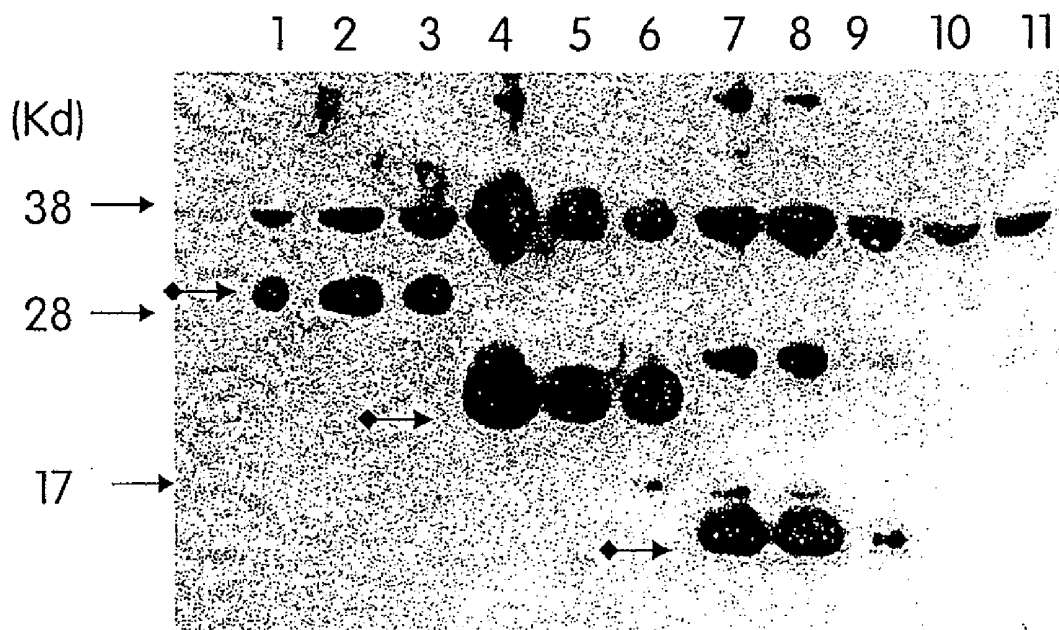




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(19) **United States**(12) **Patent Application Publication**
Scanlan et al.(10) **Pub. No.: US 2010/0172910 A1**(43) **Pub. Date: Jul. 8, 2010**(54) **HUMAN SARCOMA-ASSOCIATED
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Research Ltd.**, New York, NY (US)(21) Appl. No.: **12/683,374**(22) Filed: **Jan. 6, 2010****Related U.S. Application Data**(60) Division of application No. 10/529,655, filed on Nov.
28, 2006, now Pat. No. 7,662,917, filed as application
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(52) **U.S. Cl.** **424/139.1**; 530/387.9; 436/501;
530/391.3; 435/7.2; 530/387.3; 530/391.7(57) **ABSTRACT**

The invention relates to sarcoma-associated antigens and the nucleic acid molecules that encode them. The invention further relates to the use of the nucleic acid molecules, polypeptides and fragments thereof associated with sarcoma in methods and compositions for the diagnosis and treatment of diseases, such as cancer. More specifically, the invention relates to the discovery of a novel cancer/testis (CT) antigen, NY-SAR-35.



