cttctcagta gggttgcat ggacaagatc tataaaggcc aagtggaggt aaccagagat 600
gaatacaacg tgggaagcac tgatggtcag ccagggtgct ttacctgctg tttggatgca 660
ggccttgcca gaaccaccac tgacaataaa gtttttgggg ctctgagagt gctgtggatg 720
gaggtttctc tatccctcac agtgcctaac gattccctga gtaaaggga gacctggccc 780
aggaaggagc agtgcctgc aagagggagc ctgagccgtg gaggctggg agcctttgag 840
gtgggcagcc agggcgtgga ggcagcagca agcccaaacg gtcaatacgg gccagctgg 900
ggcctggcgg cggagggcac ggaggggagct agggcacagg caccaaagcg ggatttgtcc 960
tatagcagga ctgactctca cagagactgt tctcctgtct gtcacaacat gtccctgagg 1020
ggtcaccttg tcccaagaa gccctcaaag gagaagcagg gacagcagaa actggacagc 1080
aagttttatg agagctgggc cacagccttg ctacagcta tattcccggt gcttggcatc 1140
ttggtgcttg ttgaatcttt gctgatgaat gacccaatgc gtgaatgcat cctcagcacc 1200
tctggcttct cagggcctcg cgccaggctc ctgggggtcc tggccctggg cgggcttctc 1260
ctccatcttg gtgcacctgt tattgtaatg gcgtggattg tccttgcttt gctattcaca 1320
cggagcagga ccagggtga tcctgcagac gtgctgcccc ctggtgcatt tgagaagact 1380
cgcattcatg cactgcccc gcctcttggg ttgactttag atgacgggtga agtgatcacc 1440
acaagattgc tcaatgatgc ttctgtgcaa aaagtcgtgg tccggatatc tgaatcctcc 1500
tcctgcctcc acaatgggct gctatccggg aacggctgtg aggtccatta ccgcaggggc 1560
aggctcttcc aggacgtca gatgcctgct cagagcccag cttatcgggg ggatctgcga 1620
gctcctgtca acgcccagc aattcagaac cggagtcagc tcagcccagg tggaaagatc 1680
aagtggcggc agcacaggca gctggaaggc acccacagaa agaaatcgag cactatgttc 1740

2015201738 07 Apr 2015

152/223

342-10PCT.txt

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agaaagatcc actccatctt taactccagc ccacagagaa agacggcggc cgagagcccc 1800
ttctacgaag gagccagccc cgcagtgaag ctgattcgaa gcagttccat gtatgtggtc 1860
ggggaccacg gggagaaatt cagcgagtcc ttaaagaagt acaaaagcac cagtagcatg 1920
gacaccagcc tgtactacct gcggcaggag gaggaccggg cgtggatgta ttcgcgcacc 1980
caggactgcc tgcagtacct gcaggagctg ctggccttgc gcaaaaaata tctcagcagc 2040
ttcagtgatc tgaagcccca ccgcaccagc gggatttcct caacctctc caaatcctcc 2100
aagggagggg aaaagactcc tgtccggtct actcccaaag aaataaagaa agcaacccca 2160
aagaaatact cgcagttcag tgctgatgtg gccgaggcca ttgccttctt tgactccatc 2220
attgcagagc tggatacaga gagacgaccc cgggctgctg aggccagcct gccaaatgaa 2280
gatgtggact ttgacgtggc caccagctcc agggagcaca gcttgcattc taactggatc 2340
ctgcgggcac cgcgcagaca ctccgaggat atcgctgccc aactgtgca tactgtagac 2400
ggccagtttc gaaggagcac cgagcacagg accgtgggca ctcagaggag actcgagagg 2460
caccctattt atttgccaa ggctgtggaa ggggccttca acacctggaa atttaagccc 2520
aaagcctgca aaaaagacct ggggagctcc agacagatcc ttttcaactt ctcaggagaa 2580
gatatggagt gggatgcaga gctctttgcg ttggagcccc agttgtctcc tggggaggac 2640
tactatgaga cagagaaccc caaaggacag tggctgcttc gagaaagact ttgggagcgg 2700
acgactgggt ccctgagaag ctgtccgctt tcagcgcagc atgaggtatt tggtagagtt 2760
gaaaatgcca attgtaacac agtcaacca ctcagcacac tgcctgctgg tgccgtgcca 2820
gtgccaaaca gacctgtggc ttccagggg acaggtctca ggacactctc agagcttgag 2880
tttctctgcg tgggctga 2898

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<210> 192
 <211> 965
 <212> PRT
 <213> Homo sapiens

<400> 192

Met Trp Val Arg Cys Ala Leu Leu Val Ala Arg Asp Cys Gly Cys Ala
 1 5 10 15

Glu Arg Val Cys Pro Ser Val Val Arg Asp Arg Val Cys Val Val Gly
 20 25 30

Ala Gly Lys Ile His Thr Lys Glu Lys Asn Ile Ala His Leu Leu Glu
 35 40 45

Met Lys Tyr Phe Lys Phe Asn Ile Ser Leu Ala Asn Ala Glu Phe Ile
 50 55 60

Ser Gln Asp Ser Trp Leu Ala Trp Val Gly Phe Val Lys Val Val Lys
 65 70 75 80

2015201738 07 Apr 2015

153/223

342-10PCT.txt

Tyr Lys Ala Tyr Cys₈₅ Lys Arg Tyr Gln Val₉₀ Thr Phe Arg Arg Gln Cys₉₅
Glu Gly Lys Thr₁₀₀ Asp Tyr Tyr Ala Trp₁₀₅ Lys His Leu Val₁₁₀ Val Gln Asp
Lys Asn Lys₁₁₅ Ser Asn Thr His Lys₁₂₀ Tyr Arg Met Ile Ile₁₂₅ Cys Val Ile
Asn Thr₁₃₀ Asp Thr Ile Cys Glu₁₃₅ Met Ala Tyr Ala His₁₄₀ Ile Glu Trp Asp
Met Ile Val Cys Ala Ala Tyr Ala His Glu Leu₁₅₅ Pro Lys Tyr Gly Val₁₆₀
Lys Val Gly Leu Thr₁₆₅ Asn Asp Ala Ala Ala Cys Cys Thr Gly Leu₁₇₅ Leu
Leu Ala Cys Arg₁₈₀ Leu Leu Ser Arg Phe₁₈₅ Gly Met Asp Lys Ile₁₉₀ Tyr Lys
Gly Gln Val₁₉₅ Glu Val Thr Arg Asp₂₀₀ Glu Tyr Asn Val Gly₂₀₅ Ser Thr Asp
Gly Gln Pro Gly Ala Phe Thr₂₁₅ Cys Cys Leu Asp Ala Gly Leu Ala Arg
Thr Thr Thr Asp Asn Lys₂₃₀ Val Phe Gly Ala Leu₂₃₅ Arg Val Leu Trp Met₂₄₀
Glu Val Ser Leu Ser₂₄₅ Leu Thr Val Pro Asn₂₅₀ Asp Ser Leu Ser Lys₂₅₅ Gly
Lys Pro Gly Pro Arg Lys Glu Gln Leu₂₆₅ Pro Ala Arg Gly Ser Leu Ser
Arg Gly Val₂₇₅ Leu Gly Ala Phe Glu₂₈₀ Val Gly Ser Gln Gly₂₈₅ Val Glu Ala
Ala Ala Ser Pro Asn Gly Gln Tyr Gly Pro Ser Trp Gly Leu Ala Ala
Glu Gly Thr Glu Gly Ala Arg Pro Gln Ala Pro₃₁₅ Lys Arg Asp Leu Ser₃₂₀
Tyr Ser Arg Thr Asp₃₂₅ Ser His Arg Asp Cys₃₃₀ Ser Pro Val Cys His₃₃₅ Asn
Met Ser Leu Arg Gly His Leu Val Pro₃₄₅ Lys Lys Pro Ser Lys₃₅₀ Glu Lys

2015201738 07 Apr 2015

154/223

342-10PCT.txt

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

2015201738 07 Apr 2015

155/223

342-10PCT.txt

Glu Lys Phe Ser Glu Ser Leu Lys Lys Tyr Lys Ser Thr Ser Ser Met
625 630 635 640

Asp Thr Ser Leu Tyr Tyr Leu Arg Gln Glu Glu Asp Arg Ala Trp Met
645 650 655

Tyr Ser Arg Thr Gln Asp Cys Leu Gln Tyr Leu Gln Glu Leu Leu Ala
660 665 670

Leu Arg Lys Lys Tyr Leu Ser Ser Phe Ser Asp Leu Lys Pro His Arg
675 680 685

Thr Gln Gly Ile Ser Ser Thr Ser Ser Lys Ser Ser Lys Gly Gly Lys
690 695 700

Lys Thr Pro Val Arg Ser Thr Pro Lys Glu Ile Lys Lys Ala Thr Pro
705 710 715 720

Lys Lys Tyr Ser Gln Phe Ser Ala Asp Val Ala Glu Ala Ile Ala Phe
725 730 735

Phe Asp Ser Ile Ile Ala Glu Leu Asp Thr Glu Arg Arg Pro Arg Ala
740 745 750

Ala Glu Ala Ser Leu Pro Asn Glu Asp Val Asp Phe Asp Val Ala Thr
755 760 765

Ser Ser Arg Glu His Ser Leu His Ser Asn Trp Ile Leu Arg Ala Pro
770 775 780

Arg Arg His Ser Glu Asp Ile Ala Ala His Thr Val His Thr Val Asp
785 790 795 800

Gly Gln Phe Arg Arg Ser Thr Glu His Arg Thr Val Gly Thr Gln Arg
805 810 815

Arg Leu Glu Arg His Pro Ile Tyr Leu Pro Lys Ala Val Glu Gly Ala
820 825 830

Phe Asn Thr Trp Lys Phe Lys Pro Lys Ala Cys Lys Lys Asp Leu Gly
835 840 845

Ser Ser Arg Gln Ile Leu Phe Asn Phe Ser Gly Glu Asp Met Glu Trp
850 855 860

Asp Ala Glu Leu Phe Ala Leu Glu Pro Gln Leu Ser Pro Gly Glu Asp
865 870 875 880

Tyr Tyr Glu Thr Glu Asn Pro Lys Gly Gln Trp Leu Leu Arg Glu Arg
885 890 895

2015201738 07 Apr 2015

156/223

342-10PCT.txt

Leu Trp Glu Arg Thr Thr Gly Ser Leu Arg Ser Cys Pro Leu Ser Ala
900 905 910

Gln His Glu Val Phe Gly Arg Val Glu Asn Ala Asn Cys Asn Thr Val
915 920 925

Asn Pro Leu Ser Thr Leu Pro Ala Gly Ala Val Pro Val Pro Asn Arg
930 935 940

Pro Val Ala Ser Gln Gly Thr Gly Leu Arg Thr Leu Ser Glu Leu Glu
945 950 955 960

Phe Leu Cys Val Gly
965

<210> 193
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 193
cgagaggcac cccatttatt tg

22

<210> 194
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 194
ttctctgtct catagtagtc ctcccc

26

<210> 195
<211> 1363
<212> DNA
<213> Homo sapiens

<400> 195
aacaggcccc atgctgctct ggacggctgt gctgctcttt ggtaagtcaa cgagcatggg 60
catccccctct tggagcacta aggaccttcc ctgtgttggg aaaactgtct ggctgtacct 120
ccaagcctgg ccaaaccctg tgtttgaagg agatgccctg actctgcat gtcagggatg 180
gaagaataca cactgtctc aggtgaagtt ctacagagat ggaaaattcc ttcatttctc 240
taaggaaaac cagactctgt ccatgggagc agcaacagt cagagccgtg gccagtacag 300
ctgctctggg caggtgatgt atattccaca gacattcaca caaacttcag agactgcat 360
ggttcaagtc caagagctgt ttccacctcc tgtgctgagt gccatcccct ctctgagcc 420
ccgagagggt agcctggtga ccctgagatg tcagacaaag ctgcaccccc tgaggtcagc 480
cttgaggctc cttttctcct tccacaagga cgccacacc ttgcaggaca ggggccctca 540

2015201738 07 Apr 2015

157/223

342-10PCT.txt

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cccagaactc tgcattcccgg gagccaagga gggagactct gggctttact ggtgtgaggt 600
ggcccctgag ggtggccagg tccagaagca gagccccag ctggagggtca gagtgcaggc 660
tcctgtatcc cgtcctgtgc tcactctgca ccacgggcct gctgaccctg ctgtggggga 720
catggtgcag ctctctgtg aggcacagag gggctcccct ccgatcctgt attccttcta 780
ccttgatgag aagattgtgg ggaaccactc agctccctgt ggtggaacca cctccctcct 840
cttcccagtg aagtcagaac aggatgctgg gaactactcc tgcgaggctg agaacagtgt 900
ctccagagag aggagtgagc ccaagaagct gtctctgaag ggttctcaag tcttgttcac 960
tcccgccagc aactggctgg ttccttggct tcctgcgagc ctgcttggcc tgatggttat 1020
tgctgctgca cttctggttt atgtgagatc ctggagaaaa gctgggcccc ttccatccca 1080
gataccaccc acagctccag gtggagagca gtgccacta tatgccaacg tgcattacca 1140
gaaagggaaa gatgaaggtg ttgtctactc tgtggtgcat agaacctcaa agaggagtga 1200
agccagggtc gctgagttca ccgtggggag aaagcacaaa gcttcacca aattccaccc 1260
caccctggat ctccacacca agcggctcag ggtaaatggt cgagttcagg aagcttatgt 1320
ggccttggtc aacacctgct ccttcacccc cagcctgaag tga 1363

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<210> 196
 <211> 450
 <212> PRT
 <213> Homo sapiens
 <400> 196

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

Gly Ile Pro Ser Trp Ser Thr Lys Asp Leu Pro Cys Val Gly Lys Thr
20 25 30

Val Trp Leu Tyr Leu Gln Ala Trp Pro Asn Pro Val Phe Glu Gly Asp
35 40 45

Ala Leu Thr Leu Arg Cys Gln Gly Trp Lys Asn Thr Pro Leu Ser Gln
50 55 60

Val Lys Phe Tyr Arg Asp Gly Lys Phe Leu His Phe Ser Lys Glu Asn
65 70 75 80

Gln Thr Leu Ser Met Gly Ala Ala Thr Val Gln Ser Arg Gly Gln Tyr
85 90 95

Ser Cys Ser Gly Gln Val Met Tyr Ile Pro Gln Thr Phe Thr Gln Thr
100 105 110

Ser Glu Thr Ala Met Val Gln Val Gln Glu Leu Phe Pro Pro Pro Val
115 120 125

2015201738 07 Apr 2015

158/223

342-10PCT.txt

Leu Ser Ala Ile Pro Ser Pro Glu Pro Arg Glu Gly Ser Leu Val Thr
130 135 140

Leu Arg Cys Gln Thr Lys Leu His Pro Leu Arg Ser Ala Leu Arg Leu
145 150 155 160

Leu Phe Ser Phe His Lys Asp Gly His Thr Leu Gln Asp Arg Gly Pro
165 170 175

His Pro Glu Leu Cys Ile Pro Gly Ala Lys Glu Gly Asp Ser Gly Leu
180 185 190

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

Pro Gln Leu Glu Val Arg Val Gln Ala Pro Val Ser Arg Pro Val Leu
210 215 220

Thr Leu His His Gly Pro Ala Asp Pro Ala Val Gly Asp Met Val Gln
225 230 235 240

Leu Leu Cys Glu Ala Gln Arg Gly Ser Pro Pro Ile Leu Tyr Ser Phe
245 250 255

Tyr Leu Asp Glu Lys Ile Val Gly Asn His Ser Ala Pro Cys Gly Gly
260 265 270

Thr Thr Ser Leu Leu Phe Pro Val Lys Ser Glu Gln Asp Ala Gly Asn
275 280 285

Tyr Ser Cys Glu Ala Glu Asn Ser Val Ser Arg Glu Arg Ser Glu Pro
290 295 300

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

Asn Trp Leu Val Pro Trp Leu Pro Ala Ser Leu Leu Gly Leu Met Val
325 330 335

Ile Ala Ala Ala Leu Leu Val Tyr Val Arg Ser Trp Arg Lys Ala Gly
340 345 350

Pro Leu Pro Ser Gln Ile Pro Pro Thr Ala Pro Gly Gly Glu Gln Cys
355 360 365

Pro Leu Tyr Ala Asn Val His His Gln Lys Gly Lys Asp Glu Gly Val
370 375 380

Val Tyr Ser Val Val His Arg Thr Ser Lys Arg Ser Glu Ala Arg Ser
385 390 395 400

2015201738 07 Apr 2015

159/223

342-10PCT.txt

Ala Glu Phe Thr Val Gly Arg Lys His Lys Ala Ser Pro Lys Phe His
405 410 415

Pro Thr Leu Asp Leu His Thr Lys Arg Leu Arg Val Asn Gly Arg Val
420 425 430

Gln Glu Ala Tyr Val Ala Leu Val Asn Thr Cys Ser Leu Thr Pro Ser
435 440 445

Leu Lys
450

<210> 197
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 197
gtcagggatg gaagaatac 19