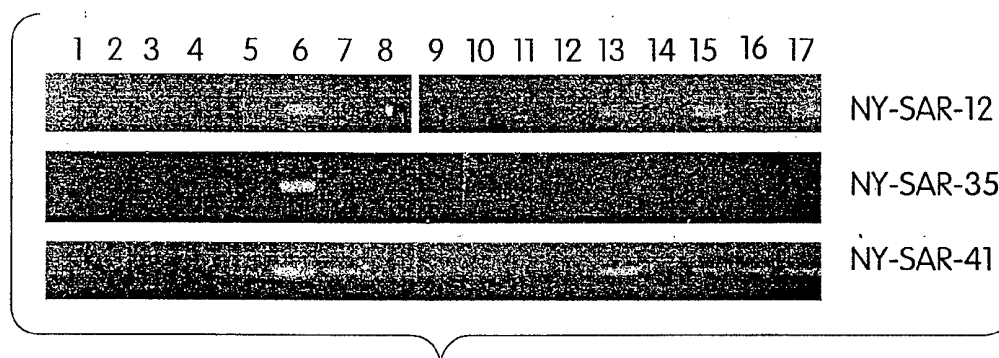


Fig. 1A

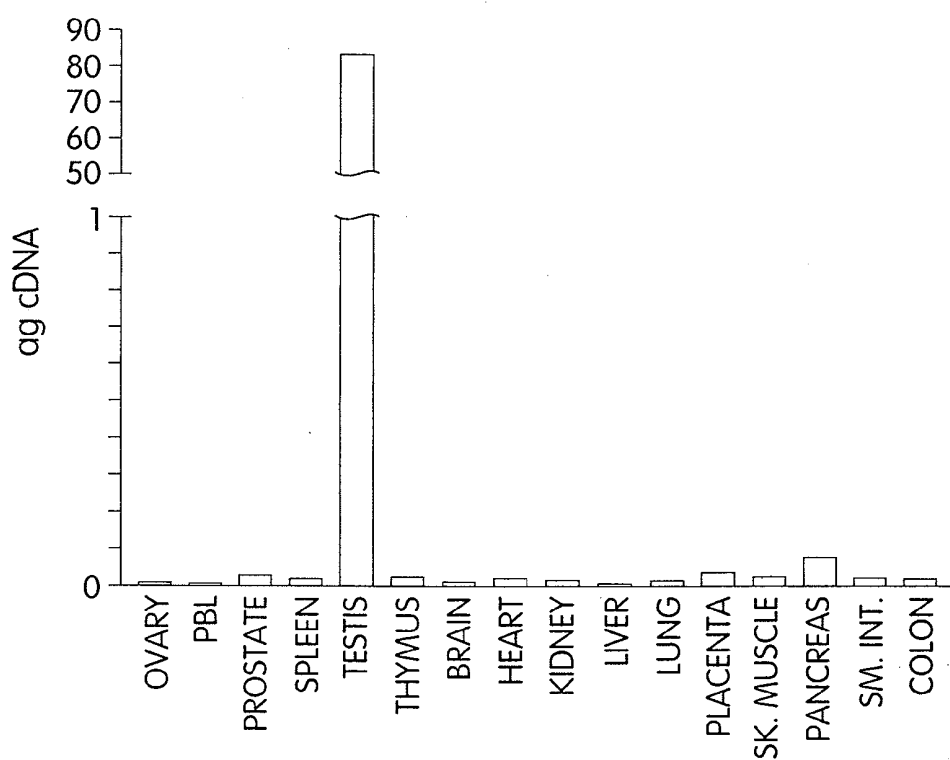


Fig. 1B

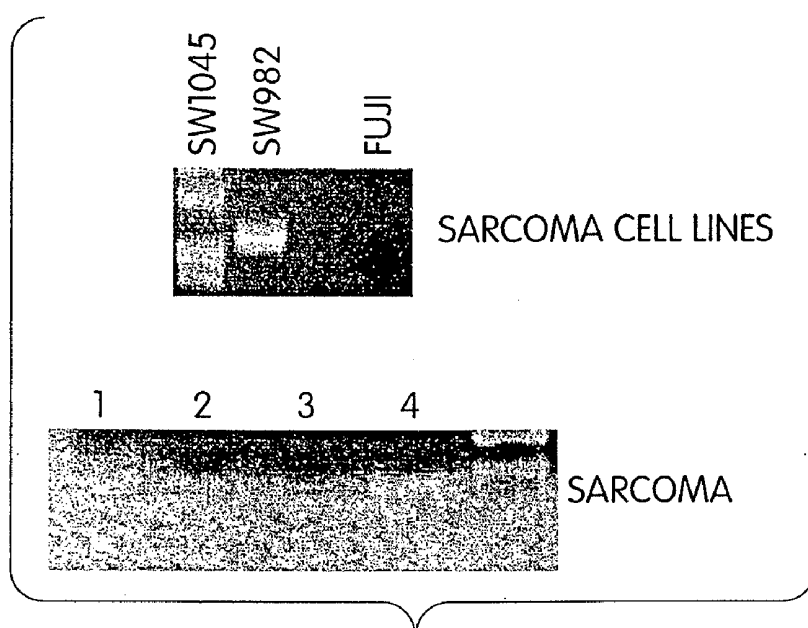


Fig. 1C

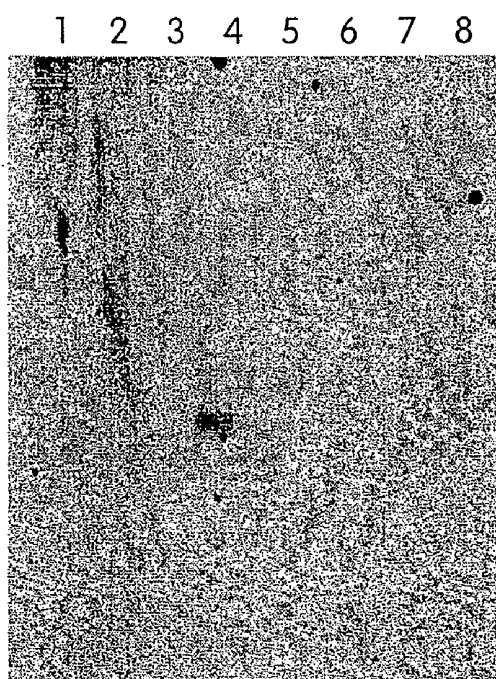


Fig. 1D

ggcttccatcctaatacgaactcgctatagggctcgagcgccg
cccgggcaaaagtctggggccacggactgccggaccgttgggctgtgaggcagcgtctcagcgaggcgccacccggagcc
atg tct tca cat agg agg aaa gcg aag ggg agg aat agg aga agt cac cgt gcc atg cgt 180
M S S H R R K A K G R N R R S H R A M R 20
gtg gct cac tta gag ctg gca act tat gag ttg gcg gca act gag tcg aat ccc gag agc 240
V A H L E L A T Y E L A A T E S N P E S 40
agc cat cct gga tac gag gcc gcc atg gct gac agg cct cag cca gga tag cgg gaa tct 300
S H P G Y E A A M A D R P Q P G W R E S 60
cat aag atg cgg gtc agc aaa ccc ttt ggg atg ctc atg ctc tcc att tgg atc ctg ctg 360
L K M R V S K P F G M L M L S I W I L L 80
ttc gtg tgc tac tac ctg tcc tac tac ctg tgc tcc ggg tcc tca tat ttt gtg ctt gca 420
F V C Y Y L S Y Y L C S G S S Y F V L A 100
aat gga cat atc ctg ccc aac agt gaa aat gct cat ggc caa tct ctg gaa gaa gat tcc 480
N G H I L P N S E N A H G Q S L E E D S 120
gca ttg gaa gct ttg ctg aat ttt ttc ttt cca aca act tgc aat ctg agg gaa aat cag 540
A L E A L L N F F F P T T C N L R E N Q 140
gtg gca aag cct tgt aat gag ctg caa gat ctt agt gag agt gaa tgt ttg aga cac aaa 600
V A K P C N E L Q D L S E S E C L R H K 160
tgc tgt ttt tca tca tcg ggg acc acg agc ttc aaa tgt ttt gct cca ttt aga gat gtg 660
C C F S S S G T T S F K C F A P F R D V 180
cct aaa cag atg atg caa atg ttt ggg ctt ggt gcg atc agc ctt atc ctg gta tgt ctg 720
P K Q M M Q M F G L G A I S L I L V C L 200
ccc att tat tgc cgc tct ctt ttc tgg agg agc gaa ccg gcc gat gat tta caa agg cag 780
P I Y C R S L F W R S E P A D D L Q R Q 220
gac aac aga gtt gta acg ggt ttg aag aaa caa aga agg aag cga aag agg aag tct gaa 840
D N R V V T G L K K Q R R K R K R K S E 240
atg tta cag aaa gca gca aga gga cgt gag gaa cat ggt gac gag tga caagagaccaa 900
M L Q K A A R G R E E H G D E * 255
gcattattttccctcaagacaacagaaaccattcagagcagaggggactgtctcagccatgcaaacctcatggag
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tcatgcatcaaaaaaaaaaaaaaaaaaaaaa 1082

Fig. 2

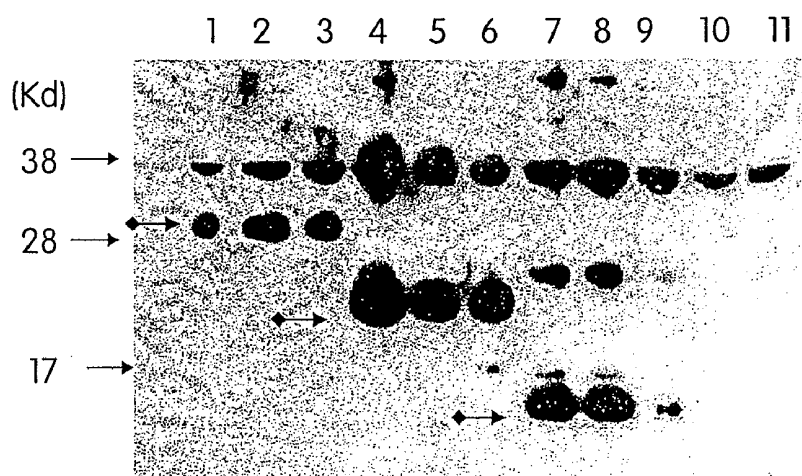


Fig. 3

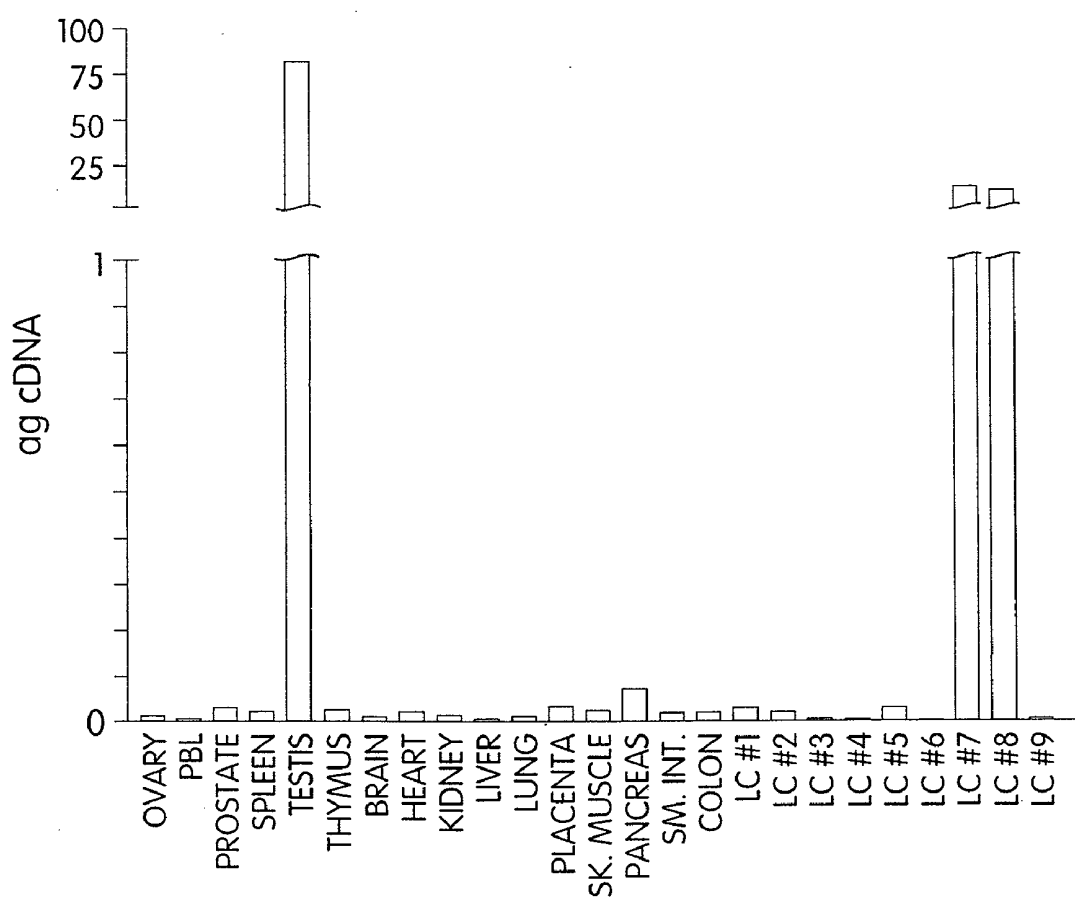


Fig. 4

HUMAN SARCOMA-ASSOCIATED ANTIGENS

RELATED APPLICATIONS

[0001] This application is a divisional of U.S. Non-Provisional patent application Ser. No. 10/529,655, which is a national stage filing under 35 U.S.C. §371 of PCT International application PCT/US03/30870, filed Sep. 30, 2003, which was published under PCT Article 21(2) in English, which is a continuation-in-part of U.S. application Ser. No. 10/260,708, filed on Sep. 30, 2002, and issued on Jul. 14, 2009 as U.S. Pat. No. 7,560,537, the entire disclosure of each of which is incorporated herein by reference.

FIELD OF THE INVENTION

[0002] The invention relates to sarcoma-associated antigens and the nucleic acid molecules that encode them. The invention further relates to the use of the nucleic acid molecules, polypeptides and fragments thereof associated with sarcoma in methods and compositions for the diagnosis and treatment of diseases, such as cancer. More specifically, the invention relates to the discovery of a novel cancer/testis (CT) antigen, NY-SAR-35.

BACKGROUND OF THE INVENTION

[0003] The identification of human tumor antigens recognized by the autologous host is yielding new and promising target molecules for immunotherapy, diagnosis and monitoring of human cancer (van der Bruggen P, et al. 1991. A gene encoding an antigen recognized by cytolytic T lymphocytes on a human melanoma. *Science* 254:1643-47; Gaugler, B., et al. Human gene MAGE-3 codes for an antigen recognized on a melanoma by autologous cytolytic T lymphocytes. *J. Exp. Med.* 1994; 179: 921-30; Kawakami, Y., et al. Cloning of the gene for a shared human melanoma antigen recognized by autologous T cells infiltrating into tumor. *Proc. Natl. Acad. Sci. USA.* 1994; 91: 3515-19 and Chen, Y.-T., et al. A testicular antigen aberrantly expressed in human cancers detected by autologous antibody screening. *Proc. Natl. Acad. Sci. USA.* 1997; 94: 1914-18). Studies of the cellular and humoral immune response to cancer have revealed an extensive repertoire of tumor antigens recognized by the immune system, collectively termed the cancer immunome (Jager D, et al. Identification of a tissue-specific putative transcription factor in breast tissue by serological screening of a breast cancer library. *Cancer Res* 2001 Mar. 1; 61(5):2055-61).