<210> 198
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 198
acaggagggtg gaaacagc 18

<210> 199
<211> 534
<212> DNA
<213> Homo sapiens

<400> 199
acaattgtgt cttcttcag atgtcatcgc tataaggagt ggggctttca tcacctcctt 60
gacgtaggat gtgtacatgg ctctccaggc cagagttgct ccaagcaagg ttgttttgca 120
gaagtttctt ctatgtgtca ttcttttcta cactgtgtac tatgtgtccc tgagcatggg 180
ctgcgtgatg tttgaggatg atgagttgaa tgcctggcct ccatttgatt tcaaaacaaa 240
tccctcatgg ctcaacataa actataaagt tcttttagtt tcaacagagg tcacctactt 300
tgtttgaggg ttgttttttg ttccagttgt ggaagaatgg gtttgggatt atgctatttc 360
agtcactatt cttcatgttg ccatcacttc aactgttatg ttggaattcc ccttgacatc 420
acattgggtg gctgctttag gtatatcaaa attgcttggt tagattctct aatgcacaga 480
aataatgtta aatagaataa ctgtggaaat atattttatt ttctcataga tttt 534

<210> 200
<211> 128
<212> PRT

2015201738 07 Apr 2015

160/223

342-10PCT.txt

<213> Homo sapiens

<400> 200

Met Ala Leu Gln Val Arg Val Ala Pro Ser Lys Val Val Leu Gln Lys
1 5 10 15

Phe Leu Leu Cys Val Ile Leu Phe Tyr Thr Val Tyr Tyr Val Ser Leu
20 25 30

Ser Met Gly Cys Val Met Phe Glu Val His Glu Leu Asn Val Leu Ala
35 40 45

Pro Phe Asp Phe Lys Thr Asn Pro Ser Trp Leu Asn Ile Asn Tyr Lys
50 55 60

Val Leu Leu Val Ser Thr Glu Val Thr Tyr Phe Val Cys Gly Leu Phe
65 70 75 80

Phe Val Pro Val Val Glu Glu Trp Val Trp Asp Tyr Ala Ile Ser Val
85 90 95

Thr Ile Leu His Val Ala Ile Thr Ser Thr Val Met Leu Glu Phe Pro
100 105 110

Leu Thr Ser His Trp Trp Ala Ala Leu Gly Ile Ser Lys Leu Leu Val
115 120 125

<210> 201

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 201

tcaaacatca cgcagcccat

20

<210> 202

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 202

tggggctttc atcacctcct tg

22

<210> 203

<211> 615

<212> DNA

<213> Homo sapiens

<400> 203

ggggatgtga tgtcaggctt gattgtgggc atattattgg tgccccagtc cattgcttat

60

2015201738 07 Apr 2015

161/223

342-10PCT.txt

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tccctgctgg ctggccaaga acctgtctat ggtctgtaca catctttttt tgccagcatc 120
atattttttc tcttggttac ctcccgtcac atctctgtgg gcatttttgg agtactgtgc 180
cttatgattg gtgagacagt tgaccgagaa ctacagaaaag ctggctatga caatgccccat 240
agtgtccttt ccttaggaat ggtttcaaatt gggagcacat tattaatatca tacatcagac 300
aggatatgtg acaaaagttg ctatgcaatt atggttggca gcactgtaac ctttatagct 360
ggagttttatc agtgattgtt ttgttaatgt ggaagcaaca ttttctatga ttaatctgct 420
gttacctgtt ttgactgagc tactacaaaa agaaaaatca ctgaattgct atgggtttct 480
gaaatatcca aaaaattaac ctgaagcagg gggaaaaatg acatcacacc attagcagg 540
attgtgtgaa acttctaaaa atgaaactga ctttatctg acttattagg aataaatact 600
ctctaatagaa ctctc 615
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<210> 204
<211> 121
<212> PRT
<213> Homo sapiens

<400> 204

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

Tyr Ser Leu Leu Ala Gly Gln Glu Pro Val Tyr Gly Leu Tyr Thr Ser
20 25 30

Phe Phe Ala Ser Ile Ile Tyr Phe Leu Leu Gly Thr Ser Arg His Ile
35 40 45

Ser Val Gly Ile Phe Gly Val Leu Cys Leu Met Ile Gly Glu Thr Val
50 55 60

Asp Arg Glu Leu Gln Lys Ala Gly Tyr Asp Asn Ala His Ser Ala Pro
65 70 75 80

Ser Leu Gly Met Val Ser Asn Gly Ser Thr Leu Leu Asn His Thr Ser
85 90 95

Asp Arg Ile Cys Asp Lys Ser Cys Tyr Ala Ile Met Val Gly Ser Thr
100 105 110

Val Thr Phe Ile Ala Gly Val Tyr Gln
115 120

<210> 205
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

2015201738 07 Apr 2015

162/223

342-10PCT.txt

<400> 205
taaatcatac atcagacagg 20

<210> 206
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 206
aaaacaggta acagcagatt 20

<210> 207
<211> 513
<212> DNA
<213> Homo sapiens

<400> 207
atggcgggcgg ccgctctcgc gagaattcgg cccgtcgggc tccaagcccg gcgcctggcg 60
tcggaggggaa agactcgagc cgaaagcccc atctctgacc ctagcaactc atacccttct 120
ggcttccctt tagcaaagcg cctggacgtc atcccccttt cagatacccc aggcctcgtc 180
ctggccactg gcttgactat tgcaggagag cctgataaga tgggacacgg ctccaccttg 240
cattcagcaa gtcgttatcc tgcaactacg atgcaccagg aagaggatgt ggtgaggcca 300
gcttttccat atgcagttag gcatcgaagg gaagatctgc tgtacctaag tggggtgggc 360
atttcatttt tagggaccgt ctttggttaa ataatttggg acctcataaa gcctccagcc 420
attcctgatc aggacatagc ttacaacagc agcctgggtgc ccataacctg gacagcctgg 480
agtgaagtca cactcccaga cttgatgttc taa 513

<210> 208
<211> 170
<212> PRT
<213> Homo sapiens

<400> 208

Met Ala Ala Ala Ala Leu Ala Arg Ile Arg Pro Val Gly Leu Gln Ala
1 5 10 15

Arg Arg Leu Ala Ser Glu Gly Lys Thr Arg Ala Glu Ser Pro Ile Ser
20 25 30

Asp Pro Ser Asn Ser Tyr Pro Ser Gly Phe Pro Leu Ala Lys Arg Leu
35 40 45

Asp Val Ile Pro Ser Ser Asp Thr Pro Gly Leu Val Leu Ala Thr Gly
50 55 60

Leu Thr Ile Ala Gly Glu Pro Asp Lys Met Gly His Gly Ser Thr Leu
65 70 75 80

163/223

342-10PCT.txt

His Ser Ala Ser Arg Tyr Pro Ala Thr Thr Met His Gln Glu Glu Asp
85 90 95
Val Val Arg Pro Ala Phe Pro Tyr Ala Val Arg His Arg Arg Glu Asp
100 105 110
Leu Leu Tyr Leu Ser Gly Val Gly Ile Ser Phe Leu Gly Thr Val Phe
115 120 125
Val Lys Ile Ile Trp Asp Leu Ile Lys Pro Pro Ala Ile Pro Asp Gln
130 135 140
Asp Ile Ala Tyr Asn Ser Ser Leu Val Pro Ile Thr Trp Thr Ala Trp
145 150 155 160
Ser Glu Val Thr Leu Pro Asp Leu Met Phe
165 170

<210> 209
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 209
tgagccctag atatacttgg 20

<210> 210
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 210
cagtcagcct ccatttct 18

<210> 211
<211> 508
<212> DNA
<213> Homo sapiens

<400> 211
tgagccctag atatacttgg cttgcattta ggggccatga tgtttagaga tgaataatgc 60
cttacatgct ggagtcaccc tcagtttgtc aaagtgttca cactgtgaga ggctcacaga 120
aatggaggct gactgaagga agagcagatt cacatctttc atcccttctt tatgctcatg 180
cttctaattt ttgttcccat gttttcttgc ccctcctctt cttagcattt attttgtctg 240
tttctctttc ccctcttctg gctccctctc catctctcct gagcacagaa atgcggctac 300
tgtatttaaat ccacagtggc cccctctggc cccctctttg tgtctcctga gcacaggccc 360
tggtccctc tccatctctc ctgacctcct gatccgcca cctcggccag ttattgctgt 420

2015201738 07 Apr 2015

164/223

342-10PCT.txt

tttataagga aaatgttttc tagtaccaca cttgtctccc tggaagggat agaagaagga 480

gggaaggaag tagggaggca gggaagag 508

<210> 212

<211> 97

<212> PRT

<213> Homo sapiens

<400> 212

Met Pro Tyr Met Leu Glu Ser Pro Ser Val Cys Gln Ser Val His Thr
1 5 10 15

Val Arg Gly Ser Gln Lys Trp Arg Leu Thr Glu Gly Arg Ala Asp Ser
20 25 30

His Leu Ser Ser Leu Leu Tyr Ala His Ala Ser Asn Phe Cys Ser His
35 40 45

Val Phe Leu Pro Leu Leu Phe Leu Ala Phe Ile Leu Ser Val Ser Leu
50 55 60

Ser Pro Leu Leu Ala Pro Ser Pro Ser Leu Leu Ser Thr Glu Met Arg
65 70 75 80

Leu Leu Tyr Leu Ile His Ser Gly Pro Leu Trp Pro Pro Leu Cys Val
85 90 95

Ser

<210> 213

<211> 25

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 213

ctgtatttaa tccacagtgg ccccc 25

<210> 214

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 214

tccctacttc cttccctcct tcttcta 27

<210> 215

<211> 1321

<212> DNA

<213> Homo sapiens

2015201738 07 Apr 2015

165/223

342-10PCT.txt

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<400> 215
cagtgtcccag gcaagcccag gagttgacat ttctctgccc agccatgggc ctcaccctgc 60
tcttgctgct gctcctggga ctagaaggtc agggcatagt tggcagcctc cctgaggtgc 120
tgcaggcacc cgtgggaagc tccattctgg tgcagtgcc ctacaggctc caggatgtca 180
aagctcagaa ggtgtggtgc cggttcttgc cggaggggtg ccagcccctg gtgtcctcag 240
ctgtggatcg cagagctcca gcgggcaggc gtacgtttct cacagacctg ggtgggggcc 300
tgctgcaggt ggaaatgggt accctgcagg aagaggatgc tggcaggtat ggctgcatgg 360
tggatggggc cagggggccc cagattttgc acagagtctc tctgaacata ctgccccag 420
aggaagaaga agagacccat aagattggca gtctggctga gaacgcattc tcagaccctg 480
caggcagtgc caaccctttg gaaccagcc aggatgagaa gagcatcccc ttgatctggg 540
gtgctgtgct cctggtaggt ctgctgggtg cagcgggtgt gctgtttgct gtgatggcca 600
agaggaaaca agggaaacagg cttggtgtct gtggccgatt cctgagcagc agagtttcag 660
gcatgaatcc ctctcagtg gtccaccacg tcagtgactc tggaccggct gctgaattgc 720
ctttggatgt accacacatt aggcttgact caccacctc atttgacaat accacctaca 780
ccagcctacc tcttgattcc ccatcaggaa aaccttcact cccagctcca tcctcattgc 840
cccctctacc tcctaaggtc ctggtctgct ccaagcctgt gacatatgcc acagtaatct 900
tcccgggagg gaacaaggtt ggagggacct cgtgtgggcc agcccagaat ccacctaaca 960
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gggttctgtg catccatcca gccagctcat gccctaggat ccttaggata tctgagcaac 1080
cagggacttt aagatctaata ccaatgtcct aactttacta gggaaagtga cgctcagaca 1140
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t 1321
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<210> 216
<211> 311
<212> PRT
<213> Homo sapiens
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<400> 216

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Met Gly Leu Thr Leu Leu Leu Leu Leu Gly Leu Glu Gly Gln
1          5          10          15

Gly Ile Val Gly Ser Leu Pro Glu Val Leu Gln Ala Pro Val Gly Ser
20          25          30

Ser Ile Leu Val Gln Cys His Tyr Arg Leu Gln Asp Val Lys Ala Gln
35          40          45
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2015201738 07 Apr 2015

166/223

342-10PCT.txt

Lys Val Trp Cys Arg Phe Leu Pro Glu Gly Cys Gln Pro Leu Val Ser
50 55 60

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

Asp Leu Gly Gly Gly Leu Leu Gln Val Glu Met Val Thr Leu Gln Glu
85 90 95

Glu Asp Ala Gly Glu Tyr Gly Cys Met Val Asp Gly Ala Arg Gly Pro
100 105 110

Gln Ile Leu His Arg Val Ser Leu Asn Ile Leu Pro Pro Glu Glu Glu
115 120 125

Glu Glu Thr His Lys Ile Gly Ser Leu Ala Glu Asn Ala Phe Ser Asp
130 135 140

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

Ile Pro Leu Ile Trp Gly Ala Val Leu Leu Val Gly Leu Leu Val Ala
165 170 175

Ala Val Val Leu Phe Ala Val Met Ala Lys Arg Lys Gln Gly Asn Arg
180 185 190

Leu Gly Val Cys Gly Arg Phe Leu Ser Ser Arg Val Ser Gly Met Asn
195 200 205

Pro Ser Ser Val Val His His Val Ser Asp Ser Gly Pro Ala Ala Glu
210 215 220

Leu Pro Leu Asp Val Pro His Ile Arg Leu Asp Ser Pro Pro Ser Phe
225 230 235 240

Asp Asn Thr Thr Tyr Thr Ser Leu Pro Leu Asp Ser Pro Ser Gly Lys
245 250 255

Pro Ser Leu Pro Ala Pro Ser Ser Leu Pro Pro Leu Pro Pro Lys Val
260 265 270

Leu Val Cys Ser Lys Pro Val Thr Tyr Ala Thr Val Ile Phe Pro Gly
275 280 285

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

Asn Asn Gln Thr Pro Ser Ser
305 310

2015201738 07 Apr 2015

167/223

342-10PCT.txt

<210> 217
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 217
aggaagaaga agagaccc 18

<210> 218
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 218
catcacagca aacagcac 18

<210> 219
<211> 3874
<212> DNA
<213> Homo sapiens

<400> 219
gagaactggg gcggcgcggc gcggcgcggt gcatttccag gcgctgctct ccgtcgcaga 60
gaaccctgag ctcggcgcgc cgagagtccc agcagggcaa gggggcgcgg cgtcctggtc 120
ctcgagcttg ggagacagat gcgcatgggc gtgggggcat gcggacctaa gctcgggtga 180
agctctcggg aagggcaaga ctgcggcgac gagatgcgag cagaggagcc ctgcgcccc 240
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cagctgctgc ccgagctctg taccttcgtg gtgcgcgtgc tgttctacct ggggcctgtc 360
tacctagctg gctacctggg gctcagcata acctggttgc tgctcggcgc cctgctgtgg 420
atgtggtggc gcaggaaccg ccgcgggaag cttgggcgcc tggccgccgc cttcgaattc 480
cttgacaatg aacgcgagtt catcagccgc gagctgcggg gccagcacct gccagcctgg 540
atccacttcc cggacgtgga gcgggctcag tgggcccaaca agatcatctc tcagacctgg 600
ccctacctaa gcatgatcat ggaaagcaag ttccgggaga aacttgagcc caagatccga 660
gagaagagca tccacctgag gacctttacc tttaaccaagc tctactttgg acagaagtgt 720
cccaggttca acggtgtcaa ggcacacact aatacgtgca accgaagacg tgtgactgtg 780
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2015201738 07 Apr 2015

168/223

342-10PCT.txt

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aagtcagatc	cctacgccaa	ggtgagcatc	ggcctacagc	atttccggag	taggaccatc	1260
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ggacaggacc	tggaggtaga	cctgtatgat	gaggataccg	acagggatga	cttcctgggc	1380
agcctgcaga	tctgccttgg	agatgtcatg	accaacagag	tggtggtatga	gtggtttgtc	1440
ctgaatgaca	caaccagcgg	gcggtctgcac	ctgctggctgg	agtggctttc	attgcttact	1500
gaccaagaag	ttctgactga	ggaccatggt	ggcctttcca	ctgccattct	cgtggctttc	1560
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ccttgatagt	aagagaggac	actgaggccc	cacaaggcct	catctcctta	aggctagtgc	1980
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taagcaaaga	gaggcaaaaa	caatgtcttg	tccaagatct	catgaccaac	aagtgggtgga	2220
gctgggatct	tttagggccc	tgagccctgc	ctggagagca	gcacagctca	tcagtcccca	2280
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gaggaacgag	agctggggag	cccatacaca	ggacctgaag	ccctaaagaa	aggccctctg	2760
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acagatttgc	catgtccccc	agaccctgct	tctgatacta	aggacgtatc	caggagtacc	2880
acaaccacca	ccagtgtctac	caccgttgcc	actgagccca	catcccaaga	gacaggccca	2940
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ccagccacca	tcttcctgac	tgtcccaggt	ccccactctc	cagggcccat	caagtcaccc	3060
agacccatga	aatgccctgc	ctccccattc	gcatggccgc	ccaagaggct	ggctcccagc	3120
atgtcctcgc	tcaactcctt	ggcctcttct	tgctttgacc	tggcagatat	cagcctcaac	3180

2015201738 07 Apr 2015

169/223

342-10PCT.txt

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attgagtatg cacctctctg cttaatcttt tctaaaatcg cctgtatgaa aaatacctcg 3240
ctggatggaa aagtagatat gaacttacat ttctgtgcaa gttgtttttt cacaaaatat 3300
cttcctaaga ggcagcatgg tgtggtagaa agaacacagg acaagggaga gagagccaaa 3360
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aagaagactt cagtgaagcg gaagacctg gaacccctgt ttgatgagac atttgaattt 3660
tttgttccca tggaagaagt aaagaagagg tcactagatg ttgcagtga aaatagtagg 3720
ccacttggtt cacacagaag aaaggagtta ggaaaagtac tgattgactt atcaaaagaa 3780
gatctgatta agggcttttc acaatggtaa gtgtgccctt tcattttatc actgttatcc 3840
tgctattcaa gacagttttc ccttttcagt actg 3874

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<210> 220
 <211> 501
 <212> PRT
 <213> Homo sapiens

<400> 220

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Met Arg Ala Glu Glu Pro Cys Ala Pro Gly Ala Pro Ser Ala Leu Gly
1          5          10          15

Ala Gln Arg Thr Pro Gly Pro Glu Leu Arg Leu Ser Ser Gln Leu Leu
20          25          30

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

Val Tyr Leu Ala Gly Tyr Leu Gly Leu Ser Ile Thr Trp Leu Leu Leu
50          55          60

Gly Ala Leu Leu Trp Met Trp Trp Arg Arg Asn Arg Arg Gly Lys Leu
65          70          75          80

Gly Arg Leu Ala Ala Ala Phe Glu Phe Leu Asp Asn Glu Arg Glu Phe
85          90          95

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

Pro Asp Val Glu Arg Val Glu Trp Ala Asn Lys Ile Ile Ser Gln Thr
115         120         125

Trp Pro Tyr Leu Ser Met Ile Met Glu Ser Lys Phe Arg Glu Lys Leu
130         135         140

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2015201738 07 Apr 2015

170/223

342-10PCT.txt

Glu Pro Lys Ile Arg Glu Lys Ser Ile His Leu Arg Thr Phe Thr Phe
145 150 155 160

Thr Lys Leu Tyr Phe Gly Gln Lys Cys Pro Arg Val Asn Gly Val Lys
165 170 175

Ala His Thr Asn Thr Cys Asn Arg Arg Arg Val Thr Val Asp Leu Gln
180 185 190

Ile Cys Tyr Ile Gly Asp Cys Glu Ile Ser Val Glu Leu Gln Lys Ile
195 200 205

Gln Ala Gly Val Asn Gly Ile Gln Leu Gln Gly Thr Leu Arg Val Ile
210 215 220

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

Phe Phe Leu Gln Lys Gln His Leu Gln Ile Asn Trp Thr Gly Leu Thr
245 250 255

Asn Leu Leu Asp Ala Pro Gly Ile Asn Asp Val Ser Asp Ser Leu Leu
260 265 270

Glu Asp Leu Ile Ala Thr His Leu Val Leu Pro Asn Arg Val Thr Val
275 280 285

Pro Val Lys Lys Gly Leu Asp Leu Thr Asn Leu Arg Phe Pro Leu Pro
290 295 300

Cys Gly Val Ile Arg Val His Leu Leu Glu Ala Glu Gln Leu Ala Gln
305 310 315 320

Lys Asp Asn Phe Leu Gly Leu Arg Gly Lys Ser Asp Pro Tyr Ala Lys
325 330 335

Val Ser Ile Gly Leu Gln His Phe Arg Ser Arg Thr Ile Tyr Arg Asn
340 345 350

Leu Asn Pro Thr Trp Asn Glu Val Phe Glu Phe Met Val Tyr Glu Val
355 360 365

Pro Gly Gln Asp Leu Glu Val Asp Leu Tyr Asp Glu Asp Thr Asp Arg
370 375 380

Asp Asp Phe Leu Gly Ser Leu Gln Ile Cys Leu Gly Asp Val Met Thr
385 390 395 400

Asn Arg Val Val Asp Glu Trp Phe Val Leu Asn Asp Thr Thr Ser Gly
405 410 415

171/223

342-10PCT.txt

Arg Leu His Leu Arg Leu Glu Trp Leu Ser Leu Leu Thr Asp Gln Glu
420 425 430

Val Leu Thr Glu Asp His Gly Gly Leu Ser Thr Ala Ile Leu Val Val
435 440 445

Phe Leu Glu Ser Ala Cys Asn Leu Pro Arg Asn Pro Phe Asp Tyr Leu
450 455 460

Asn Gly Glu Tyr Arg Ala Lys Lys Leu Ser Arg Phe Ala Arg Val Lys
465 470 475 480

Gln Gly Gln Gln Arg Pro Phe Phe Leu Cys Gln Thr Ile Cys Arg Gln
485 490 495

Glu Asp Thr Tyr Lys
500

<210> 221
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 221
tggggcctgt ctacctagct

20

<210> 222
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 222
tcttgttggc ccactcgac

19

<210> 223
<211> 1020
<212> DNA
<213> Homo sapiens

<400> 223
agacacagga cctgctgggc cacagaaagg aggctctggg tagacgcact agattactgg 60
ataaatcact tcaatttccc aatgaatatt atattgttta tttttataacc tggagttttt 120
tccttaaaaa gtagcacttt gaagcctact attgaagcat tgcctaattgt gctaccctta 180
aatgaagatg ttaataagca ggaagaaaag aatgaagatc atactcccaa ttatgctcct 240
gctaattgaga aaaaatggcaa ttattataaa gatataaaac aatatgtgtt cacaacacaa 300
aatccaaatg gcactgagtc tgaaatatct gtgagagcca caactgacct gaattttgct 360
ctaaaaaacg ataaaactgt caatgcaact acatatgaaa aatccaccat tgaagaagaa 420

172/223

342-10PCT.txt

```

acaactacta gcgaaccctc tcataaaaat attcaaagat caaccccaaa cgtgcctgca 480
ttttggacaa tgtagctaa agctataaat ggaacagcag tggatcatgga tgataaagat 540
caattatttc acccaattcc agagtctgat gtgaatgcta cacagggaga aaatcagcca 600
gatctagagg atctgaagat caaaataatg ctgggaatct cgttgatgac cctcctcctc 660
tttgtggtcc tcttggcatt ctgtagtgct aactgtgata aactgaggca tctgagttat 720
aaaagttgtg agagtcagta ctctgtcaac ccagagctgg ccacgatgtc ttactttcat 780
ccatcagaag gtgtttcaga tacatccttt tccaagagtg cagagagcag cacatTTTTg 840
gggtaccactt cttcagatat gagaagatca ggcacaagaa catcagaatc taagataatg 900
acggatatca tttccatagg ctgagataat gagatgcatg aaaacgatga gtcggttacc 960
cgggtgaagaa atcaaggaac ccgggtgaaga aatcttattg atgaataaat aactttaatt 1020

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<210> 224
 <211> 294
 <212> PRT
 <213> Homo sapiens

<400> 224

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Met Asn Phe Ile Leu Phe Ile Phe Ile Pro Gly Val Phe Ser Leu Lys
1           5           10          15

Ser Ser Thr Leu Lys Pro Thr Ile Glu Ala Leu Pro Asn Val Leu Pro
          20          25          30

Leu Asn Glu Asp Val Asn Lys Gln Glu Glu Lys Asn Glu Asp His Thr
          35          40          45

Pro Asn Tyr Ala Pro Ala Asn Glu Lys Asn Gly Asn Tyr Tyr Lys Asp
          50          55          60

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

Glu Ile Ser Val Arg Ala Thr Thr Asp Leu Asn Phe Ala Leu Lys Asn
          85          90          95

Asp Lys Thr Val Asn Ala Thr Thr Tyr Glu Lys Ser Thr Ile Glu Glu
100         105         110

Glu Thr Thr Thr Ser Glu Pro Ser His Lys Asn Ile Gln Arg Ser Thr
115         120         125

Pro Asn Val Pro Ala Phe Trp Thr Met Leu Ala Lys Ala Ile Asn Gly
130         135         140

Thr Ala Val Val Met Asp Asp Lys Asp Gln Leu Phe His Pro Ile Pro
145         150         155         160

```

173/223

342-10PCT.txt

Glu Ser Asp Val Asn Ala Thr Gln Gly Glu Asn Gln Pro Asp Leu Glu
165 170 175

Asp Leu Lys Ile Lys Ile Met Leu Gly Ile Ser Leu Met Thr Leu Leu
180 185 190

Leu Phe Val Val Leu Leu Ala Phe Cys Ser Ala Thr Leu Tyr Lys Leu
195 200 205

Arg His Leu Ser Tyr Lys Ser Cys Glu Ser Gln Tyr Ser Val Asn Pro
210 215 220

Glu Leu Ala Thr Met Ser Tyr Phe His Pro Ser Glu Gly Val Ser Asp
225 230 235 240

Thr Ser Phe Ser Lys Ser Ala Glu Ser Ser Thr Phe Leu Gly Thr Thr
245 250 255

Ser Ser Asp Met Arg Arg Ser Gly Thr Arg Thr Ser Glu Ser Lys Ile
260 265 270

Met Thr Asp Ile Ile Ser Ile Gly Ser Asp Asn Glu Met His Glu Asn
275 280 285

Asp Glu Ser Val Thr Arg
290

<210> 225
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 225
tgaatgctac acagggagaa aatc

24

<210> 226
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 226
tgaaagtaag acatcgtggc c

21

<210> 227
<211> 309
<212> DNA
<213> Homo sapiens

<400> 227
atgaccacag ccacccctct gggggatacc accttcttct cactgaacat gaccaccagg

60

174/223

342-10PCT.txt

ggagaagact tcctgtataa gagttctgga gccattgttg ctgccgttgt ggtggttgtc 120
atcatcatct tcaccgtggt tctgatcctg ctgaagatgt acaacaggaa aatgaggacg 180
aggcgggaa tagagcccaa gggccccaag ccaaccgccc cttctgccgt gggcccaaac 240
agcaacggca gccaacaccc agcaactgtg accttcagtc ctgttgacgt ccaggtggag 300
acgcgatga 309

<210> 228
<211> 102
<212> PRT
<213> Homo sapiens
<400> 228

Met Thr Thr Ala Thr Pro Leu Gly Asp Thr Thr Phe Phe Ser Leu Asn
1 5 10 15

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

Val Ala Ala Val Val Val Val Val Ile Ile Ile Phe Thr Val Val Leu
35 40 45

Ile Leu Leu Lys Met Tyr Asn Arg Lys Met Arg Thr Arg Arg Glu Leu
50 55 60

Glu Pro Lys Gly Pro Lys Pro Thr Ala Pro Ser Ala Val Gly Pro Asn
65 70 75 80

Ser Asn Gly Ser Gln His Pro Ala Thr Val Thr Phe Ser Pro Val Asp
85 90 95

Val Gln Val Glu Thr Arg
100

<210> 229
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 229
ggggatacca ccttcttct 19

<210> 230
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 230
agttgctggg tggtggct 18

2015201738 07 Apr 2015

175/223

342-10PCT.txt

<210> 231
<211> 2510
<212> DNA
<213> Homo sapiens

<400> 231
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tgcatctctg atgatgcatg atgttgacca gtttttaata tgtttggtga ctgcttgtat 120
gtcttctttt aagaagtgtc tgttcataatc ctttgccctt tcgcttctat gcaccaataa 180
caccaggct gagagtcaaa ccaagaacac aatcctgact acagtagcca taaagaaaat 240
gaaatacctg ggaatacacc taatcaaaaa catgaaagca ctctctagag ggagaactac 300
aaaacattgc tgaaagaaat cagagatgat tctctgaaaa agaagtcaga ttagaaatga 360
ttctctgaaa aagaaatcat ctctgatttc tttcagcagt gtgttttttg tttgtttgtt 420
tgttttgaga cagagtcttg ctctgtcgcc aaggctggag ggcaatggca tgatttcagc 480
tcactacaac ctctgtctcc tgggttcgag cgattctcct acctcagcct cccgagtagc 540
tgggattaca ggaggctgag aaaatgttag aaattggggg agacaagttt cccttagaga 600
gcaggaagtt actaagtagt cctggaaaga acatcagttg cagatgtgac ccctctgaga 660
ttaatatatc tgatgaaatg cctaaaacta cagtttgga agctctcagt atgaattctg 720
gaaatgcaaa ggaaaagagt ctcttcaact aagagtcttt gctgggatgg aagatttggg 780
ccgtgtggtg cctcagggaa gttctggtta cagagaaaat ggcgagtctc tcagagaaga 840
agcaagacca agtctggccc tgtccttggt catctcaaag ccatgccgaa gcattcagtt 900
attcttggtg tgcatggaa ggcattcagc tatccccata ccagcagcca gtcaacagat 960
gtgaatgtgg aagcagaaga ccacctctg ttggttcttc tcctcttcct tctttttctc 1020
tttagaacgg ccaccattga agacctagct tccattttc cagacgtttt ctctgaaatt 1080
ctctgctggc ctgccaagcc atatggattc attctgccac tgaggagtcc ttcagtgagg 1140
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gtgcatctcc atcactcctt agcagcagcc tgcataactg gcaagaatct tggatgatac 1440
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tcaacagtaa gtgaggatga gcagtgtctc ttggttttca ttgaggatag agtaagagat 1560
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agatttgtca tagtgtctgc tttctagata tctgggaaag atttgataat agttgtttgt 1680
gaatagaaag gaggatatga tgtttttatt ggccattttg cgggactctt cgacttcttg 1740
ctgctgtctc ttgaggatac attccaattc catcctggcg agatccaagt gcttacgtac 1800