[0004] The immunome is composed largely of antigens defined by T-cell epitope cloning (van der Bruggen P, et al. 1991. A gene encoding an antigen recognized by cytolytic T lymphocytes on a human melanoma. *Science* 254:1643-47; Gaugler, B., et al. Human gene MAGE-3 codes for an antigen recognized on a melanoma by autologous cytolytic T lymphocytes. *J. Exp. Med.* 1994; 179: 921-30; Kawakami, et al. Cloning of the gene for a shared human melanoma antigen recognized by autologous T cells infiltrating into tumor. *Proc. Natl. Acad. Sci. USA.* 1994; 91: 3515-19; Boel, P., et al. BAGE: a new gene encoding an antigen recognized on human melanomas by cytolytic T lymphocytes. *Immunity* 1995; 2: 167-75. (PMID: 7895173); Van den Eynde, B., et al. A new family of genes coding for an antigen recognized by autologous cytolytic T lymphocytes on a human melanoma. *J. Exp. Med.* 1995; 182: 689-98. (PMID: 7544395)), MHC peptide elution (Skipper J C, et al. An HLA-A2-restricted tyrosinase

antigen on melanoma cells results from posttranslational modification and suggests a novel pathway for processing of membrane proteins. *J Exp Med* 1996 Feb. 1; 183(2):527-34; Cox A L, et al. Identification of a peptide recognized by five melanoma-specific human cytotoxic T cell lines. *Science* 1994 Apr. 29; 264(5159):716-9; Pascolo S, et al. A MAGE-A1 HLA-A A*0201 epitope identified by mass spectrometry. *Cancer Res* 2001 May 15; 61(10):4072-7), and serological expression cloning (SEREX, Chen, Y.-T., et al. A testicular antigen aberrantly expressed in human cancers detected by autologous antibody screening. *Proc. Natl. Acad. Sci. USA.* 1997; 94: 1914-18; Jager D, et al. Identification of a tissue-specific putative transcription factor in breast tissue by serological screening of a breast cancer library. *Cancer Res* 2001 Mar. 1; 61(5):2055-61; Sahin, U., et al. Human neoplasms elicit multiple specific immune responses in the autologous host. *Proc. Natl. Acad. Sci. USA* 1995; 92: 11810-13; Scanlan, M. J., et al. Characterization of human colon cancer antigens recognized by autologous antibodies. *Int. J. Cancer* 1998; 76: 652-8; Scanlan, M. J., et al. Antigens recognized by autologous antibody in patients with renal-cell carcinoma. *Int. J. Cancer* 1999; 83: 456-64; Scanlan M J, et al. Humoral immunity to human breast cancer: antigen definition and quantitative analysis of mRNA expression. *Cancer Immunity* 1:4 [epub]), and is catalogued in three databases: the peptide database of T-cell defined tumor antigens (authored by members of the Ludwig Institute for Cancer Research (LICR) that is available on the website of Cancer Immunity, Journal of the Academy of Cancer Immunology, cancerimmunity.org/peptidedatabase/Tcellepitopes); the SYFPEITHI database of MHC ligands and peptide motifs (available on the website of Biomedical Informatics-Heidelberg, bmi-heidelberg.com/syfpeithi/) and the cancer immunome database available on the website of the LICR (licr.org/CancerImmunomeDB, formerly licr.org/SEREX.html).

[0005] SEREX is a method of immunoscreening tumor-derived cDNA expression libraries with cancer patient sera in order to identify molecules recognized by high titered IgG antibodies (Sahin, U., et al. Human neoplasms elicit multiple specific immune responses in the autologous host. *Proc. Natl. Acad. Sci. USA* 1995; 92: 11810-13). Approximately 1000 distinct antigens have been defined by SEREX analysis, including a number of etiologically and therapeutically significant cancer antigens, such as mutational antigens (e.g. p53, LKB1, BUB1; Scanlan, M. J., et al. Characterization of human colon cancer antigens recognized by autologous antibodies. *Int. J. Cancer* 1998; 76: 652-8; Scanlan, M. J., et al. Antigens recognized by autologous antibody in patients with renal-cell carcinoma. *Int. J. Cancer* 1999; 83: 456-64; Scanlan M J, et al. Humoral immunity to human breast cancer: antigen definition and quantitative analysis of mRNA expression. *Cancer Immunity* 1:4 [epub]), differentiation antigens (e.g. tyrosinase, NY-BR-1, rab 38; Jager D, et al. Identification of a tissue-specific putative transcription factor in breast tissue by serological screening of a breast cancer library. *Cancer Res* 2001 Mar. 1; 61(5):2055-61; Sahin, U., et al. Human neoplasms elicit multiple specific immune responses in the autologous host. *Proc. Natl. Acad. Sci. USA* 1995; 92: 11810-13; Jager D, et al. Serological cloning of a melanocyte rab guanosine 5'-triphosphate-binding protein and a chromosome condensation protein from a melanoma complementary DNA library. *Cancer Res* 2000 Jul. 1; 60(13):3584-91), over-expressed gene products (e.g. Her2neu, TPD52, eIF4-gamma; Scanlan M J, et al. Humoral immunity to human

breast cancer: antigen definition and quantitative analysis of mRNA expression. *Cancer Immunity* 1:4 [epub]; Chen, Y.-T., et al. Identification of human tumor antigens by serological expression cloning. In: S. A. Rosenberg (ed.). *Principles and Practice of Biologic Therapy of Cancer*, pp. 557-570. Philadelphia: Lippincott Williams & Wilkins, 2000) and cancer/testis (CT) antigens (e.g. MAGE-1, NY-ESO-1, SSX-2; Chen, Y.-T., et al. A testicular antigen aberrantly expressed in human cancers detected by autologous antibody screening. *Proc. Natl. Acad. Sci. USA* 1997; 94: 1914-18; Sahin, U., et al. Human neoplasms elicit multiple specific immune responses in the autologous host. *Proc. Natl. Acad. Sci. USA* 1995; 92: 11810-13).

[0006] CT antigens represent a group of shared, tumor-specific antigens expressed exclusively in developing germ cells of the testis and fetal ovary, as well as in placental trophoblast, and most notably, in a proportion of human cancers of diverse origins (Chen, Y.-T., et al. Identification of human tumor antigens by serological expression cloning. In: S. A. Rosenberg (ed.). *Principles and Practice of Biologic Therapy of Cancer*, pp. 557-570. Philadelphia: Lippincott Williams & Wilkins, 2000). These antigens elicit spontaneous cellular (Van den Eynde, B. J. and van der Bruggen, P. (1997) *Curr. Opin. Immunol.* 9,684-693) and humoral immune responses (Stockert, E., et al. (1998) *J. Exp. Med.* 187, 1349-1354) in some cancer patients. On the basis of tissue-restricted expression and immunogenicity, CT antigens are attractive targets for vaccine-based immunotherapies. In general, CT antigens are expressed in 20-40% of specimens from a given tumor type (Sahin U, et al. 1998. Expression of multiple cancer/testis antigens in breast cancer and melanoma: basis for polyvalent CT vaccine strategies. *Int J Cancer* 78:387-89; Scanlan M J et al. 2000. Expression of cancer-testis antigens in lung cancer: definition of bromodomain testis-specific gene (BRDT) as a new CT gene, CT9. *Cancer Lett.* 150:155-64; Van den Eynde BJ and van der Bruggen P. 1997. T cell defined tumor antigens. *Curr Opin Immunol* 9:684-693). One exception to this is synovial sarcoma, in which 80% of specimens express NY-ESO-1 (Jungbluth A A, et al. 2001. Monophasic and biphasic synovial sarcomas abundantly express cancer/testis antigen NY-ESO-1 but not MAGE-A1 or CT7. *Int J Cancer* 94:252-6) and MAGE antigens (Antonescu C R, et al. MAGE antigen expression in monophasic and biphasic synovial sarcoma. *Hum Pathol* 2002 February; 33(2):225-9); the expression of which are often homogeneous throughout the tumor. Thus, identification of additional CT antigens and other genes having a tumor-associated expression profile is needed for the development of additional therapeutics and diagnostics to permit effective treatment and diagnosis of a broader group of cancer patients.

SUMMARY OF THE INVENTION

[0007] The humoral immune response of sarcoma patients to CT antigens was examined using the SEREX method. Sera from patients which showed a humoral immune response to CT antigens were subsequently used to screen cDNA libraries derived from CT-rich synovial sarcoma cell lines as well as normal testis. Although there was little overlap in the identity of clones isolated with different sarcoma sera, more than 30% of the isolated clones were previously identified during SEREX analysis of other tumor types. Approximately 60% of these antigens also reacted with sera from normal individuals. This is in conformity with other findings (Scanlan, M. J., et al.