2015201738 07 Apr 2015

176/223

342-10PCT.txt

tgtctcctta gctgccttag agtaaacgat catcagttca atggaccaa atcaccttca	1860
gccatgtggg ttcttcatca tcatggattt cttttggttg acaaacattc tggctctcag	1920
atgcaaaaag tcacactggg aaatgaactg taagtgggtga aattagtttt ggtattttaat	1980
ttaaaactac atttatagtt tttctcttct cttctatggt gcaatgaatg taaagtattt	2040
gggatccagt gcttataaac ctttccttcc tttgtgcaca gaatgtaact agcaagccca	2100
ttagcaccca gataattcta tcatgttagt ttcccatcct ggaaaatctt tgtacagtgg	2160
gaagttcccc gatgtgtttt tctttcttag gtgaagggtt ggctatatca ctttattgaa	2220
ttttgcattc cttagacttt taaaatatac taatgtattc tagtcttact ctaaagacct	2280
ttgatgttaa aggaatcctt catttatctt atattcccta tctcataggg ccacaattat	2340
tttaatacag agatgatttt caaaatattt taacaactgg tacaggacag atgccagcca	2400
ctcagaaggg atgcctgctg taaacaagca gtatgtatgg ttgtaccaat gcctattggc	2460
tgaacattat gctactttca gatattaaaa tgggtgttctt ttgaatcgtg	2510

<210> 232
 <211> 164
 <212> PRT
 <213> Homo sapiens
 <400> 232

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

07 Apr 2015

2015201738

177/223

342-10PCT.txt

Asp Arg Val Gly Ser Arg Arg Gly Thr Glu Arg Thr Ser Ser Leu Ala
145 150 155 160

Leu Gln Cys Ser

<210> 233
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 233
gaggctgaga aaatgttaga

20

<210> 234
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 234
tccatcccag caaagact

18

<210> 235
<211> 1977
<212> DNA
<213> Homo sapiens

<400> 235
cgtgggcttg aggacctgga gagagtagat cctgaagaac tttttcagtc tgctgaagag 60
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tcctgtgaga aacactcatt tgattgtgaa aagacttgaa ttctatgcta agcagggttc 180
caagtagcta aatgaatgat ctcaagaag ctctcttgct gctgctgcta ctcgtttaca 240
tttattgatt acttacgatg attcagggtac tgttgtaagt gctttacatg ctgttatacg 300
agactcttgg gagaaatcac tttaatgaag cttgagacac atggcattgc catgcaatga 360
tttttcccc ctcttcacgg gatcagaggg aactaataga atgtgacaat gattctttag 420
cagggactgc tgaggcttct gggtcctttt taagatctgc agtgaaagaa gatgagaaac 480
atggatatgc ctttcttttg gtccccctct tcctttatct gatctctact tccttctata 540
aatatattag ggctacattg tccctttgta tttcaaaca ggcaaaaaga ggttgtaatt 600
acactttact gcaatcctca gtttctccag ggaacaggaa tgcaaaggct ttgaaggcct 660
ctctattttgc tgacatggtc agctgggtgc catgggcaa gtccttctgt tgccctcctc 720
tgtcaccaag taagctaggt ctttctgag gctcaggtt gctgtgatga tgatcacttt 780
taggcagaag gttagaggcc tcatgagtg tatatggact ttattaggct ttagatttga 840
tggggaataa gggatgtgat ttgtcttttg ggaactcatc tttgattcat cattgtctct 900

342-10PCT.txt

tggtatcttg	gaatttccat	gtcattacag	tctacagaat	gaaagagtaa	cctgtcccag	960
aggagaggca	ggtgaaagac	tccacagcat	gctcattctc	attctgtctt	ctcagtgaca	1020
ccgaggttta	ctgagtgcc	actatgtgcc	aagcactgtg	ctcagggctt	tctttgtatg	1080
catgatctca	gtgaatctca	ccaagcctca	tctggaaaac	ggggacaaat	taacaacagg	1140
atggcaaatt	gaaaaacacg	taaccatggt	ctacagatgg	aaaggggtgc	ttggttatta	1200
tgaaggcccc	ctcgcaagcg	tgtgggacat	gggtgtgttc	tctgggttgt	actgatcaga	1260
tcaaggacct	ccccaccct	tctcacactc	tgcccacttc	cgccctttgc	ttatcagacc	1320
cttagccagt	gactcattcc	agaaccagaa	ccttggtgaa	atctcaaccg	acaccagaga	1380
tcggtgtctt	cagtcctaga	ctgatggaga	aaatccagaa	tatatactag	aagctccaaa	1440
tgctctgggt	ttcagctcct	ctgtgctgtg	gacactgact	ttggctcaga	actccgattt	1500
agtacaaaag	gctcattttt	atttcagggg	cactcttcct	aaagcaaacc	taataaatga	1560
aatatggaat	tcacagatac	acacacacat	taaaaaatta	acctagtgtg	tctgtgagga	1620
gtaggcagaa	attcactgta	taaaagaatg	cttcatttca	tagagaattt	gtgttaagat	1680
tccattagat	agtacatttc	tcaaagattt	ttgaggttgt	atttgcttta	ccaaaacttg	1740
gtttatgtaa	gtggaaaaag	catgttgcaa	aataacttgg	tgtctatgat	tcagtttatg	1800
taaaataata	aatgtatgta	ggaatacgtg	tgttgaaaga	tgtacatcaa	tttgctaaca	1860
atggttatct	ctgacgtggg	gggatttgag	atgtgttttt	ctttttgggt	gtatttttct	1920
ctattgtttg	acttaacaca	gaacatgttt	ggttacaaca	ataaagttat	tgaagac	1977

<210> 236
 <211> 130
 <212> PRT
 <213> Homo sapiens

<400> 236

Met Ile Phe Pro Pro Ser Ser Arg Asp Gln Arg Glu Leu Ile Glu Cys
 1 5 10 15

Asp Asn Asp Ser Leu Ala Gly Thr Ala Glu Ala Ser Gly Ser Phe Leu
 20 25 30

Arg Ser Ala Val Lys Glu Asp Glu Lys His Gly Tyr Ala Leu Leu Leu
 35 40 45

Val Pro Leu Phe Leu Tyr Leu Ile Ser Thr Ser Phe Tyr Lys Tyr Ile
 50 55 60

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

Asn Tyr Thr Leu Leu Gln Ser Ser Val Ser Pro Gly Asn Arg Asn Ala
 85 90 95

07 Apr 2015 2015201738

179/223

342-10PCT.txt

Lys Ala Leu Lys Ala Ser Leu Phe Ala Asp Met Val Ser Trp Val Pro
100 105 110

Trp Ala Lys Ser Phe Cys Cys Pro Pro Leu Ser Pro Ser Lys Leu Gly
115 120 125

Pro Phe
130

<210> 237
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 237
atgattcttt agcaggga 18

<210> 238
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 238
ctctttttgc cttgtttg 18

<210> 239
<211> 1293
<212> DNA
<213> Homo sapiens

<400> 239
aggccgaggg gttcggcgac gcggagggag ggagagtctg ggccgcgcgg gagccgcagg 60
gcgccctagc cttcgcaaa acgatggcgg aggaagaagg accacctgta gagctgcgcc 120
aaagaaaaaa gccaaagtct tcagaaaata aggaatctgc caaagaagag aaaatcagtg 180
acattccaat tcctgaaaga gtcctcaaac atgtattatt tcaacgcttt gcaaagattt 240
tcattggctg tcttgacgcg gttactagtgt gtatgatgta tgctctctac ttatcagcat 300
accatgaacg gaaattctgg ttttccaaca ggcaggagct tgaacgggaa atcacgtttc 360
aggggtgacag tgccatttat tactcctatt ataaagatat gttaaaggca ccttcatttg 420
aaagaggtgt ttacgaactg acacacaata acaaaactgt atctctgaag actataaatg 480
cagtgacgca aatgtctctg tatccggaac ttattgctag cattttatat caagccactg 540
gtagcaatga gattattgag ccagtgtatt tctatattgg cattgttttt ggattgcaag 600
gaatatatgt tactgcttta tttgttaca gttggcttat gagtgggaca tggctagcag 660
gaatgcttac tgttgcgtgg ttcgttatta acagttgcac agaccctgg tacagtgtgg 720
gaggtgacaa cacaggatat taataccagg aggcaggaat cattgggacc gtcttggaag 780

2015201738 07 Apr 2015

180/223

342-10PCT.txt

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ctggctacca cattcaatta actttgctat taatttcattg taatccctat atctgtcttc 840
atatttgaag aggaaaagat actttctcat gtaaacataa tggtttttaa gaataagact 900
ctcttatgct acttaaaca aagaataaga ctctcttttag agatcttagt gagaattgta 960
agaaataaaa taaacagaag tctgactgcc ttatttgatg tctactgatg atgttgtatt 1020
gctggagtag aagttaaata gaaaaattga cctgggtatat tctactcaaa tgtatctttt 1080
gacaattgaa atgttcttaa tagctaagtt ttaaaaaatg cgtttgtttg ctttttgttt 1140
atattttatt ggtatgtatc ttgtactgca aaatacattt taatgccatg aaagaatatg 1200
ctgtctcttt attcatcagc tttatagctt ttatttatat atgacttctt agaaaagtat 1260
aaaaagatat taaagtcatt ccattatatt atg 1293

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<210> 240
 <211> 219
 <212> PRT
 <213> Homo sapiens
 <400> 240

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

Pro Lys Ser Ser Glu Asn Lys Glu Ser Ala Lys Glu Glu Lys Ile Ser
20 25 30

Asp Ile Pro Ile Pro Glu Arg Ala Pro Lys His Val Leu Phe Gln Arg
35 40 45

Phe Ala Lys Ile Phe Ile Gly Cys Leu Ala Ala Val Thr Ser Gly Met
50 55 60

Met Tyr Ala Leu Tyr Leu Ser Ala Tyr His Glu Arg Lys Phe Trp Phe
65 70 75 80

Ser Asn Arg Gln Glu Leu Glu Arg Glu Ile Thr Phe Gln Gly Asp Ser
85 90 95

Ala Ile Tyr Tyr Ser Tyr Tyr Lys Asp Met Leu Lys Ala Pro Ser Phe
100 105 110

Glu Arg Gly Val Tyr Glu Leu Thr His Asn Asn Lys Thr Val Ser Leu
115 120 125

Lys Thr Ile Asn Ala Val Gln Gln Met Ser Leu Tyr Pro Glu Leu Ile
130 135 140

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

Val Tyr Phe Tyr Ile Gly Ile Val Phe Gly Leu Gln Gly Ile Tyr Val
165 170 175

342-10PCT.txt

Thr Ala Leu Phe Val Thr Ser Trp Leu Met Ser Gly Thr Trp Leu Ala
180 185 190

Gly Met Leu Thr Val Ala Trp Phe Val Ile Asn Ser Cys Thr Asp Pro
195 200 205

Trp Tyr Ser Val Gly Gly Asp Asn Thr Gly Tyr
210 215

<210> 241
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 241
accgctgcaa gacagccaa 19

<210> 242
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 242
gcagaaacga tggcggagga 20

<210> 243
<211> 1291
<212> DNA
<213> Homo sapiens

<400> 243
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gacagctgca tggaaaacaa aattctgctg ggagtaaata gaggcctgtg cctgcttata 120
tcattggtag ccatctcacc ctgggtccaa aatcgacagc cacactcggg gctcttataa 180
tcaggggtca taagctgcta tgtcacctac ctacatttct cagctctgtc cagcaaacct 240
gcagaagtag ttctagatga acatgggaaa aatgttataa tctgtgtgcc tgactttggt 300
caagacctgt acagagatga aaacttggtg actatactgg ggaccagcct cttaatcgga 360
tgtatcttgt attcatgttt gacatcaaca acaagatcga gttctgacgc tctgcagggg 420
cgatacgag ctctgaatt ggagatagct cgctgttggt tttgcttcag tcctgggtgga 480
gaggacactg aagagcagca gccggggaag gagggaccac gggtcattta tgacgagaag 540
aaaggcaccg tctacatcta ctctacttc cacttcgtgt tcttcctagc ttccctgtat 600
gtgatgatga ccgtcaccaa ctgggtcaac tacgaaagtg ccaacatcga gagcttcttc 660
agcgggagct ggtccatctt ctgggtcaag atggcctcct gctggatatg cgtgctgttg 720

2015201738 07 Apr 2015

182/223

342-10PCT.txt

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tacctgtgta cgctggctgc tccccctctgc tgccccaccc gggagttctc tgtgtgatga 780
tatcggcggt cccctgggct ttgtgggcct acagcctgga aagtgccatc ttttgaacag 840
tgtccccggg gcagggactg gcgccctgtg cctgagtggg tctgaaaaag ctttgagaga 900
gaaaaaaaaa aatctcctga ttagcttttt acttttgaaa ttcaaaaaga aactaccagt 960
ttgtcccaaa ggaattgaaa ttttcaacca aactgatcat ggttgaaata tcttaccctt 1020
aggaactgga taccagttat gttgacttcc ttctgcatgt ttttgccaaa acagaatttg 1080
gggcacagca tcttttcaca gggataaaaa tatcttgtgg ggccagtcac tctcatcctc 1140
ggaatagaaa aacatgccaa aatcttgagt cccagcgcc taacagaatc cagaccctc 1200
tcactcactt ccgcctctta gagccttgtc cccagggggc tttgaggaca ggactcagcc 1260
tgcagggccc ctggtattta taggggtccaa g 1291
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<210> 244
<211> 257
<212> PRT
<213> Homo sapiens

<400> 244

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

Thr Gln Lys Asp Ser Cys Met Glu Asn Lys Ile Leu Leu Gly Val Asn
20 25 30

Gly Gly Leu Cys Leu Leu Ile Ser Leu Val Ala Ile Ser Pro Trp Val
35 40 45

Gln Asn Arg Gln Pro His Ser Gly Leu Leu Gln Ser Gly Val Ile Ser
50 55 60

Cys Tyr Val Thr Tyr Leu Thr Phe Ser Ala Leu Ser Ser Lys Pro Ala
65 70 75 80

Glu Val Val Leu Asp Glu His Gly Lys Asn Val Thr Ile Cys Val Pro
85 90 95

Asp Phe Gly Gln Asp Leu Tyr Arg Asp Glu Asn Leu Val Thr Ile Leu
100 105 110

Gly Thr Ser Leu Leu Ile Gly Cys Ile Leu Tyr Ser Cys Leu Thr Ser
115 120 125

Thr Thr Arg Ser Ser Ser Asp Ala Leu Gln Gly Arg Tyr Ala Ala Pro
130 135 140

Glu Leu Glu Ile Ala Arg Cys Cys Phe Cys Phe Ser Pro Gly Gly Glu
145 150 155 160

183/223

342-10PCT.txt

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

Asp Glu Lys Lys Gly Thr Val Tyr Ile Tyr Ser Tyr Phe His Phe Val
180 185 190

Phe Phe Leu Ala Ser Leu Tyr Val Met Met Thr Val Thr Asn Trp Phe
195 200 205

Asn Tyr Glu Ser Ala Asn Ile Glu Ser Phe Phe Ser Gly Ser Trp Ser
210 215 220

Ile Phe Trp Val Lys Met Ala Ser Cys Trp Ile Cys Val Leu Leu Tyr
225 230 235 240

Leu Cys Thr Leu Val Ala Pro Leu Cys Cys Pro Thr Arg Glu Phe Ser
245 250 255

Val

<210> 245
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<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 245
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<210> 246
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<212> DNA
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<220>
<223> Oligonucleotide

<400> 246
ttctgctggg agtaaattg 18

<210> 247
<211> 2412
<212> DNA
<213> Homo sapiens

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gggggaggag gaggggagct aggtggtgac atcacagtcg aaggttataa aagcttccag 180
ccaaacggca ttgaagttga agatacaacc tgacagcaca gcctgagatc ttggggatcc 240
ctcagcctaa caccacaga cgtcagctgg tggattcccg ctgcatcaag gcctaccac 300

342-10PCT.txt

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aatTTTTTTT	taagcgcca	gataataaat	aatgtaacct	ttgcggttta	agaggataaa	1320
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gtcatgcacc	ctaaaaatgg	ctctgtcact	gtgagtggct	tcagtaggat	tttgagaata	2280
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2015201738 07 Apr 2015

185/223

342-10PCT.txt

ccccctttta ccctccattt gtgtttattg catatccact ataacaacat taaaggacct 2400
ttaaaaggaa gt 2412

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<212> PRT
<213> Homo sapiens
<400> 248

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Val Pro Arg Ala Gln Pro Leu Ala Pro Gln Asp Phe Glu Glu Glu Glu
20 25 30

Ala Asp Glu Thr Glu Thr Ala Trp Pro Pro Leu Pro Ala Val Pro Cys
35 40 45

Asp Tyr Asp His Cys Arg His Leu Gln Val Pro Cys Lys Glu Leu Gln
50 55 60

Arg Val Gly Pro Ala Ala Cys Leu Cys Pro Gly Leu Ser Ser Pro Ala
65 70 75 80

Gln Pro Pro Asp Pro Pro Arg Met Gly Glu Val Arg Ile Ala Ala Glu
85 90 95

Glu Gly Arg Ala Val Val His Trp Cys Ala Pro Phe Ser Pro Val Leu
100 105 110

His Tyr Trp Leu Leu Leu Trp Asp Gly Ser Glu Ala Ala Gln Lys Gly
115 120 125

Pro Pro Leu Asn Ala Thr Val Arg Arg Ala Glu Leu Lys Gly Leu Lys
130 135 140

Pro Gly Gly Ile Tyr Val Val Cys Val Val Ala Ala Asn Glu Ala Gly
145 150 155 160

Ala Ser Arg Val Pro Gln Ala Gly Gly Glu Gly Leu Glu Gly Ala Asp
165 170 175

Ile Pro Ala Phe Gly Pro Cys Ser Arg Leu Ala Val Pro Pro Asn Pro
180 185 190

Arg Thr Leu Val His Ala Ala Val Gly Val Gly Thr Ala Leu Ala Leu
195 200 205

Leu Ser Cys Ala Ala Leu Val Trp His Phe Cys Leu Arg Asp Arg Trp
210 215 220

342-10PCT.txt

Gly Cys Pro Arg Arg Ala Ala Ala Arg Ala Ala Gly Ala Leu
 225 230 235

<210> 249
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<220>
 <223> Oligonucleotide

<400> 249
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18

<210> 250
 <211> 18
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<220>
 <223> Oligonucleotide

<400> 250
 gccgtctcag tctcatct

18

<210> 251
 <211> 1024
 <212> DNA
 <213> Homo sapiens

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 acagtccgct gcgggccccg ggcgcctctc gaggccacgc gacggcccg accggctctt 240
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 ggttttattt tggttaacaag aagcacaatg tcttttttat ttttttttt tagtaaaactt 780
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 ttcacagcct cattcctgcc ttttctcagc cattacctcc caaacatagc agtttttctg 960
 agtttcatca cttttgattc attttgctg tttttgaact ttatataaat ggattttatac 1020

2015201738 07 Apr 2015

187/223

342-10PCT.txt

atta

1024

<210> 252
<211> 162
<212> PRT
<213> Homo sapiens

<400> 252

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

Val Arg Cys Gly Pro Gly Ala Pro Leu Glu Ala Thr Arg Arg Pro Ala
20 25 30

Pro Ala Leu Pro Pro Arg Gly Leu Pro Cys Tyr Ser Ser Gly Gly Ala
35 40 45

Pro Ser Asn Ser Gly Pro Gln Gly His Gly Glu Ile His Arg Val Pro
50 55 60

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

Gly Arg Phe Lys Ser Met Glu Glu Ile Pro Pro Arg Ile Pro Pro Glu
85 90 95

Met Ile Asp Thr Ala Arg Asn Lys Ala Arg Val Lys Ala Cys Tyr Ile
100 105 110

Met Ile Gly Leu Thr Ile Ile Ala Cys Phe Ala Val Ile Val Ser Ala
115 120 125

Lys Arg Ala Val Glu Arg His Glu Ser Leu Thr Ser Trp Asn Leu Ala
130 135 140

Lys Lys Ala Lys Trp Arg Glu Glu Ala Ala Leu Ala Ala Gln Ala Lys
145 150 155 160

Ala Lys

<210> 253
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 253
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19

<210> 254
<211> 22

2015201738 07 Apr 2015

188/223

342-10PCT.txt

<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 254
ttcccatctt ctactgttgc tg 22

<210> 255
<211> 852
<212> DNA
<213> Homo sapiens

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aagcttcctc tcagtgacca caatatgaat gggaacagca agatggcaaa agcttgctga 240
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gcagccaccc ctccatgtgg gccacagggg aggagcttag gaagccgcct tggcaagggt 720
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caacacaggg aa 852

<210> 256
<211> 110
<212> PRT
<213> Homo sapiens

<400> 256
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Pro Ser Pro Gln Val Leu Leu Leu Leu Leu Arg Glu Ala Pro Ser Thr
20 25 30
Ala Ala Ala Val Ala Gly Trp Leu Val Val Ala Ser Met Ala Leu Leu
35 40 45
Gln Leu His Ala Val Gly Gly Val Ala Leu Thr Ser Ser His Pro Ser
50 55 60

07 Apr 2015
2015201738

189/223

342-10PCT.txt

Met Trp Ala Thr Gly Glu Glu Leu Arg Lys Pro Pro Trp Gln Gly Ser
65 70 75 80

Ala Gly Ser Ala Ser Gly Val Glu Glu Leu Thr Gly Lys His Ser Cys
85 90 95

Pro Gly Pro Glu Glu Pro Ala Thr Val Gln Lys Ala Pro Ala
100 105 110

<210> 257
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 257
ttgctgttcc cattcata 18

<210> 258
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 258
gataaagtct ggttcctcc 19

<210> 259
<211> 4231
<212> DNA
<213> Homo sapiens

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gagtgccggg ctctgaggca cggccgtcga cttaaagcgtt gcatcctgtt acctggagac 180
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342-10PCT.txt

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342-10PCT.txt

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<210> 260
<211> 359
<212> PRT
<213> Homo sapiens

<400> 260

Met Gln Val Pro Asn Ser Thr Gly Pro Asp Asn Ala Thr Leu Gln Met
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Leu Arg Asn Pro Ala Ile Ala Val Ala Leu Pro Val Val Tyr Ser Leu
20 25 30

Val Ala Ala Val Ser Ile Pro Gly Asn Leu Phe Ser Leu Trp Val Leu
35 40 45

2015201738 07 Apr 2015

192/223

342-10PCT.txt

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

2015201738 07 Apr 2015

193/223

342-10PCT.txt

Arg Arg Glu Ser Leu Phe Ser Ala Arg Thr Thr Ser Val Arg Ser Glu
325 330 335

Ala Gly Ala His Pro Glu Gly Met Glu Gly Ala Thr Arg Pro Gly Leu
340 345 350

Gln Arg Gln Glu Ser Val Phe
355

<210> 261
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 261
cctgttacct ggagaccct 19

<210> 262
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 262
accagcgagt acaccacg 18

<210> 263
<211> 717
<212> DNA
<213> Homo sapiens

<400> 263
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ggaagaaact cgcattgtct actggatcaa ggacagacag ctaccaacc gtgacagcac 120
catactggaa cttcaaaaag ttctgaaaac atgttgtgct cagagcatga aaattttctg 180
ctgtcttttg aactttgtct acaaacagtt agaagatgca gccaagggc tcaccatggg 240
tggcgatgtt gaagaacatg aagaccttac tgctgatagc accatcttca aatttgtgga 300
agcttataca gagtgggagg tgaagagggtg gtcagacaac aatctgataa tgaaacaaac 360
aaatgtgaag agaagacgct tagatgatgt tggccctgaa ttggaaaagg ctgtctggga 420
gctcggtgc ccaccagca ttcagtgtct gctacctcct gtctgttatg cttgtgtctg 480
gttttttcaa gttttaattt tttttttaat tcttagtttt tgtgggtaca tagtaggtgt 540
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catggagaat ggggtaccca tcacatcaag catttatcct ttgtgttaca aacggtccag 660
ttagactctt ttagttatta ttaaaatgta caattaaatt atttttgact atagtca 717

194/223

342-10PCT.txt

<210> 264
<211> 171
<212> PRT
<213> Homo sapiens

<400> 264

Met Thr Glu Glu Thr Arg Ile Val Tyr Trp Ile Lys Asp Arg Gln Leu
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Thr Asn Arg Asp Ser Thr Ile Leu Glu Leu Gln Lys Val Leu Lys Thr
20 25 30

Cys Cys Ala Gln Ser Met Lys Ile Phe Cys Cys Leu Trp Asn Phe Val
35 40 45

Tyr Lys Gln Leu Glu Asp Ala Ala Gln Gly Leu Thr Met Gly Gly Asp
50 55 60

Val Glu Glu His Glu Asp Leu Thr Ala Asp Ser Thr Ile Phe Lys Phe
65 70 75 80

Val Glu Ala Tyr Thr Glu Trp Glu Val Lys Arg Trp Ser Asp Asn Asn
85 90 95

Leu Ile Met Lys Gln Thr Asn Val Lys Arg Arg Arg Leu Asp Asp Val
100 105 110

Gly Pro Glu Leu Glu Lys Ala Val Trp Glu Leu Gly Cys Pro Pro Ser
115 120 125

Ile Gln Cys Leu Leu Pro Pro Val Cys Tyr Ala Cys Val Trp Phe Phe
130 135 140

Gln Val Leu Ile Phe Phe Leu Ile Leu Ser Phe Cys Gly Tyr Ile Val
145 150 155 160

Gly Val Tyr Ile Tyr Gly Leu His Glu Met Phe
165 170

<210> 265
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 265
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<210> 266
<211> 20
<212> DNA
<213> Artificial Sequence

2015201738 07 Apr 2015

195/223
342-10PCT.txt

<220>
<223> Oligonucleotide

<400> 266
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<210> 267
<211> 390
<212> DNA
<213> Homo sapiens

<400> 267
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gatctggagg ttggagggtt agctggacag ccccttaaag ttttactcc acgtaaaaaa 180
ggttctgggg aagtgggtga tgcttctcag tcgcccagca gaagcaatga tggccagcat 240
tcctgcattg gccacagcag agatctctgc tgctacactg ctacagaccct cataatctcc 300
tacacatcaa atggctcttc tccttttagca actccaccct tccaccctat tcctggaaac 360
tgctacgaca gtgttgatta taaaatatag 390

<210> 268
<211> 129
<212> PRT
<213> Homo sapiens

<400> 268
Met Glu Val Ile Leu Pro Asp Lys Pro Gln Val Asp Ala Leu Ala Phe
1 5 10 15

Leu Ala Ala Val Thr Met Leu Trp Ile Thr Leu Pro Met Ser Pro Phe
20 25 30

Ala Glu Ala Glu Lys Leu Ala Trp Asp Leu Glu Val Gly Gly Leu Ala
35 40 45

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

Val Gly Asp Ala Ser Gln Ser Pro Ser Arg Ser Asn Asp Gly Gln His
65 70 75 80

Ser Cys Ile Gly His Ser Arg Asp Leu Cys Cys Tyr Thr Ala Gln Thr
85 90 95

Leu Ile Ile Ser Tyr Thr Ser Asn Gly Leu Ser Pro Leu Ala Thr Pro
100 105 110

Pro Phe His Pro Ile Pro Gly Asn Cys Tyr Asp Ser Val Asp Tyr Lys
115 120 125

2015201738 07 Apr 2015

196/223
342-10PCT.txt

Ile

<210> 269
<211> 2856
<212> DNA
<213> Homo sapiens

<400> 269
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cctgaactgg cagttccact cttcctagtg tttctcagtt tctatcttgt cacttttctg 120
gggaatgggg ggatgatcat tctaattcaa gtggatgccc aactccacac ccccggtgac 180
ttcttcctga gccaccttgc tttcctggat gcctgctgtg cctcagtaat cacccttcag 240
attctggcca cactggccac agacaagaca gttatctcct atggctgccg tgctgtgcag 300
ttctctttct tcaccatatg tgcaggcaca gagtgttacc tgctgtcagt gatggcctat 360
gaccgctttg ttgccattag caatccactg cactgtaaca tgaccatgac tccaggtacc 420
tgcagggtct ttttggccag tgccttcac tctgtgggtgt caggggccat tctgcatacc 480
acgtgcacct tcaccctctc cttctgttgt gacaatcaga tcaacttctt cttctgtgac 540
ctcccacccc tgctgaagct cgcctgcagc agcatgacac aaactgagat tgtcattctc 600
ctttgtgcaa aatgcatgtt cctagccaat gtcattggta tctgatctg ctacatgctc 660
attatcagag ccattttgag ggtgaagtcg gcaggaggcc tctgatagc atctgctcat 720
ttcgatgcat atgtatatga gacaggcatc aactacaaca cagtttatgg ctcaggaaag 780
gcagtagggg ggtcctggag gagcctgcgg gaaaccaacc acatgagacc aggaaatact 840
tcaaaacact cagcagccca gctgcatcaa tgcctcatcc agcaagttgg caggtggccc 900
ttgcagagca tgcccttccc cgtttctgca gggccacctt ataagtcagt gcagcctctc 960
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gcagcctccg gagcagccac tatgctgaca aaggggctgc ccgacatcac tgtgggactg 1380
cagatttatg actcctgcat ctcagggatc caggctctgg ggagcaccct ggccctgctg 1440
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gtggttggag ggatgacctt cctggagtca gagcccatgt ctgagctgct ctccatctac 1560
agagtccctc agggccaaag actcacaaa aactttgaag taaaagaact tgtctgcaca 1620
tatctggtag gacagcttcc ttatggcctg gtcagttatg acaacagcaa ctttgagtgg 1680
ctggatcagc agctgcagaa gcagatcggg ggcgaggggac ttcctgttgg cgctgcgccc 1740