Antigens recognized by autologous antibody in patients with renal-cell carcinoma. *Int. J. Cancer* 1999; 83: 456-64 and Scanlan M J, et al. Humoral immunity to human breast cancer: antigen definition and quantitative analysis of mRNA expression. *Cancer Immunity* 2000; 1:4 [epub]). Thus, only a fraction of the serologically-defined immunome is associated with a cancer-related immune response. The studies described herein have led to the identification of antigens, which include antigens not before associated with cancer along with several novel gene products associated with a sarcoma-related immune response. One such novel CT antigen is NY-SAR-35, which appears to be a cell surface/secreted molecule.

[0008] According to one aspect of the invention, isolated nucleic acid molecules are provided. The isolated nucleic acid molecules are selected from the group consisting of (a) nucleic acid molecules which hybridize under high stringency conditions to a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 1-14 and 97-107 and which code for a sarcoma-associated antigen, (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and (c) complements of (a) or (b).

[0009] In some embodiments, the isolated nucleic acid molecule includes a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 1-14 and 97-107. In some embodiments the isolated nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 10, 11, 99, 102 and 104. In other embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 10. In yet other embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 11. In still other embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 102. In still further embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 104.

[0010] In some embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NOs: 121, 123, 125, 127, 129 or 131. In some embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 121. In other embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 123. In still other embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 125. In yet other embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 131.

[0011] According to another aspect of the invention, additional isolated nucleic acid molecules are provided. The isolated nucleic acid molecules are selected from the group consisting of: (a) unique fragments of a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 10, 11, 99, 102 and 104, which encodes an immunogenic peptide and (b) complements of (a). In some embodiments the isolated nucleic acid molecules are selected from the group consisting of: (a) unique fragments of a nucleotide sequence set forth as SEQ ID NO: 10, which encodes an immunogenic peptide and (b) complements of (a). In other embodiments the isolated nucleic acid molecules are selected from the group consisting of: (a) unique fragments of a nucleotide sequence set forth as SEQ ID NO: 11, which

encodes an immunogenic peptide and (b) complements of (a). In yet other embodiments the isolated nucleic acid molecules are selected from the group consisting of: (a) unique fragments of a nucleotide sequence set forth as SEQ ID NO: 102, which encodes an immunogenic peptide and (b) complements of (a). In still other embodiments the isolated nucleic acid molecules are selected from the group consisting of: (a) unique fragments of a nucleotide sequence set forth as SEQ ID NO: 104, which encodes an immunogenic peptide and (b) complements of (a). In some embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 121. In other embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 123. In still other embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 125. In yet other embodiments the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO: 131.

[0012] In certain embodiments, the isolated nucleic acid molecule includes a nucleotide sequence that is at least about 90% identical to a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-14 and 97-107; preferably the nucleotide sequence is at least about 95% identical, more preferably the nucleotide sequence is at least about 97% identical, still more preferably the nucleotide sequence is at least about 98% identical, and yet more preferably the nucleotide sequence is at least about 99% identical.

[0013] According to further aspects of the invention, expression vectors that include any of the foregoing isolated nucleic acid molecules operably linked to a promoter are provided, as are host cells transformed or transfected with these expression vectors. In certain embodiments, the host cell expresses a MHC molecule, and in some of these embodiments the MHC molecule is expressed recombinantly.

[0014] According to another aspect of the invention, isolated polypeptides are provided that are encoded by the isolated nucleic acid molecules described herein. In certain embodiments, the isolated polypeptide includes an amino acid sequence as set forth in SEQ ID NOs: 46-60, 109-120 or a fragment thereof that is at least eight amino acids in length. In certain embodiments, the isolated polypeptides are antigenic polypeptides that are capable of eliciting antibodies to a sarcoma-associated antigen. In some embodiments the isolated polypeptide includes an amino acid sequence as set forth in SEQ ID NO: 55 or a fragment thereof that is at least eight amino acids in length. In other embodiments the isolated polypeptide includes an amino acid sequence as set forth in SEQ ID NO: 56 or a fragment thereof that is at least eight amino acids in length. In yet other embodiments the isolated polypeptide includes an amino acid sequence as set forth in SEQ ID NO: 111 or a fragment thereof that is at least eight amino acids in length. In still other embodiments the isolated polypeptide includes an amino acid sequence as set forth in SEQ ID NO: 114 or a fragment thereof that is at least eight amino acids in length. In yet other embodiments the isolated polypeptide includes an amino acid sequence as set forth in SEQ ID NO: 116 or a fragment thereof that is at least eight amino acids in length. In still other embodiments the isolated polypeptide includes an amino acid sequence as set forth in SEQ ID NO: 122. In yet other embodiments the isolated polypeptide includes an amino acid sequence as set forth in SEQ ID NO: 124. In still further embodiments the isolated polypeptide includes an amino acid sequence as set forth in SEQ ID NO: 126. In yet other embodiments the

polypeptide includes the amino acid sequence set forth as SEQ ID NOs: 128, 130 or 132.

[0015] Another aspect of the invention provides binding polypeptides that selectively bind to the foregoing isolated polypeptides. In some embodiments these binding polypeptides are isolated also. In other embodiments, the binding polypeptides are antibodies or antigen-binding fragments thereof.

[0016] According to another aspect of the invention, methods of diagnosing cancer in a subject are provided. The methods include obtaining a biological sample from the subject, and determining the presence of an antibody in the biological sample that binds specifically to one or more sarcoma-associated antigens encoded by a nucleotide sequence selected from the group consisting of SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108. The presence of such antibodies indicates that the subject has cancer. In some embodiments the one or more sarcoma-associated antigens is/are encoded by a nucleotide sequence selected from the group consisting of SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108. In still other embodiments the one or more sarcoma-associated antigens is/are encoded by a nucleotide sequence selected from the group consisting of SEQ ID NOs: 10, 11, 15, 102, 104 and 108. In some embodiments the sarcoma-associated antigens is encoded by a nucleotide sequence set forth as SEQ ID NO: 10.

[0017] In some embodiments, the step of determining the presence of an antibody includes contacting the biological sample with one or more sarcoma-associated antigens that are specifically bound by the antibody and are encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of (1) nucleotide sequences set forth as SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108 and (2) nucleotide sequences that are at least 90% identical to the nucleotide sequences of (1), and then determining the binding of the antibody to the sarcoma-associated antigen. In other embodiments, the step of determining the presence of an antibody includes contacting the biological sample with one or more sarcoma-associated antigens that are specifically bound by the antibody and are encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of (1) nucleotide sequences set forth as SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108 and (2) nucleotide sequences that are at least 90% identical to the nucleotide sequences of (1), and then determining the binding of the antibody to the sarcoma-associated antigen.

[0018] In some embodiments, the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 10, 11, 15, 102, 104 and 108, and in other embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 10. In other embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 121. In still other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 123. In other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 125. In yet other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NOs: 127, 129 or 131.

[0019] In other embodiments, the sarcoma-associated antigen is a polypeptide that includes the amino acid sequence of any of SEQ ID NOs: 48, 50-53, 55-90, 111, 114, 116 and 120

or a fragment thereof that is at least eight amino acids in length. In still other embodiments, the sarcoma-associated antigen is a polypeptide that includes the amino acid sequence of any of SEQ ID NOs: 50-52, 55-58, 60-90, 114, 116, 120 or a fragment thereof that is at least eight amino acids in length. In still other embodiments, the sarcoma-associated antigen is a polypeptide that includes the amino acid sequence of any of SEQ ID NOs: 55, 56, 60, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length.

[0020] In some embodiments, the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 55 or a fragment thereof that is at least eight amino acids in length. In certain embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 122. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 124. In yet other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 126. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 128, 130 or 132.

[0021] In certain embodiments, the biological sample is serum. In other embodiments, the one or more sarcoma-associated antigens are produced recombinantly, and/or the one or more sarcoma-associated antigens are bound to a substrate. In some embodiments, the step of determining the binding of the antibody with the one or more sarcoma-associated antigens is performed with an ELISA-based method. In still other embodiments a serum antibody detection assay (SADA) is used.

[0022] According to still another aspect of the invention, methods for diagnosing cancer in a subject are provided. The methods include obtaining a biological sample from a subject, and determining the expression of a sarcoma-associated antigen or a nucleic acid molecule that encodes it. The nucleic acid molecule includes a nucleotide sequence selected from the group consisting of SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108 in the biological sample. The nucleic acid molecule in some embodiments includes a nucleotide sequence selected from the group consisting of SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108 in the biological sample. The expression of the sarcoma-associated antigen or the nucleic acid molecule that encodes it in the sample is diagnostic for cancer in the subject.

[0023] In certain embodiments, the sarcoma-associated nucleic acid molecule comprises the nucleotide sequence selected from the group consisting of SEQ ID NOs: 10, 11, 15, 102, 104 and 108. In some embodiments the sarcoma-associated nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 10. In other embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 121. In still other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 123. In yet other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 125. In yet other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NOs: 127, 129 or 131.