2015201738 07 Apr 2015

197/223

342-10PCT.txt

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agccgtgtag ccaggcaaca gtctgatgag gaagctgtgg gaggagtgca gggatacagg 1800
tggtctggat taggggcttc catccaaagt gccagagaag gggcttggca tcgcacaggg 1860
ctggagaaca tgaccactgc ccacctgtct gccttcaaac ttcctgatct aactgccact 1920
taccaagcct acctggcagc caaagccctg tgggttgccct atcagaactt gatgtcctgc 1980
tctgagagag agggaccatt cctgggaggc acgtatgcca atgcatggga agccaggctt 2040
tctcaggtta acttcaccac caaagcccaa gaagaggttt tcttcgcca agatggggaa 2100
gtgctgacaa cgtttgacat taaaaacatc tatgtttctcc cagacctgtc aggacagaca 2160
gccattgttg gacactttga cttcagagca ctttctggaa aagagcttct gttggatgac 2220
agcgcaattg tctgggcaga aggaccctta aagattagag ctgagagaac cctaagaacc 2280
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atggccatgg aggtctttgt catcttggca tcagcaggag gcctcatgtc ctccctcttc 2760
ttttccaaat gctacatcat ccttctccat cctgaaaaga acacaaaaga ccaaattgtt 2820
ggccggcatc atcgcaagtg ggaaaaactg aagtga 2856

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<210> 270
 <211> 951
 <212> PRT
 <213> Homo sapiens
 <400> 270

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

Ser Phe Tyr Leu Val Thr Phe Leu Gly Asn Gly Gly Met Ile Ile Leu
 35 40 45

Ile Gln Val Asp Ala Gln Leu His Thr Pro Val Tyr Phe Phe Leu Ser
 50 55 60

His Leu Ala Phe Leu Asp Ala Cys Cys Ala Ser Val Ile Thr Pro Gln
 65 70 75 80

Ile Leu Ala Thr Leu Ala Thr Asp Lys Thr Val Ile Ser Tyr Gly Cys
 85 90 95

07 Apr 2015

198/223

342-10PCT.txt

Arg Ala Val Gln Phe Ser Phe-Phe Thr Ile Cys Ala Gly Thr Glu Cys
100 105 110

Tyr Leu Leu Ser Val Met Ala Tyr Asp Arg Phe Val Ala Ile Ser Asn
115 120 125

Pro Leu His Cys Asn Met Thr Met Thr Pro Gly Thr Cys Arg Val Phe
130 135 140

Leu Ala Ser Ala Phe Ile Cys Gly Val Ser Gly Ala Ile Leu His Thr
145 150 155 160

Thr Cys Thr Phe Thr Leu Ser Phe Cys Cys Asp Asn Gln Ile Asn Phe
165 170 175

Phe Phe Cys Asp Leu Pro Pro Leu Leu Lys Leu Ala Cys Ser Ser Met
180 185 190

Thr Gln Thr Glu Ile Val Ile Leu Leu Cys Ala Lys Cys Met Phe Leu
195 200 205

Ala Asn Val Met Val Ile Leu Ile Cys Tyr Met Leu Ile Ile Arg Ala
210 215 220

Ile Leu Arg Val Lys Ser Ala Gly Gly Leu Leu Ile Ala Ser Ala His
225 230 235 240

Phe Asp Ala Tyr Val Tyr Glu Thr Gly Ile Asn Tyr Asn Thr Val Tyr
245 250 255

Gly Ser Gly Lys Ala Val Gly Trp Ser Trp Arg Ser Leu Arg Glu Thr
260 265 270

Asn His Met Arg Pro Gly Asn Thr Ser Lys His Ser Ala Ala Gln Leu
275 280 285

His Gln Cys Leu Ile Gln Gln Val Gly Arg Trp Pro Leu Gln Ser Met
290 295 300

Pro Phe Pro Val Ser Ala Gly Pro Pro Tyr Lys Ser Val Gln Pro Leu
305 310 315 320

Pro Gly Asp Pro Arg Pro Leu Leu Cys Ile Thr Gly Leu Phe Leu Thr
325 330 335

Leu Lys Met Met Gly Cys Gly Pro Arg Arg Pro Arg Asp Arg Lys Ser
340 345 350

Asp Phe Phe Ile Asn Thr Asp Pro Gly Ala Gly Ser Pro Glu Glu Gln
355 360 365

2015201738 07 Apr 2015

199/223

342-10PCT.txt

Arg Cys Gly Trp Glu Gly His Pro Ser His Ser Tyr Thr Leu Gly Leu
370 375 380

Ser Leu Pro Val Asn Phe Gly Leu Lys Cys Pro Trp Trp Thr Leu Ser
385 390 395 400

Gly Pro Pro Ala Thr Cys Gln Arg Pro Asp Leu Gln Thr Pro Ser Pro
405 410 415

Pro Lys Glu Ile Cys Ser Ser Gly Leu Arg Pro Leu Thr His Ser Ala
420 425 430

Gly Pro Asp Arg Ser Gln Val Pro Ala Ala Ser Gly Ala Ala Thr Met
435 440 445

Leu Thr Lys Gly Leu Pro Asp Ile Thr Val Gly Leu Gln Ile Tyr Asp
450 455 460

Ser Cys Ile Ser Gly Ile Gln Ala Leu Gly Ser Thr Leu Ala Leu Leu
465 470 475 480

Ser Asn Gln Leu Pro Pro Thr Thr Asn Tyr Ala Cys Gly Ser Gln Gln
485 490 495

His Leu Leu Gly Val Val Gly Gly Met Thr Phe Leu Glu Ser Glu Pro
500 505 510

Met Ser Glu Leu Leu Ser Ile Tyr Arg Val Pro Gln Gly Gln Arg Leu
515 520 525

Thr Lys Asn Phe Glu Val Lys Glu Leu Val Cys Thr Tyr Leu Val Gly
530 535 540

Gln Leu Pro Tyr Gly Leu Val Ser Tyr Asp Asn Ser Asn Phe Glu Trp
545 550 555 560

Leu Asp Gln Gln Leu Gln Lys Gln Ile Gly Gly Glu Gly Leu Pro Val
565 570 575

Gly Ala Ala Pro Ser Arg Val Ala Arg Gln Gln Ser Asp Glu Glu Ala
580 585 590

Val Gly Gly Val Gln Gly Tyr Arg Trp Ser Gly Leu Gly Ala Ser Ile
595 600 605

Gln Ser Ala Arg Glu Gly Ala Trp His Arg Thr Gly Leu Glu Asn Met
610 615 620

Thr Thr Ala His Leu Ser Ala Phe Lys Leu Pro Asp Leu Thr Ala Thr
625 630 635 640

2015201738 07 Apr 2015

200/223

342-10PCT.txt

Tyr Gln Ala Tyr Leu₆₄₅ Ala Ala Lys Ala Leu₆₅₀ Trp Val Ala Tyr Gln Asn
Leu Met Ser Cys₆₆₀ Ser Glu Arg Glu Gly₆₆₅ Pro Phe Leu Gly Gly₆₇₀ Thr Tyr
Ala Asn Ala₆₇₅ Trp Glu Ala Arg Leu₆₈₀ Ser Gln Val Asn Phe₆₈₅ Thr Thr Lys
Ala Gln Glu Glu Val Phe₆₉₅ Phe Ala Lys Asp Gly Glu₇₀₀ Val Leu Thr Thr
Phe₇₀₅ Asp Ile Lys Asn Ile₇₁₀ Tyr Val Leu Pro Asp₇₁₅ Leu Ser Gly Gln Thr₇₂₀
Ala Ile Val Gly His₇₂₅ Phe Asp Phe Arg Ala₇₃₀ Pro Ser Gly Lys Glu Leu₇₃₅
Leu Leu Asp Asp₇₄₀ Ser Ala Ile Val Trp₇₄₅ Ala Glu Gly Pro Leu₇₅₀ Lys Ile
Arg Ala Glu₇₅₅ Arg Thr Leu Arg Thr Lys Thr Thr Gln His₇₆₅ Leu Ser His
Pro Lys₇₇₀ Leu Gln Glu Ser Leu₇₇₅ Pro Leu Ser Ala Thr₇₈₀ Lys Asn Val Leu
Trp Lys Pro Gly Ser Gln₇₉₀ Pro Tyr Leu Arg Ser₇₉₅ Gln Asn Ala Ala Thr₈₀₀
Lys Ala Phe Pro Asp₈₀₅ Pro Glu Glu Lys Ser₈₁₀ Gln Cys His Gln Phe₈₁₅ Leu
Phe Leu Pro Ser₈₂₀ Asp Ser Val Ala Cys₈₂₅ Gln Lys Cys Ser Asp₈₃₀ Asn Gln
Trp Pro Asn₈₃₅ Val Gln Lys Gly Glu₈₄₀ Cys Ile Pro Lys Thr₈₄₅ Leu Asp Phe
Leu Phe₈₅₀ Tyr His Lys Pro Leu₈₅₅ Asp Thr Ala Leu Ala₈₆₀ Val Cys Thr Ala
Leu₈₆₅ Leu Phe Leu Leu Ala₈₇₀ Leu Ala Ile Leu Gly₈₇₅ Ile Phe His Val Val₈₈₀
Cys Ser Cys Val Trp₈₈₅ Val Ser Phe Ile Pro Ala His Met His Ala₈₉₅ His
Ser Lys Asp Thr₉₀₀ Met Ala Met Glu Val₉₀₅ Phe Val Ile Leu Ala Ser Ala₉₁₀

201/223

342-10PCT.txt

Gly Gly Leu Met Ser Ser Leu Phe Phe Ser Lys Cys Tyr Ile Ile Leu
 915 920 925

Leu His Pro Glu Lys Asn Thr Lys Asp Gln Met Phe Gly Arg His His
 930 935 940

Arg Lys Trp Glu Lys Leu Lys
 945 950

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 <211> 956
 <212> DNA
 <213> Homo sapiens

<400> 271
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 gcaatgctgc tggctggccg catcaggctc cggaggatcg atgccttctg cacctgcctg 300
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 tcagcggtag ccgccacca tctcaggtgt ctcgatctgg gggagtttcc tgttttcaga 780
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<210> 272
 <211> 231
 <212> PRT
 <213> Homo sapiens

<400> 272

Ala Ala Leu Tyr Gly Ala Ser Gly His Phe Ala Pro Gly Thr Thr Val
 1 5 10 15

Pro Leu Ala Leu Pro Pro Gly Gly Asn Gly Ser Ala Thr Pro Asp Asn
 20 25 30

2015201738 07 Apr 2015

202/223

342-10PCT.txt

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

Pro Glu His Met Ala Glu Lys Leu Cys Glu Ala Trp Ala Phe Gly Gln
50 55 60

Ser His Gln Thr Gly Val Val Ala Leu Gly Leu Leu Thr Cys Leu Leu
65 70 75 80

Ala Met Leu Leu Ala Gly Arg Ile Arg Leu Arg Arg Ile Asp Ala Phe
85 90 95

Cys Thr Cys Leu Trp Ala Leu Leu Leu Gly Leu His Leu Ala Glu Gln
100 105 110

His Leu Gln Ala Ala Ser Pro Ser Trp Leu Asp Thr Leu Lys Phe Ser
115 120 125

Thr Thr Ser Leu Cys Cys Leu Val Gly Phe Thr Ala Ala Val Ala Thr
130 135 140

Arg Lys Ala Thr Gly Pro Arg Arg Phe Arg Pro Arg Arg Phe Phe Pro
145 150 155 160

Gly Asp Ser Ala Gly Leu Phe Pro Thr Ser Pro Ser Leu Ala Ile Pro
165 170 175

His Pro Ser Val Gly Gly Ser Pro Ala Ser Leu Phe Ile Pro Ser Pro
180 185 190

Pro Ser Phe Leu Pro Leu Ala Asn Gln Ala Ala Leu Pro Val Ser Ser
195 200 205

Thr Asp Leu Thr Leu Leu Ile Cys Leu Ala Ala Ser Ala Gly Pro Ser
210 215 220

Leu Trp Glu Pro Tyr Pro Leu
225 230

<210> 273

<211> 1806

<212> DNA

<213> Homo sapiens

<400> 273

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tacccccctg ccggcctgcc gtccttcac gcggagagcc atggagggag tgagcgcgct 180

gctggccccg tgccccacgg ccggcctggc cggcggcctg ggggtcacgg cgtgcgccgc 240

ggccggcgtg ttgctctacc ggatcgcgcg gaggatgaag ccaacgcaca cgatgggtcaa 300

2015201738 07 Apr 2015

203/223

342-10PCT.txt

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cgcccagtag	ttggagcacc	tgaaccacgt	ggtgagcagc	gcgcccagcc	tgcgcgaccc	480
ttcgcagccg	cagcagtggg	tgagcagcca	agtcctgctg	tgcaagaggt	gcaaccacca	540
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ccaagcggct	gtggagtact	acatcaagca	ccagaaccgc	cagctgcgcg	ccctgttgct	720
cagccaccag	ttcaagcgcc	gggaggccga	ccagaccac	gcacagaact	tctcctccgc	780
cgtgaagtcc	ccggtccagg	tcctcctgct	ccgtgccctc	gccttcctgg	cctgcgcctt	840
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cttcacggcg	gctgtggcca	caaggaaggc	aacggggcca	cggaggttcc	ggccccgaag	1320
gttctttcca	ggagactctg	ccggcctttt	ccccaccagc	cccagcttgg	ccatccctca	1380
cccagagtgc	ggaggctctc	cagcgtctct	gttcacccc	agcccgccca	gcttcctgcc	1440
cctcgccaac	caagcagctc	ttccgggtctc	ctcgacggac	ctcaccctcc	tcatttgcct	1500
ggccgcctca	gccgggccct	ctctctggga	accataccct	ctctgactcg	agcagactcc	1560
ggctatctgt	tcagcggtag	ccgcccacca	tctcaggtgt	ctcgatctgg	gggagtttcc	1620
tgttttcaga	ttactttctt	cttcttgctg	gggaagctgc	ccctccgtcc	catcctttcc	1680
cagggccttc	cgggggcggc	tcggtgggcc	tccagtccgg	ctctctggcc	acgggaggcc	1740
ctcatcagcc	tgccggtcaa	cctgaggggac	gaagtgtgtt	gtccggcacc	cctggagagg	1800
cccaaa						1806

<210> 274
 <211> 461
 <212> PRT
 <213> Homo sapiens

<400> 274

Met Glu Gly Val Ser Ala Leu Leu Ala Arg Cys Pro Thr Ala Gly Leu
 1 5 10 15

Ala Gly Gly Leu Gly Val Thr Ala Cys Ala Ala Ala Gly Val Leu Leu
 20 25 30

2015201738 07 Apr 2015

204/223

342-10PCT.txt

Tyr Arg Ile Ala Arg Arg Met Lys Pro Thr His Thr Met Val Asn Cys
35 40 45

Trp Phe Cys Asn Gln Asp Thr Leu Val Pro Tyr Gly Asn Arg Asn Cys
50 55 60

Trp Asp Cys Pro His Cys Glu Gln Tyr Asn Gly Phe Gln Glu Asn Gly
65 70 75 80

Asp Tyr Asn Lys Pro Ile Pro Ala Gln Tyr Leu Glu His Leu Asn His
85 90 95

Val Val Ser Ser Ala Pro Ser Leu Arg Asp Pro Ser Gln Pro Gln Gln
100 105 110

Trp Val Ser Ser Gln Val Leu Leu Cys Lys Arg Cys Asn His His Gln
115 120 125

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

Arg Tyr Asp Glu Glu Val Glu Val Tyr Arg His His Leu Glu Gln Met
145 150 155 160

Tyr Lys Leu Cys Arg Pro Cys Gln Ala Ala Val Glu Tyr Tyr Ile Lys
165 170 175

His Gln Asn Arg Gln Leu Arg Ala Leu Leu Leu Ser His Gln Phe Lys
180 185 190

Arg Arg Glu Ala Asp Gln Thr His Ala Gln Asn Phe Ser Ser Ala Val
195 200 205

Lys Ser Pro Val Gln Val Ile Leu Leu Arg Ala Leu Ala Phe Leu Ala
210 215 220

Cys Ala Phe Leu Leu Thr Thr Ala Leu Tyr Gly Ala Ser Gly His Phe
225 230 235 240

Ala Pro Gly Thr Thr Val Pro Leu Ala Leu Pro Pro Gly Gly Asn Gly
245 250 255

Ser Ala Thr Pro Asp Asn Gly Thr Thr Pro Gly Ala Glu Gly Trp Arg
260 265 270

Gln Leu Leu Gly Leu Leu Pro Glu His Met Ala Glu Lys Leu Cys Glu
275 280 285

Ala Trp Ala Phe Gly Gln Ser His Gln Thr Gly Val Val Ala Leu Gly
290 295 300

2015201738 07 Apr 2015

205/223

342-10PCT.txt

Leu Leu Thr Cys Leu Leu Ala Met Leu Leu Ala Gly Arg Ile Arg Leu
305 310 315 320

Arg Arg Ile Asp Ala Phe Cys Thr Cys Leu Trp Ala Leu Leu Leu Gly
325 330 335

Leu His Leu Ala Glu Gln His Leu Gln Ala Ala Ser Pro Ser Trp Leu
340 345 350

Asp Thr Leu Lys Phe Ser Thr Thr Ser Leu Cys Cys Leu Val Gly Phe
355 360 365

Thr Ala Ala Val Ala Thr Arg Lys Ala Thr Gly Pro Arg Arg Phe Arg
370 375 380

Pro Arg Arg Phe Phe Pro Gly Asp Ser Ala Gly Leu Phe Pro Thr Ser
385 390 395 400

Pro Ser Leu Ala Ile Pro His Pro Ser Val Gly Gly Ser Pro Ala Ser
405 410 415

Leu Phe Ile Pro Ser Pro Pro Ser Phe Leu Pro Leu Ala Asn Gln Ala
420 425 430

Ala Leu Pro Val Ser Ser Thr Asp Leu Thr Leu Leu Ile Cys Leu Ala
435 440 445

Ala Ser Ala Gly Pro Ser Leu Trp Glu Pro Tyr Pro Leu
450 455 460

<210> 275
<211> 600
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (460)..(461)
<223> any

<220>
<221> misc_feature
<222> (530)..(531)
<223> any

<220>
<221> misc_feature
<222> (574)..(575)
<223> any

<220>
<221> misc_feature
<222> (577)..(578)
<223> any

2015201738 07 Apr 2015

206/223
342-10PCT.txt

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<400> 275
tcaagtctga cttgcatcta cactgcgggc aagatgcggc tgcaagaccg catcgccacg      60
ttcttcttcc caaaaggcat gatgctcacc acggctgcgc tgatgctctt cttcttacac      120
ctgggcatct tcatacagaga cgtgcacaac ttctgcatca cctaccacta tgaccacatg      180
agctttcact acacggtcgt cctgatgttc tcccagggtga tcagcatctg ctgggctgcc      240
atgggggtcac tctatgctga gatgacagaa aacaagtacg tctgcttctc cgccctgacc      300
atcctgagtg agtggcagga gggggagggg gcaagaggga gcggggagct ttggaaccct      360
gagatgtggc aaggagtagc cagggaaggg tactggggct catggggggc tctgtcccc      420
gcccagtgct caacggagcc atgctcttca accgcctgtt cttggagttt ctggccatcg      480
agtaccggga ggagcaccac tgaggcctgg ggagtcggaa cagggtctaan gagggggaag      540
caaaaggctg cctcgggtgt ttaataaag ctgntgntta tttccaaaaa aaaaaaaaaa      600
```

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<210> 276
<211> 174
<212> PRT
<213> Homo sapiens
```

```
<220>
<221> MISC_FEATURE
<222> (128)..(129)
<223> i
```

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<220>
<221> MISC_FEATURE
<222> (151)..(152)
<223> any
```