[0024] In other embodiments, the sarcoma-associated antigen comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 48, 50-53, 55-90, 111, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. In yet other embodiments, the sarcoma-associated antigen comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 50-52, 55-58, 60-90, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. In yet other embodiments, the sarcoma-associated antigen includes a

ciated antigen comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 50-52, 55-58, 60-90, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. The sarcoma-associated antigen in some embodiments includes an amino acid sequence selected from the group consisting of SEQ ID NOs: 55, 56, 60, 114, 116 and 120. In some embodiments the sarcoma-associated antigen includes an amino acid sequence set forth as SEQ ID NO: 55 or a fragment thereof that is at least eight amino acids in length. In certain embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 122. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 124. In yet other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 126. In still further embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NOs: 128, 130 or 132.

[0025] According to yet another aspect of the invention, methods for determining onset, progression, or regression of cancer in a subject are provided. The methods include obtaining from a subject a first biological sample, determining the expression of a sarcoma-associated antigen or the nucleic acid molecule that encodes it in the first sample, obtaining from the subject a second biological sample, determining the expression of the sarcoma-associated antigen or the nucleic acid molecule that encodes it in the second sample, and comparing the expression in the first sample to the expression in the second sample as a determination of the onset, progression, or regression of the cancer. The nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of (1) nucleotide sequences set forth as SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108 and (2) nucleotide sequences that are at least 90% identical to the nucleotide sequences of (1). In some embodiments the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of (1) nucleotide sequences set forth as SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108 and (2) nucleotide sequences that are at least 90% identical to the nucleotide sequences of (1).

[0026] In some embodiments, the nucleic acid molecule that encodes the sarcoma-associated antigen includes a nucleotide sequence selected from the group consisting of SEQ ID NOs: 10, 11, 15, 102, 104 and 108. In other embodiments the nucleic acid molecule includes the nucleotide sequence of SEQ ID NO: 10. In yet other embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 121. In still other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 123. In yet other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 125. In still other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NOs: 127, 129 or 131. In other embodiments, the sarcoma-associated antigen includes a polypeptide sequence selected from the group consisting of polypeptide sequences set forth as SEQ ID NOs: 48, 50-53, 55-90, 111, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. In still other embodiments, the sarcoma-associated antigen includes a polypeptide sequence selected from the group consisting of polypeptide sequences set forth as SEQ ID NOs: 50-52, 55-58, 60-90, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. In yet other embodiments, the sarcoma-associated antigen includes a

polypeptide sequence selected from the group consisting of polypeptide sequences set forth as SEQ ID NOs: 55, 56, 60, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. In some embodiments the sarcoma-associated antigen includes the amino acid sequence of SEQ ID NO: 55 or a fragment thereof that is at least eight amino acids in length. In certain embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 122. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 124. In yet other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 126. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NOs: 128, 130 or 132.

[0027] In some embodiments of the foregoing methods, the step of determining the expression of the sarcoma-associated antigen or the nucleic acid molecule that encodes it includes contacting the biological sample with an agent that selectively binds to the sarcoma-associated antigen or the nucleic acid molecule that encodes it. For methods in which the agent that selectively binds is a nucleic acid molecule, it is preferred that the expression of the sarcoma-associated nucleic acid molecule is determined by nucleic acid hybridization or nucleic acid amplification; some embodiments of the methods utilize real-time RT-PCR or RT-PCR as methods of nucleic acid amplification, or use a nucleic acid microarray as a method for nucleic acid hybridization. For methods in which the agent that selectively binds is a polypeptide, the polypeptide preferably is an antibody or antigen-binding fragment thereof. More preferably, the antibody is a monoclonal antibody, particularly a chimeric, human, or humanized antibody, a single chain antibody, or the antigen-binding fragment is a F(ab')₂, Fab, Fd, or Fv fragment. In certain embodiments, the antibody or antigen-binding fragment is labeled with a detectable label, preferably a fluorescent or radioactive label.

[0028] In certain embodiments of the foregoing methods, the sample is selected from the group consisting of tissue, cells, and blood. In some embodiments, the cancer is a sarcoma.

[0029] In another aspect of the invention, kits for detecting antibodies reactive to a sarcoma-associated antigen in a biological sample are provided. The kits include one or more sarcoma-associated antigens encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108, and instructions for the use of the sarcoma-associated antigens in the detection of antibodies in the biological sample. In some embodiments the one or more sarcoma-associated antigens is/are encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108. In some embodiments, the sarcoma-associated nucleic acid molecule comprises the nucleotide sequence set forth as SEQ ID NO: 10, 11, 15, 102, 104 or 108. In other embodiments, the sarcoma-associated nucleic acid molecule comprises the nucleotide sequence set forth as SEQ ID NO: 10. In other embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 121. In still other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 123. In yet other embodiments the nucleic acid molecule includes the nucle-

otide sequence set forth in SEQ ID NO: 125. In still further embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NOs: 127, 129 or 131. In other embodiments, the sarcoma-associated antigens are bound to a substrate. In further embodiments, the kit also includes a labeling reagent and labeling reagent substrate, and/or a blocking reagent. Additional kit embodiments include secondary antibodies for detection of the antibody bound to the antigen.

[0030] In a further aspect of the invention, other kits for the diagnosis of cancer in a subject are provided. The kits include one or more binding agents that specifically bind to a sarcoma-associated antigen or the nucleic acid molecule that encodes it. In this aspect, the nucleic acid molecule includes a nucleotide sequence selected from the group consisting of SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108. In some embodiments the nucleic acid molecule includes a nucleotide sequence selected from the group consisting of SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108. The kit also includes instructions for the use of the binding agents in the diagnosis of cancer. The one or more binding agents are nucleic acid molecules or polypeptides. If the latter, the polypeptides preferably are antibodies or antigen-binding fragments thereof. In other embodiments, the one or more agents are bound to a substrate. Further embodiments of the kits include one or more agents that bind specifically to a cancer-associated antigen other than those encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 10, 11, 15, 102, 104 and 108. In some embodiments, the kit is configured for diagnosis of sarcomas.

[0031] According to another aspect of the invention, methods for treating a subject with a disorder characterized by the aberrant expression of a sarcoma-associated antigen or the nucleic acid molecule that encodes it are provided. The methods include administering to a subject an effective amount of an antibody or antigen-binding fragment thereof that specifically binds to the sarcoma-associated antigen. In this aspect, the antigen includes an amino acid sequence selected from the group consisting of SEQ ID NOs: 48, 50-53, 55-90, 111, 114, 116 and 120 or a fragment thereof that is eight or more amino acids in length. In some embodiments the antigen includes an amino acid sequence selected from the group consisting of SEQ ID NOs: 50-52, 55-58, 60-90, 114, 116 and 120 or a fragment thereof that is eight or more amino acids in length. In other embodiments the antigen includes an amino acid sequence selected from the group consisting of SEQ ID NOs: 55, 56, 60, 114, 116 and 120 or a fragment thereof that is eight or more amino acids in length. In some embodiments, the antibody or antigen-binding fragment thereof specifically binds to the extracellular domain of a sarcoma-associated antigen that includes the amino acid sequence of SEQ ID NO: 55 or a fragment thereof that is eight or more amino acids in length. In certain embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 122. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 124. In yet other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 126. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 128, 130 or 132. In yet other embodiments the sarcoma-

associated antigen includes the amino acid sequence set forth as SEQ ID NO: 134 or a fragment thereof that is eight or more amino acids in length.

[0032] In certain embodiments, the disorder is cancer, preferably sarcoma. In other embodiments, the antibody used in the methods is a monoclonal antibody, preferably a chimeric, human, or humanized antibody; a single chain antibody; or the antigen-binding fragment is a F(ab')₂, Fab, Fd, or Fv fragment.

[0033] In other embodiments, the antibody or antigen-binding fragment thereof is bound to a cytotoxic agent. Preferred cytotoxic agents include: calicheamicin, esperamicin, methotrexate, doxorubicin, melphalan, chlorambucil, ARA-C, vindesine, mitomycin C, cisplatin, etoposide, bleomycin and 5-fluorouracil. Other cytotoxic agents include radioisotopes, including those that emit α , β , and/or γ radiation. Preferred radioisotopes include: ²²⁵Ac, ²¹¹At, ²¹²Bi, ²¹³Bi, ¹⁸⁶Rh, ¹⁸⁸Rh, ¹⁷⁷Lu, ⁹⁰Y, ¹³¹I, ⁶⁷Cu, ¹²⁵I, ¹²³I, ⁷⁷Br, ¹⁵³Sm, ¹⁶⁶Bo, ⁶⁴Cu, ²¹²Pb, ²²⁴Ra and ²²³Ra.

[0034] According to another aspect of the invention, methods for treating a subject with a disorder characterized by the aberrant expression of a sarcoma-associated antigen or a nucleic acid molecule that encodes it are provided. The methods include administering an amount of an agent that selectively binds to the sarcoma-associated antigen or the nucleic acid molecule that encodes it effective to treat the disorder. The nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of (a) an isolated nucleic acid molecule comprising a nucleotide sequence that is at least 90% identical to the nucleotide sequence selected from the group consisting of SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108, and (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code. In some embodiments the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of (a) an isolated nucleic acid molecule comprising a nucleotide sequence that is at least 90% identical to the nucleotide sequence selected from the group consisting of SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108, and (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code. In certain embodiments the disorder is cancer, preferably sarcoma. In yet other embodiments the sarcoma-associated nucleic acid molecule comprises the nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 10, 11, 15, 102, 104 and 108. In some embodiments the sarcoma-associated nucleic acid molecule comprises the nucleotide sequence set forth as SEQ ID NO: 10.

[0035] In other embodiments the sarcoma-associated nucleic acid molecule codes for a sarcoma-associated antigen which comprises the polypeptide sequence selected from the group consisting of polypeptide sequences set forth as SEQ ID NOs: 48, 50-53, 55-90, 111, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. In still other embodiments the sarcoma-associated nucleic acid molecule codes for a sarcoma-associated antigen which comprises the polypeptide sequence selected from the group consisting of polypeptide sequences set forth as SEQ ID NOs: 50-52, 55-58, 60-90, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. In some embodiments the sarcoma-associated nucleic acid molecule codes for a sarcoma-associated antigen which comprises the polypeptide sequence set forth as SEQ ID NO: 55, 56, 60,

114, 116 or 120 or a fragment thereof that is at least eight amino acids in length. In another embodiment the sarcoma-associated nucleic acid molecule codes for a sarcoma-associated antigen which comprises the polypeptide sequence set forth as SEQ ID NO: 55 or a fragment thereof that is at least eight amino acids in length. In certain embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 122. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 124. In yet other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 126. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NOs: 128, 130 or 132.

[0036] In certain embodiments, the binding agent is an antisense or RNAi molecule. In other embodiments, the binding agent is a polypeptide, preferably an antibody or antigen-binding fragment thereof. Preferred antibodies include monoclonal antibodies, including chimeric, human, or humanized antibodies, and single chain antibodies; preferred antigen-binding fragments include F(ab')₂, Fab, Fd, or Fv fragments. In other embodiments, the antibody or antigen-binding fragment is bound to a cytotoxic agent.

[0037] According to yet another aspect of the invention, methods for treating a subject with a disorder characterized by the aberrant expression of a sarcoma-associated antigen or the nucleic acid molecule that encodes it are provided. The methods include administering to the subject an amount of an agent effective to stimulate an immune response to a sarcoma-associated antigen encoded by a nucleic acid molecule comprising a nucleotide sequence that is at least 90% identical to the nucleotide sequence selected from the group consisting of SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108. In some embodiments the sarcoma-associated antigen is encoded by a nucleic acid molecule comprising a nucleotide sequence that is at least 90% identical to the nucleotide sequence selected from the group consisting of SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108. In some embodiments, the disorder is cancer, particularly sarcoma. In other embodiments the sarcoma-associated nucleic acid molecule comprises the nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 10, 11, 15, 102, 104 and 108. In some embodiments the sarcoma-associated nucleic acid molecule comprises the nucleotide sequence set forth as SEQ ID NO: 10. In other embodiments the sarcoma-associated antigen is encoded by a nucleic acid molecule comprising a nucleotide sequence set forth as SEQ ID NO: 133.

[0038] In yet other embodiments the sarcoma-associated antigen includes an amino acid sequence selected from the group consisting of SEQ ID NOs: 48, 50-53, 55-90, 111, 114, 116 and 120, or a fragment thereof that is at least eight amino acids in length. In still other embodiments the sarcoma-associated antigen includes an amino acid sequence selected from the group consisting of SEQ ID NOs: 50-52, 55-58, 60-90, 114, 116 and 120, or a fragment thereof that is at least eight amino acids in length. In some embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 55, or a fragment thereof that is at least eight amino acids in length. In certain embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 122. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 124. In yet other embodiments the sarcoma-

associated antigen includes the amino acid sequence set forth as SEQ ID NO: 126. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NOs: 128, 130 or 132. In still further embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 134, or a fragment thereof that is at least eight amino acids in length.

[0039] In some embodiments, the agent that stimulates an immune response is a nucleic acid that encodes a sarcoma-associated antigen operably linked to a promoter for expressing the sarcoma-associated antigen; a polypeptide comprising the sarcoma-associated antigen; or a host cell that expresses the sarcoma-associated antigen, particularly a host cell that also expresses a MHC molecule. In some embodiments, the agent which stimulates an immune response is a peptide fragment of the sarcoma-associated antigen, or is a complex of a peptide fragment of the sarcoma-associated antigen and a MHC molecule. In other embodiments, the agent also includes an adjuvant or cytokine.

[0040] In another aspect of the invention, kits for diagnosing a disorder associated with the aberrant expression of a sarcoma-associated antigen or a nucleic acid molecule that encodes it are provided. The kits include one or more nucleic acid molecules that hybridize to the nucleic acid molecule that encodes the sarcoma-associated antigen comprising a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108 under high stringency conditions, and instructions for the use of the nucleic acid molecules in the diagnosis of a disorder associated with aberrant expression of the sarcoma-associated antigen or the nucleic acid molecule that encodes it. In some embodiments the one or more nucleic acid molecules that hybridize to the nucleic acid molecule that encodes the sarcoma-associated antigen comprises a nucleotide sequence selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108. In some embodiments, the one or more nucleic acid molecules are detectably labeled. In some embodiments the nucleic acid molecule that encodes the sarcoma-associated antigen comprises the nucleotide sequence set forth as SEQ ID NO: 10, 11, 15, 102, 104 or 108. In other embodiments the nucleic acid molecule that encodes the sarcoma-associated antigen comprises the nucleotide sequence set forth as SEQ ID NO: 10. In other embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 121. In still other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 123. In yet other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 125. In still other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NOs: 127, 129 or 131.

[0041] In certain embodiments, the one or more nucleic acid molecules consist of a first primer and a second primer, wherein the first primer and the second primer are constructed and arranged to selectively amplify at least a portion of a nucleic acid molecule that encodes the sarcoma-associated antigen and comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs: 10, 11, 15, 102, 104 and 108. In other embodiments, the nucleic acids in the kit are bound to a substrate.

[0042] In still another aspect of the invention, methods for identifying a cancer-associated antigen are provided. The methods include obtaining a biological sample from one or

more subjects, determining the reactivity of the biological sample to one or more known cancer-associated antigens, using the reactive biological sample to screen an expression library to determine the presence of cancer-associated antigens reactive with the biological sample, and isolating a clone that encodes the cancer-associated antigen from the expression library. In certain embodiments the biological sample is serum. In some embodiments the expression library is derived from a tumor, preferably from a tumor cell line.

[0043] In still other embodiments, the methods also include determining the identity of the cancer-associated antigen encoded by the isolated clone, preferably by DNA sequencing.

[0044] The invention in a further aspect provides a composition including an agent that stimulates an immune response to a sarcoma-associated antigen. In some embodiments sarcoma-associated antigens are those encoded by a nucleic acid molecule selected from the group consisting of an isolated nucleic acid molecule comprising a nucleotide sequence that is at least 90% identical to the nucleotide sequence selected from the group consisting of SEQ ID NOs: 3, 5-8, 10-45, 99, 102, 104 and 108, and nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code. In some embodiments the sarcoma-associated antigens are those encoded by a nucleic acid molecule selected from the group consisting of an isolated nucleic acid molecule comprising a nucleotide sequence that is at least 90% identical to the nucleotide sequence selected from the group consisting of SEQ ID NOs: 5-7, 10-13, 15-45, 102, 104 and 108, and nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code. In particular embodiments, the nucleic acid molecule includes a nucleotide sequence selected from the group consisting of SEQ ID NOs: 10, 11, 15, 102, 104 and 108. In some embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 10. In other embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 133.

[0045] In some embodiments, sarcoma-associated antigen comprises a polypeptide sequence selected from the group consisting of SEQ ID NOs: 48, 50-53, 55-90, 111, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. In other embodiments, sarcoma-associated antigen comprises a polypeptide sequence selected from the group consisting of SEQ ID NOs: 50-52, 55-58, 60-90, 114, 116 and 120 or a fragment thereof that is at least eight amino acids in length. In some embodiments the sarcoma-associated antigen includes the amino acid sequence of SEQ ID NO: 55, 56, 60, 114, 116 or 120 or a fragment thereof that is at least eight amino acids in length. In other embodiments the sarcoma-associated antigen includes the amino acid sequence of SEQ ID NO: 55 or a fragment thereof that is at least eight amino acids in length. In certain embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 122. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 124. In yet other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 126. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NOs: 128, 130 or 132. In yet other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 134.

[0046] The agent, in some embodiments, is a nucleic acid that encodes a sarcoma-associated antigen operably linked to a promoter for expressing the sarcoma-associated antigen. In other embodiments, the agent is a polypeptide comprising the sarcoma-associated antigen. In still other embodiments, the agent is a host cell that expresses the sarcoma-associated antigen; preferably the host cell also expresses a MHC molecule. In yet other embodiments, the agent is a complex of a peptide derived from the sarcoma-associated antigen and a MHC molecule.

[0047] The composition also includes, in certain embodiments, an adjuvant or cytokine and/or one or more cytotoxic or chemotherapeutic agents. The compositions optionally includes a pharmaceutically acceptable carrier.