```
<220>
<221> MISC_FEATURE
<222> (166)..(168)
<223> any
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<400> 276
Met Met Leu Thr Thr Ala Ala Leu Met Leu Phe Phe Leu His Leu Gly
1          5          10          15
Ile Phe Ile Arg Asp Val His Asn Phe Cys Ile Thr Tyr His Tyr Asp
20          25          30
His Met Ser Phe His Tyr Thr Val Val Leu Met Phe Ser Gln Val Ile
35          40          45
Ser Ile Cys Trp Ala Ala Met Gly Ser Leu Tyr Ala Glu Met Thr Glu
50          55          60
Asn Lys Tyr Val Cys Phe Ser Ala Leu Thr Ile Leu Ser Glu Trp Gln
65          70          75          80
```

2015201738 07 Apr 2015

207/223

342-10PCT.txt

Glu Gly Glu Gly Ala Arg Gly Ser Gly Glu Leu Trp Asn Pro Glu Met
85 90 95

Trp Gln Gly Val Ala Arg Glu Gly Tyr Trp Gly Ser Trp Gly Ala Leu
100 105 110

Ser Pro Ala Gln Cys Ser Thr Glu Pro Cys Ser Ser Thr Ala Cys Xaa
115 120 125

Trp Ser Phe Trp Pro Ser Ser Thr Gly Arg Ser Thr Thr Glu Ala Trp
130 135 140

Gly Val Gly Thr Gly Leu Xaa Arg Gly Lys Gln Lys Ala Ala Ser Gly
145 150 155 160

Val Leu Ile Lys Leu Xaa Xaa Ile Ser Lys Lys Lys Lys Lys
165 170

<210> 277
<211> 457
<212> DNA
<213> Homo sapiens

<400> 277
aaacactgca ggctacgaat cggctcattgc atagggttttc catgaatcag gaagattcag 60
tccttggtaaa ttcatgccca ggaacatcgc tgccactgct attattctag cagctgttcc 120
catactccaa tgagtccagt taaacatttg ccttcttggg tcatgtaaag gtggcctgaa 180
gactgccaga agaggctgaa gaactgccaa agtcatcact atacagccga ggtatgggtg 240
gtaacctgca tgcctactcc agcctcccct gtatataaac ggcataacaa aagcaatgca 300
ggtagaggaca gttgtggtga acatgagcat ccgatgcacc tgaaaccaag ctgcttcacc 360
aagcaagaaa gcttttgacc aaactggctt gaagaaccgg gcaaccagta cacctatgct 420
aacagtagtc atccatgcca caaacattaa ggcacca 457

<210> 278
<211> 144
<212> PRT
<213> Homo sapiens

<400> 278

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

Arg Phe Phe Lys Pro Val Trp Ser Lys Ala Phe Leu Leu Gly Glu Ala
20 25 30

Ala Trp Phe Gln Val His Arg Met Leu Met Phe Thr Thr Thr Val Leu
35 40 45

Thr Cys Ile Ala Phe Val Met Pro Phe Ile Tyr Arg Gly Gly Trp Ser
50 55 60

2015201738 07 Apr 2015

208/223

342-10PCT.txt

Arg His Ala Gly Tyr His Pro Tyr Leu Gly Cys Ile Val Met Thr Leu
65 70 75 80

Ala Val Leu Gln Pro Leu Leu Ala Val Phe Arg Pro Pro Leu His Asp
85 90 95

Pro Arg Arg Gln Met Phe Asn Trp Thr His Trp Ser Met Gly Thr Ala
100 105 110

Ala Arg Ile Ile Ala Val Ala Ala Met Phe Leu Gly Met Asn Leu Pro
115 120 125

Gly Leu Asn Leu Pro Asp Ser Trp Lys Thr Tyr Ala Met Thr Asp Ser
130 135 140

<210> 279
<211> 293
<212> DNA
<213> Homo sapiens

<400> 279
tttttttttt tttttttaag gctgaagcaa ataggaacgt atatttctca tgaatccaaa 60
gcaaagacac aggaagtgtt ggcatctttt tgggtggctgg tagctcttga ctttctcttc 120
aagggttgcca catgccttag cagcagctca tgacttcacg ttctcaccgt attcgaaggc 180
aggaagcatg gagtagctgg cagctgcgtt tgacacagac tgccctcgga ccccttctcc 240
gcgcagtgcg actcgcaatt gtctggagca cgttggcagc agccctcgtg ccg 293

<210> 280
<211> 45
<212> PRT
<213> Homo sapiens

<400> 280

Arg His Glu Gly Cys Cys Gln Arg Ala Pro Asp Asn Cys Glu Ser His
1 5 10 15

Cys Ala Glu Lys Gly Ser Glu Gly Ser Leu Cys Gln Thr Gln Leu Pro
20 25 30

Ala Thr Pro Cys Phe Leu Pro Ser Asn Thr Val Arg Thr
35 40 45

<210> 281
<211> 15
<212> PRT
<213> Homo sapiens

<400> 281

Cys Gln Lys Gln Arg Asn Trp His Gly Ile Trp Arg Leu Glu Val
1 5 10 15

2015201738 07 Apr 2015

209/223

342-10PCT.txt

<210> 282
<211> 13
<212> PRT
<213> Homo sapiens

<400> 282

Met Ala Lys Gln Gly Glu Met Asn Thr Ser Thr Ser Cys
1 5 10

<210> 283
<211> 13
<212> PRT
<213> Homo sapiens

<400> 283

Pro Lys Arg Gly Gly Arg Ala Gly Arg Glu His Ser Cys
1 5 10

<210> 284
<211> 91
<212> PRT
<213> Homo sapiens

<400> 284

Arg Phe Gln Arg Asn Thr Gly Glu Met Ser Ser Asn Ser Thr Ala Leu
1 5 10 15

Ala Leu Val Arg Pro Ser Ser Ser Gly Leu Ile Asn Ser Asn Thr Asp
20 25 30

Asn Asn Leu Ala Val Tyr Asp Leu Ser Arg Asp Ile Leu Asn Asn Phe
35 40 45

Pro His Ser Ile Ala Arg Gln Lys Arg Ile Leu Val Asn Leu Ser Met
50 55 60

Val Glu Asn Lys Leu Val Glu Leu Glu His Thr Leu Leu Ser Lys Gly
65 70 75 80

Phe Arg Gly Ala Ser Pro His Arg Lys Ser Thr
85 90

<210> 285
<211> 15
<212> PRT
<213> Homo sapiens

<400> 285

Cys Lys Tyr Arg Arg Phe Gln Arg Asn Thr Gly Glu Met Ser Ser
1 5 10 15

<210> 286
<211> 14
<212> PRT

07 Apr 2015
2015201738

210/223

342-10PCT.txt

<213> Homo sapiens

<400> 286

1 Lys Lys Gly Phe Arg Gly Ala Ser Pro His Arg Lys Ser Thr
5 10

<210> 287

<211> 19

<212> PRT

<213> Homo sapiens

<400> 287

1 Met Ala Cys Ile Tyr Pro Thr Thr Phe Tyr Thr Ser Leu Pro Thr Lys
5 10 15

Ser Leu Asn

<210> 288

<211> 121

<212> PRT

<213> Homo sapiens

<400> 288

1 Ala Pro Pro Ser Cys Arg Glu Cys Tyr Gln Ser Leu His Tyr Arg Gly
5 10 15

Glu Met Gln Gln Tyr Phe Thr Tyr His Thr His Ile Glu Arg Ser Cys
20 25 30

Tyr Gly Asn Leu Ile Glu Glu Cys Val Glu Ser Gly Lys Ser Tyr Tyr
35 40 45

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

Pro Arg Gly Lys Gln Trp Leu Cys Phe Thr Lys Ile Gly Gln Trp Gly
65 70 75 80

Val Asn Thr Gln Val Leu Glu Asp Ile Lys Arg Glu Gln Ile Ile Ala
85 90 95

Lys Ala Lys Ala Ser Lys Pro Thr Thr Pro Pro Glu Asn Arg Pro Arg
100 105 110

His Phe His Ser Phe Ile Gln Lys Leu
115 120

<210> 289

<211> 15

<212> PRT

<213> Homo sapiens

<400> 289

2015201738 07 Apr 2015

211/223

342-10PCT.txt

Cys Glu Asn Arg Pro Arg His Phe His Ser Phe Ile Gln Lys Leu
1 5 10 15

<210> 290
<211> 13
<212> PRT
<213> Homo sapiens

<400> 290

Cys Ile Tyr Pro Thr Thr Phe Tyr Thr Ser Leu Pro Thr
1 5 10

<210> 291
<211> 14
<212> PRT
<213> Homo sapiens

<400> 291

Cys Lys Glu Asp Glu Leu Val Arg Asp Ser Pro Ala Arg Lys
1 5 10

<210> 292
<211> 12
<212> PRT
<213> Homo sapiens

<400> 292

Ala Leu Gly Thr Arg Leu Ser Gln His Thr Asp Val
1 5 10

<210> 293
<211> 11
<212> PRT
<213> Homo sapiens

<400> 293

Asp Phe Asn Cys Pro Cys Leu Val His Tyr Asn
1 5 10

<210> 294
<211> 53
<212> PRT
<213> Homo sapiens

<400> 294

Ser Ser Ser Val Asp Pro Glu Lys Phe Leu Asp Phe Ala Asn Met Thr
1 5 10 15

Pro Ser Gln Val Gln Leu Phe Leu Ala Lys Val Pro Cys Lys Glu Asp
20 25 30

Glu Leu Val Arg Asp Ser Pro Ala Arg Lys Ala Val Ser Arg Tyr Leu
35 40 45

2015201738 07 Apr 2015

212/223

342-10PCT.txt

Arg Cys Leu Ser Gln
50

<210> 295
<211> 146
<212> PRT
<213> Homo sapiens

<400> 295

Arg Cys Leu Arg Pro Cys Phe Asp Gln Thr Val Phe Leu Gln Arg Arg
1 5 10 15

Tyr Trp Ser Asn Tyr Val Asp Leu Glu Gln Lys Leu Phe Asp Glu Thr
20 25 30

Cys Cys Glu His Ala Arg Asp Phe Ala His Arg Cys Val Leu His Phe
35 40 45

Phe Ala Ser Met Arg Ser Glu Leu Gln Ala Arg Gly Leu Arg Arg Gly
50 55 60

Asn Ala Gly Arg Arg Leu Glu Leu Pro Ala Val Pro Glu Pro Pro Glu
65 70 75 80

Gly Leu Asp Ser Gly Ser Gly Lys Ala His Leu Arg Ala Ile Ser Ser
85 90 95

Arg Glu Gln Val Asp Arg Leu Leu Ser Thr Trp Tyr Ser Ser Lys Pro
100 105 110

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

His Arg Ala Pro Thr Leu Ala Leu Gly Thr Arg Leu Ser Gln His Thr
130 135 140

Asp Val
145

<210> 296
<211> 1035
<212> PRT
<213> Homo sapiens

<400> 296

Met Pro Cys Gly Phe Ser Pro Ser Pro Val Ala His His Leu Val Pro
1 5 10 15

Gly Pro Pro Asp Thr Pro Ala Gln Gln Leu Arg Cys Gly Trp Thr Val
20 25 30

Gly Gly Trp Leu Leu Ser Leu Val Arg Gly Leu Leu Pro Cys Leu Pro
35 40 45

2015201738 07 Apr 2015

213/223

342-10PCT.txt

Pro Gly Ala Arg Thr Ala Glu Gly Pro Ile Met Val Leu Ala Gly Pro
50 55 60

Leu Ala Val Ser Leu Leu Leu Pro Ser Leu Thr Leu Leu Val Ser His
65 70 75 80

Leu Ser Ser Ser Gln Asp Val Ser Ser Glu Pro Ser Ser Glu Gln Gln
85 90 95

Leu Cys Ala Leu Ser Lys His Pro Thr Val Ala Phe Glu Asp Leu Gln
100 105 110

Pro Trp Val Ser Asn Phe Thr Tyr Pro Gly Ala Arg Asp Phe Ser Gln
115 120 125

Leu Ala Leu Asp Pro Ser Gly Asn Gln Leu Ile Val Gly Ala Arg Asn
130 135 140

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

Glu Trp Ala Ser Ser Glu Asp Thr Arg Arg Ser Cys Gln Ser Lys Gly
165 170 175

Lys Thr Glu Glu Glu Cys Gln Asn Tyr Val Arg Val Leu Ile Val Ala
180 185 190

Gly Arg Lys Val Phe Met Cys Gly Thr Asn Ala Phe Ser Pro Met Cys
195 200 205

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

Gly Val Ala Arg Cys Pro Tyr Asp Pro Arg His Asn Ser Thr Ala Val
225 230 235 240

Ile Ser Ser Gln Gly Glu Leu Tyr Ala Ala Thr Val Ile Asp Phe Ser
245 250 255

Gly Arg Asp Pro Ala Ile Tyr Arg Ser Leu Gly Ser Gly Pro Pro Leu
260 265 270

Arg Thr Ala Gln Tyr Asn Ser Lys Trp Leu Asn Glu Pro Asn Phe Val
275 280 285

Ala Ala Tyr Asp Ile Gly Leu Phe Ala Tyr Phe Phe Leu Arg Glu Asn
290 295 300

Ala Val Glu His Asp Cys Gly Arg Thr Val Tyr Ser Arg Val Ala Arg
305 310 315 320

2015201738 07 Apr 2015

214/223

342-10PCT.txt

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

2015201738 07 Apr 2015

215/223
342-10PCT.txt

Leu Trp Thr Gln Asn Ile Thr Ala Cys Pro Val Arg Asn Val Thr Arg
595 600 605

Asp Gly Gly Phe Gly Pro Trp Ser Pro Trp Gln Pro Cys Glu His Leu
610 615 620

Asp Gly Asp Asn Ser Gly Ser Cys Leu Cys Arg Ala Arg Ser Cys Asp
625 630 635 640

Ser Pro Arg Pro Arg Cys Gly Gly Leu Asp Cys Leu Gly Pro Ala Ile
645 650 655

His Ile Ala Asn Cys Ser Arg Asn Gly Ala Trp Thr Pro Trp Ser Ser
660 665 670

Trp Ala Leu Cys Ser Thr Ser Cys Gly Ile Gly Phe Gln Val Arg Gln
675 680 685

Arg Ser Cys Ser Asn Pro Ala Pro Arg His Gly Gly Arg Ile Cys Val
690 695 700

Gly Lys Ser Arg Glu Glu Arg Phe Cys Asn Glu Asn Thr Pro Cys Pro
705 710 715 720

Val Pro Ile Phe Trp Ala Ser Trp Gly Ser Trp Ser Lys Cys Ser Ser
725 730 735

Asn Cys Gly Gly Gly Met Gln Ser Arg Arg Arg Ala Cys Glu Asn Gly
740 745 750

Asn Ser Cys Leu Gly Cys Gly Val Glu Phe Lys Thr Cys Asn Pro Glu
755 760 765

Gly Cys Pro Glu Val Arg Arg Asn Thr Pro Trp Thr Pro Trp Leu Pro
770 775 780

Val Asn Val Thr Gln Gly Gly Ala Arg Gln Glu Gln Arg Phe Arg Phe
785 790 795 800

Thr Cys Arg Ala Pro Leu Ala Asp Pro His Gly Leu Gln Phe Gly Arg
805 810 815

Arg Arg Thr Glu Thr Arg Thr Cys Pro Ala Asp Gly Ser Gly Ser Cys
820 825 830

Asp Thr Asp Ala Leu Val Glu Val Leu Leu Arg Ser Gly Ser Thr Ser
835 840 845

Pro His Thr Val Ser Gly Gly Trp Ala Ala Trp Gly Pro Trp Ser Ser
850 855 860

2015201738 07 Apr 2015

216/223

342-10PCT.txt

Cys Ser Arg Asp Cys Glu Leu Gly Phe Arg Val Arg Lys Arg Thr Cys
865 870 875 880

Thr Asn Pro Glu Pro Arg Asn Gly Gly Leu Pro Cys Val Gly Asp Ala
885 890 895

Ala Glu Tyr Gln Asp Cys Asn Pro Gln Ala Cys Pro Val Arg Gly Ala
900 905 910

Trp Ser Cys Trp Thr Ser Trp Ser Pro Cys Ser Ala Ser Cys Gly Gly
915 920 925

Gly His Tyr Gln Arg Thr Arg Ser Cys Thr Ser Pro Ala Pro Ser Pro
930 935 940

Gly Glu Asp Ile Cys Leu Gly Leu His Thr Glu Glu Ala Leu Cys Ala
945 950 955 960

Thr Gln Ala Cys Pro Glu Gly Trp Ser Pro Trp Ser Glu Trp Ser Lys
965 970 975

Cys Thr Asp Asp Gly Ala Gln Ser Arg Ser Arg His Cys Glu Glu Leu
980 985 990

Leu Pro Gly Ser Ser Ala Cys Ala Gly Asn Ser Ser Gln Ser Arg Pro
995 1000 1005

Cys Pro Tyr Ser Glu Ile Pro Val Ile Leu Pro Ala Ser Ser Met
1010 1015 1020

Glu Glu Ala Thr Asp Cys Ala Gly Phe Asn Leu Ile
1025 1030 1035

<210> 297
<211> 16
<212> PRT
<213> Homo sapiens

<400> 297

Cys Pro Tyr Asp Pro Arg His Asn Ser Thr Ala Val Ile Ser Ser Gln
1 5 10 15

<210> 298
<211> 11
<212> PRT
<213> Homo sapiens

<400> 298

Cys Pro Glu Val Arg Arg Asn Thr Pro Trp Thr
1 5 10

2015201738 07 Apr 2015

217/223

342-10PCT.txt

<210> 299
<211> 35
<212> PRT
<213> Homo sapiens

<400> 299

Glu Arg Val Trp Ser Asp Asp His Lys Asp Phe Asp Cys Asn Thr Arg
1 5 10 15

Gln Pro Gly Cys Ser Asn Val Cys Phe Asp Glu Phe Phe Pro Val Ser
20 25 30

His Val Arg
35

<210> 300
<211> 38
<212> PRT
<213> Homo sapiens

<400> 300

His Ser Phe Tyr Pro Lys Tyr Ile Leu Pro Pro Val Val Lys Cys His
1 5 10 15

Ala Asp Pro Cys Pro Asn Ile Val Asp Cys Phe Ile Ser Lys Pro Ser
20 25 30

Glu Lys Asn Ile Phe Thr
35

<210> 301
<211> 15
<212> PRT
<213> Homo sapiens

<400> 301

Cys Leu Pro Asp Arg Pro Arg Asp His Val Lys Lys Thr Ile Leu
1 5 10 15

<210> 302
<211> 13
<212> PRT
<213> Homo sapiens

<400> 302

Glu Arg Val Trp Ser Asp Asp His Lys Asp Phe Asp Cys
1 5 10

<210> 303
<211> 38
<212> PRT
<213> Homo sapiens

<400> 303

Asn Asn Asp Val Ser Cys Asp His Pro Ser Asn Thr Val Pro Ser Gly

218/223

342-10PCT.txt
10

1 5 15

Ser Asn Gln Asp Leu Gly Ala Gly Ala Gly Glu Asp Ala Arg Ser Asp
20 25 30

Asp Ser Ser Ser Arg Ile
35

<210> 304
<211> 15
<212> PRT
<213> Homo sapiens

<400> 304

Cys Asp His Pro Ser Asn Thr Val Pro Ser Gly Ser Asn Gln Asp
1 5 10 15

<210> 305
<211> 12
<212> PRT
<213> Homo sapiens

<400> 305

Cys Val Pro His Ser Arg Ser Arg Gly Pro Asn Leu
1 5 10

<210> 306
<211> 12
<212> PRT
<213> Homo sapiens

<400> 306

Cys Glu Leu Ser Gln Thr Pro His Pro His Ser Arg
1 5 10

<210> 307
<211> 14
<212> PRT
<213> Homo sapiens

<400> 307

Cys Leu Asp Ser Ala Gly Asn Asn Ala Gly Ile Gln Trp Gly
1 5 10

<210> 308
<211> 14
<212> PRT
<213> Homo sapiens

<400> 308

Cys Asn Arg Val Ser Lys Asn Pro Glu Met Leu Gln Thr Gly
1 5 10

<210> 309
<211> 2115

2015201738 07 Apr 2015

219/223

342-10PCT.txt

<212> DNA
<213> Homo sapiens

<400> 309

atgcgtatat	gttatgaatg	ccaaaatgaa	agaacattgt	ggcgaatgtgt	ttcccaggat	60
ggggctgact	acagtgtggg	cgtgtgtgtc	cctgattctt	gtgtgaaga	ggatgtgact	120
ctgatgtctc	ggctggatac	tttaagattc	agaaatactt	catttttggc	cccttccttc	180
tttcttttta	caataaattc	ttcctccttg	tctggtggga	gtgtgaccag	atgtgctgct	240
ggaaagatcc	ccctggacac	atgtgtgcc	gtatgtctgt	tcacacctt	gctgggtctc	300
atcctccctc	cggctggaac	agtctgcgtg	gcagctaggg	aatgggggtc	agcctgcagg	360
acatcgcggg	aacacgggga	acctctggcc	acttacggga	gtctgccact	gagcgaggcg	420
gagagcaatg	aacaaagaag	cagaatccca	cggacacact	gccgggcaca	tctcctcctg	480
tcagcagcct	ccagcagagg	aaaaaggttt	ctaggagccg	tggctcatgc	tctggagtgc	540
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2015201738 07 Apr 2015

220/223

342-10PCT.txt

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gaatgttctg gttaa 2115

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<211> 704
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20 25 30

Ser Cys Ala Glu Glu Asp Val Thr Leu Met Ser Arg Leu Asp Thr Leu
35 40 45

Arg Phe Arg Asn Thr Ser Phe Leu Ala Pro Ser Leu Phe Leu Phe Thr
50 55 60

Ile Asn Ser Ser Ser Leu Ser Gly Gly Ser Val Thr Arg Cys Ala Ala
65 70 75 80

Gly Lys Ile Pro Leu Asp Thr Phe Ala Ala Val Cys Leu Phe Ile Thr
85 90 95

Leu Leu Gly Leu Ile Leu Pro Pro Ala Gly Thr Val Cys Val Ala Ala
100 105 110

Arg Glu Trp Gly Ser Ala Cys Arg Thr Ser Arg Glu His Gly Glu Pro
115 120 125

Leu Ala Thr Tyr Gly Ser Leu Pro Leu Ser Glu Ala Glu Ser Asn Glu
130 135 140

Gln Arg Ser Arg Ile Pro Arg Thr His Cys Arg Ala His Leu Leu Leu
145 150 155 160

Ser Ala Ala Ser Ser Arg Gly Lys Arg Phe Leu Gly Ala Val Ala His
165 170 175

Ala Leu Glu Cys Phe Ser Trp Gln Lys Asn Val Pro Ala Ile Trp Thr
180 185 190

Thr Lys Ala Pro Gly Gly Thr Cys Ser Ala Leu Asn Gly Ile Arg Val
195 200 205

2015201738 07 Apr 2015

221/223

342-10PCT.txt

Leu Ser Leu Leu Trp Ile Ile Ser Gly His Thr Ser Gln Met Thr Ala
210 215 220

Trp Leu Ser Leu Gly Trp Lys Asp Gly Gly His Glu Arg Pro Leu Val
225 230 235 240

Met Ser Gly Pro Ser Val Gly Ile Gly Asp Thr Arg Glu Ala Thr Ser
245 250 255

Gly Trp Leu Ser Ala Ser Ser Phe Leu Lys Met His Gln Asn Ser Asp
260 265 270

Lys Gly Ile Thr Pro Lys Gly Ile Leu Arg Tyr Phe Leu Ser His Leu
275 280 285

Val Arg Leu Gln Pro Leu His Leu Tyr Ser Met Cys Leu Leu Val Gly
290 295 300

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

His Trp Asp Asn Cys Arg Gln Ala Trp Trp Thr Asn Leu Leu Leu Leu
325 330 335

Asn Asn Phe Val Ser Val Lys Asn Ala Cys Asn Gly Trp Thr Trp Tyr
340 345 350

Leu Ala Asn Asp Phe Gln Phe His Leu Thr Thr Pro Val Ile Ile Phe
355 360 365

Ile His Val Lys Ser Thr Gln Ile Leu Ile Leu Leu Gly Ala Met Leu
370 375 380

Phe Leu Ala Ser Phe Thr Ala Thr Ala Leu Ile Thr Leu Ala Tyr Lys
385 390 395 400

Leu Pro Val Val Ala Pro Ser Glu Thr Arg Thr Ser Arg Gly Gly Leu
405 410 415

Leu Asn Ala Arg Leu Phe Thr Leu Cys Pro Leu Val His Gly Lys Ser
420 425 430

Gly Tyr Glu Thr Phe Gly Leu Asp Gly Lys Ala Asp Cys Leu Leu Ala
435 440 445

Ser Lys Leu Leu Asn Leu Ser Thr Cys Thr Gly Asn Glu Gln Val Cys
450 455 460

Pro Lys Cys Thr Phe Gly Leu Ala Asp Tyr Ser Asn Gly His Leu Arg
465 470 475 480

222/223

342-10PCT.txt

Asp Leu Asp Ser Leu Cys His Val Gln Ile Lys His Asn Ile Leu Ala
485 490 495

Tyr Phe Leu Val Phe Phe Ser Glu Glu Ala Ile Val Leu Tyr Phe Val
500 505 510

Glu Tyr Tyr Thr Lys Pro Tyr Cys Arg Phe Gly Pro Val Leu Val Gly
515 520 525

Leu Phe Leu Ser Ile Tyr Met His Gln Asn His Gln Glu Asn Ile Leu
530 535 540

Arg Thr Lys Leu Gln Leu Ser Thr Lys Pro Ser Thr Gly Pro Cys Gly
545 550 555 560

Arg Arg Leu Trp Ala Glu Ser Ser Leu Arg Ala Thr Glu Asp Met Glu
565 570 575

Val Trp Lys Arg Leu Gln Ala Leu Leu Ser Gly Ser His Pro Val Pro
580 585 590

Leu Lys Val Thr Asn Arg Thr His Arg Arg Ala Lys Gln Ile Lys Gly
595 600 605

Phe Asn Gly Lys Glu Ser Ser Pro Gly Leu Val Asn Arg Val Leu Ser
610 615 620

Trp Asp Ile Trp Ser Phe Leu Ser Ser Ile Ser Tyr Ala Arg Tyr Leu
625 630 635 640

Val His Pro Ile Leu Ile Ile Leu Tyr Asn Gly Leu Gln Glu Thr Leu
645 650 655

Ile His His Thr Asp Thr Asn Met Phe Tyr Leu Phe Ser Gly His Arg
660 665 670

Val Leu Thr Phe Val Thr Gly Leu Ala Leu Thr Leu Phe Ile Glu Lys
675 680 685

Pro Cys Gln Glu Leu Lys Gln His Leu Leu Gly His Glu Cys Ser Gly
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<213> Artificial Sequence

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223/223

342-10PCT.txt

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