[0048] In another aspect of the invention, compositions are provided that include an agent that selectively binds to a sarcoma-associated antigen or a nucleic acid molecule that encodes it. The nucleic acid molecule includes a nucleotide sequence selected from the group consisting of: (a) an isolated nucleic acid molecule comprising a nucleotide sequence that is at least 90% identical to the nucleotide sequence selected from the group consisting of SEQ ID NOs: 3, 5-8, 10-13, 99, 102 and 104 and (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code. In some embodiments the nucleic acid molecule includes a nucleotide sequence selected from the group consisting of: (a) an isolated nucleic acid molecule comprising a nucleotide sequence that is at least 90% identical to the nucleotide sequence selected from the group consisting of SEQ ID NOs: 5-7, 10-13, 102 and 104 and (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code. In some embodiments the nucleic acid molecule includes a nucleotide sequence selected from the group consisting of SEQ ID NOs: 10, 11, 102 and 104; in other embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 10. In other embodiments the nucleic acid molecule includes the nucleotide sequence set forth as SEQ ID NO: 121. In still other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 123. In yet other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NO: 125. In still other embodiments the nucleic acid molecule includes the nucleotide sequence set forth in SEQ ID NOs: 127, 129 or 131. In other embodiments, the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 55, 56, 114 or 116 or a fragment thereof that is at least eight amino acids in length. In some embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 55. In certain embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 122. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 124. In yet other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NO: 126. In still other embodiments the sarcoma-associated antigen includes the amino acid sequence set forth as SEQ ID NOs: 128, 130 or 132. The agents in this aspect of the invention include nucleic acids and polypeptides, preferably antibodies or antigen-binding fragments thereof. Preferred antibodies include monoclonal antibodies (particularly chimeric,

human, or humanized antibodies), and single chain antibodies; preferred antibody fragments include F(ab')₂, Fab, Fd, or Fv fragments.

[0049] In certain embodiments, the antibody or antigen-binding fragment is conjugated to cytotoxic or chemotherapeutic agent. In other embodiments, the composition includes one or more cytotoxic or chemotherapeutic agent. In still other embodiments, the composition includes a pharmaceutically acceptable carrier.

[0050] The use of the nucleotide and amino acid sequence as set forth as SEQ ID NOs: 133 and 134, respectively, in any of the compositions and methods described herein are also provided.

[0051] The invention also involves the use of the genes, gene products, fragments thereof, agents which bind thereto, and other compositions and molecules described herein in the preparation of medicaments. A particular medicament is for treating cancer.

[0052] These and other aspects of the invention will be described in further detail in connection with the detailed description of the invention.

BRIEF DESCRIPTION OF THE DRAWING

[0053] FIG. 1 provides the mRNA expression patterns of serologically defined sarcoma antigens. FIG. 1A shows the results of the RT-PCR analysis of NY-SAR-12, -35, and -41 in a panel of 17 normal tissues (Lanes 1, brain; 2, kidney; 3, liver; 4, pancreas; 5, placenta; 6, testis; 7, fetal brain; 8, small intestine; 9, heart; 10, prostate; 11, adrenal gland; 12, spleen; 13, colon; 14, stomach; 15, lung; 16, bladder; and 17, ovary). FIG. 1B provides the results of the quantitative real-time RT-PCR analysis of NY-SAR-35 in various normal tissues. FIG. 1C shows the results of the RT-PCR analysis of NY-SAR-35 expression in sarcoma cell lines and sarcoma tissue (Lane 1, fibrosarcoma; 2, rhabdomyosarcoma; 3, leiomyosarcoma; and 4, normal testis). FIG. 1D provides the results of the Northern blot analysis of NY-SAR-35 in various normal tissues (Lane 1, spleen; 2, thymus; 3, prostate; 4, testis; 5, ovary; 6, small intestine; 7, colon mucosa; and 8, peripheral blood leukocytes).

[0054] FIG. 2 provides the nucleotide and predicted amino acid sequence of NY-SAR-35 from each of the four ATG codons. The underlined letters indicate the signal peptide and the italicized letters indicate the transmembrane domain. The letters shown in gray represent the trefoil domain, while the letters that are underlined and italicized represent the other hydrophilic turn.

[0055] FIG. 3 provides the results of Western blot assay of recombinant NY-SAR-35 proteins in *E. coli*. Three colonies of each domain cloned plasmid were picked and cultured by IPTG induction. After a four hour induction, total proteins from each of the colonies were separated by SDS-gel electrophoresis. The protein gel was immunoblotted on a membrane with a His-epitope monoclonal antibody. Lanes 1, 2, and 3—whole protein (from the first ATG codon); Lanes 4, 5 and 6—MH7 protein; Lanes 7, 8, and 9—extracellular protein and Lanes 10 and 11—*E. coli* lysate as negative control.

[0056] FIG. 4 provides the real-time RT-PCR analysis of NY-SAR-35 mRNA in various normal tissues and non-small cell lung cancer specimens. NY-SAR-35 was expressed in normal testis (83.2 ag) at a level that was >1,000 times the level detected in all other normal tissues. In 2 of 9 cases of non-small cell lung cancer examined, the level of NY-SAR-35 expression was equivalent to 0.15 (12.5 ag) and 0.13 (10.8

ag) times the level detected in normal testis, or approximately 100 times the level detected in normal tissues.

DETAILED DESCRIPTION OF THE INVENTION

[0057] The screening of cDNA expression libraries derived from human tumors with autologous antibody (SEREX) has proven to be a powerful method for defining the structure of tumor antigens recognized by the humoral immune system, and has led to the identification of new targets for cancer immunotherapy. The current study examined the humoral immune response of sarcoma patients to CT antigens. Sera from patients which showed a humoral immune response to CT antigens were subsequently used to screen cDNA libraries derived from CT-rich sarcoma cell lines, leading to the identification of antigens not before associated with cancer along with several novel antigens associated with a sarcoma-related immune response, including a novel CT antigen, NY-SAR-35.

[0058] Sarcoma-associated antigens were identified with an optimized SEREX analysis method. Cell lines that were rich in CT antigen expression were chosen as the source of cDNA. Additionally, sera was obtained from a group of patients that were actively mounting a humoral immune response to a panel of known CT antigens. This optimized SEREX analysis led to the identification of 113 antigens reactive with serum IgG of sarcoma patients. The antigens identified were further evaluated for cancer-restricted expression and the frequency of eliciting antibody responses in normal individuals as well as cancer patients.

[0059] In the first round of immunoscreenings, twenty-four of 72 antigens (33%) were found to have a serological profile that was not restricted to cancer patients, as evidenced by their reactivity with normal sera, while 48 antigens had a cancer-related serological profile, reacting only with sera from cancer patients. Notable antigens belonging to this latter category include the CT antigens, NY-SAR-36/SSX-1, NY-SAR-43/SSX-4 and NY-SAR-35. Although the antibody response in these studies to NY-SAR-4/FH was most frequent, occurring in 5/39 (13%) sarcoma patients, no individual antigen was serodominant. NY-SAR-4 is equivalent to fumarate hydratase (FH), an enzyme of the tricarboxylic acid cycle. This serological response to NY-SAR-4/FH may be of interest given the recent finding that germ line mutations in the FH gene are associated with a predisposition to uterine and cutaneous leiomyomata, and also renal cell carcinoma (Tomlinson IP, et al. Germline mutations in FH predispose to dominantly inherited uterine fibroids, skin leiomyomata and papillary renal cell cancer. *Nat Genet* 2002 April; 30(4):406-10).

[0060] In addition, 6 tissue-restricted antigens, LAGE-1/NY-SAR-17, SSX1/NY-SAR-36, SSX4/NY-SAR-43, NESG1/NY-SAR-12, NY-SAR-35, and NY-SAR-41 were identified. Two of these antigens, NY-SAR-35, and NY-SAR-41 are novel gene products, and a third, NESG1/NY-SAR-12 (Li Z, Yao K, Cao Y. Molecular cloning of a novel tissue-specific gene from human nasopharyngeal epithelium. *Gene* 1999 Sep. 3; 237(1):235-40), has not been previously studied in relation to cancer. NY-SAR-35 further represents a newly defined CT antigen expressed exclusively in normal testis, melanoma, sarcoma, lung cancer and breast cancer.

[0061] The second round of immunoscreenings performed led to the identification of 41 additional SEREX-defined sarcoma antigens, 11 of which are novel gene products (NY-SAR-77, -79, -80, -84, -88, -92, -95, -97, -104, 105 and -113). Within this group of 41 sarcoma antigens are three known

testis-restricted antigens (NY-SAR-78/TSP-NY, NY-SAR-89/SSX2 and NY-SAR-99/SSX3), two differentially expressed antigens that are novel gene products (NY-SAR-92 and NY-SAR-97) and a tissue-restricted antigen that has not been previously studied in relation to cancer (NY-SAR-96/MCSP).

[0062] Table 1, below, provides a list of the sarcoma-associated antigens and their corresponding sequence identification numbers. The antigens listed include those that were found to be uncharacterized gene products as well as those sarcoma-associated antigens that exhibited cancer-restricted expression and were not found in the SEREX Database.

TABLE 1

Sarcoma-Associated Antigens (Uncharacterized Gene Products and Cancer-Related Antigens not Found in the SEREX Database)	
NY-SAR-Antigen	Sequence Identification Number (nucleotide and amino acid sequence, respectively)
3	SEQ ID NOS: 1 and 46
10	SEQ ID NOS: 2 and 47
16	SEQ ID NOS: 3 and 48
22	SEQ ID NOS: 4 and 49
23	SEQ ID NOS: 5 and 50
24	SEQ ID NOS: 6 and 51
27	SEQ ID NOS: 7 and 52
28	SEQ ID NOS: 8 and 53
29	SEQ ID NOS: 9 and 54
35	SEQ ID NOS: 10 and 55
41	SEQ ID NOS: 11 and 56
48	SEQ ID NOS: 12 and 57
62	SEQ ID NOS: 13 and 58
71	SEQ ID NOS: 14 and 59
12	SEQ ID NOS: 15 and 60
4	SEQ ID NOS: 16 and 61
5	SEQ ID NOS: 17 and 62
8	SEQ ID NOS: 18 and 63
9	SEQ ID NOS: 19 and 64
20	SEQ ID NOS: 20 and 65
21	SEQ ID NOS: 21 and 66
25	SEQ ID NOS: 22 and 67
26	SEQ ID NOS: 23 and 68
30	SEQ ID NOS: 24 and 69
34	SEQ ID NOS: 25 and 70
36	SEQ ID NOS: 26 and 71
37	SEQ ID NOS: 27 and 72
38	SEQ ID NOS: 28 and 73
39	SEQ ID NOS: 29 and 74
40	SEQ ID NOS: 30 and 75
42	SEQ ID NOS: 31 and 76
43	SEQ ID NOS: 32 and 77
46	SEQ ID NOS: 33 and 78
49	SEQ ID NOS: 34 and 79
50	SEQ ID NOS: 35 and 80
51	SEQ ID NOS: 36 and 81
52	SEQ ID NOS: 37 and 82
56	SEQ ID NOS: 38 and 83
57	SEQ ID NOS: 39 and 84
59	SEQ ID NOS: 40 and 85
60	SEQ ID NOS: 41 and 86
63	SEQ ID NOS: 42 and 87
67	SEQ ID NOS: 43 and 88
69	SEQ ID NOS: 44 and 89
70	SEQ ID NOS: 45 and 90
77	SEQ ID NOS: 97 and 109
79	SEQ ID NOS: 98 and 110
80	SEQ ID NOS: 99 and 111
84	SEQ ID NOS: 100 and 112
88	SEQ ID NOS: 101 and 113
92	SEQ ID NOS: 102 and 114
95	SEQ ID NOS: 103 and 115
97	SEQ ID NOS: 104 and 116
104	SEQ ID NOS: 105 and 117

TABLE 1-continued

Sarcoma-Associated Antigens (Uncharacterized Gene Products and Cancer-Related Antigens not Found in the SEREX Database)	
NY-SAR-Antigen	Sequence Identification Number (nucleotide and amino acid sequence, respectively)
105	SEQ ID NOs: 106 and 118
113	SEQ ID NOs: 107 and 119
96	SEQ ID NOs: 108 and 120

[0063] The invention relates, in part, to the sarcoma-associated antigens defined herein and the nucleic acid molecules that encode them. The invention further relates to the use of the nucleic acid molecules, polypeptides and fragments thereof associated with sarcoma in methods and compositions for the diagnosis and treatment of diseases, such as cancer.

[0064] As used herein, the term “sarcoma-associated antigens” means polypeptides that elicit specific immune responses to the polypeptide when expressed by a tumor cell and thus, include sarcoma-associated polypeptides (including proteins) and fragments of sarcoma-associated polypeptides, that are recognized by the immune system (e.g., by antibodies and/or T lymphocytes). In part, the invention relates to sarcoma-associated antigens as well as the nucleic acid molecules that encode the sarcoma-associated antigens. As used herein, the “nucleic acid molecules that encode” means the nucleic acid molecules that code for the immunogenic sarcoma-associated polypeptides or immunogenic fragments thereof. These nucleic acid molecules may be DNA or may be RNA (e.g. mRNA). The sarcoma-associated nucleic acid molecules of the invention also encompass variants of the nucleic acid molecules described herein. These variants may be splice variants or allelic variants of certain sequences provided. Variants of the nucleic acid molecules of the invention are intended to include homologs and alleles which are described further below. Further, as used herein, the term “sarcoma-associated molecules” includes sarcoma-associated antigens (polypeptides and fragments thereof) as well as sarcoma-associated nucleic acids. In all embodiments, human sarcoma-associated antigens and the encoding nucleic acid molecules thereof, are preferred.

[0065] In one aspect, the invention provides isolated nucleic acid molecules that encode the sarcoma-associated antigens defined herein. The isolated nucleic acid molecules of this aspect of the invention comprise: (a) nucleotide sequences selected from the group consisting of nucleotide sequences set forth as SEQ ID NOs: 1-14 and 97-107 (b) isolated nucleic acid molecules which hybridize under highly stringent conditions to the nucleic acid molecules of (a) and which code for a sarcoma-associated antigen, (c) nucleic acid molecules that differ from (a) or (b) due to the degeneracy of the genetic code, and (d) complements of (a), (b) or (c).

[0066] As used herein the term “isolated nucleic acid molecule” means: (i) amplified in vitro by, for example, polymerase chain reaction (PCR); (ii) recombinantly produced by cloning; (iii) purified, as by cleavage and gel separation; or (iv) synthesized by, for example, chemical synthesis. An isolated nucleic acid is one which is readily manipulable by recombinant DNA techniques well known in the art. Thus, a nucleotide sequence contained in a vector in which 5' and 3' restriction sites are known or for which polymerase chain

reaction (PCR) primer sequences have been disclosed is considered isolated but a nucleic acid sequence existing in its native state in its natural host is not. An isolated nucleic acid may be substantially purified, but need not be. For example, a nucleic acid that is isolated within a cloning or expression vector is not pure in that it may comprise only a tiny percentage of the material in the cell in which it resides. Such a nucleic acid is isolated, however, as the term is used herein because it is readily manipulable by standard techniques known to those of ordinary skill in the art.

[0067] The sarcoma-associated nucleic acid molecules of the invention also intended to encompass homologs and alleles which can be identified by conventional techniques. Identification of human and other organism homologs of sarcoma-associated polypeptides will be familiar to those of skill in the art. In general, nucleic acid hybridization is a suitable method for identification of homologous sequences of another species (e.g., human, cow, sheep), which correspond to a known sequence. Standard nucleic acid hybridization procedures can be used to identify related nucleic acid sequences of selected percent identity. For example, one can construct a library of cDNAs reverse transcribed from the mRNA of a selected tissue and use the nucleic acids that encode sarcoma-associated antigens identified herein to screen the library for related nucleotide sequences. The screening preferably is performed using high-stringency conditions to identify those sequences that are closely related by sequence identity. Nucleic acids so identified can be translated into polypeptides and the polypeptides can be tested for activity.

[0068] The term “high stringency” as used herein refers to parameters with which the art is familiar. Nucleic acid hybridization parameters may be found in references that compile such methods, e.g. Molecular Cloning: A Laboratory Manual, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989, or Current Protocols in Molecular Biology, F. M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. More specifically, high-stringency conditions, as used herein, refers, for example, to hybridization at 65° C. in hybridization buffer (3.5×SSC, 0.02% Ficoll, 0.02% polyvinyl pyrrolidone, 0.02% Bovine Serum Albumin, 2.5 mM NaH₂PO₄(pH7), 0.5% SDS, 2 mM EDTA). SSC is 0.15M sodium chloride/0.15M sodium citrate, pH7; SDS is sodium dodecyl sulphate; and EDTA is ethylenediaminetetracetic acid. After hybridization, the membrane upon which the DNA is transferred is washed, for example, in 2×SSC at room temperature and then at 0.1-0.5×SSC/0.1×SDS at temperatures up to 68° C.

[0069] There are other conditions, reagents, and so forth that can be used, which result in a similar degree of stringency. The skilled artisan will be familiar with such conditions, and thus they are not given here. It will be understood, however, that the skilled artisan will be able to manipulate the conditions in a manner to permit the clear identification of homologs and alleles of the sarcoma-associated nucleic acids of the invention (e.g., by using lower stringency conditions). The skilled artisan also is familiar with the methodology for screening cells and libraries for expression of such molecules, which then are routinely isolated, followed by isolation of the pertinent nucleic acid molecule and sequencing.

[0070] In general, homologs and alleles typically will share at least 90% nucleotide identity and/or at least 95% amino acid identity to the sequences of sarcoma-associated nucleic acids and polypeptides, respectively, in some instances will share at least 95% nucleotide identity and/or at least 97%

amino acid identity, in other instances will share at least 97% nucleotide identity and/or at least 98% amino acid identity, in other instances will share at least 99% nucleotide identity and/or at least 99% amino acid identity, and in other instances will share at least 99.5% nucleotide identity and/or at least 99.5% amino acid identity. The homology can be calculated using various, publicly available software tools developed by NCBI (Bethesda, Md.) that can be obtained through the internet. Exemplary tools include the BLAST system available from the website of the National Center for Biotechnology Information (NCBI) at the National Institutes of Health. Pairwise and ClustalW alignments (BLOSUM30 matrix setting) as well as Kyte-Doolittle hydropathic analysis can be obtained using the MacVector sequence analysis software (Oxford Molecular Group). Watson-Crick complements of the foregoing nucleic acids also are embraced by the invention.

[0071] In another aspect of the invention, unique fragments are provided which include unique fragments of the nucleotide sequences of the invention and complements thereof. The invention, in a preferred embodiment, provides unique fragments of SEQ ID NO: 10, 11, 15, 102, 104 or 108 and complements thereof. In another preferred embodiment, provides unique fragments of SEQ ID NO: 10 and complements thereof. In other embodiments the unique fragment includes the nucleotide sequence set forth as SEQ ID NO: 121. In still other embodiments the unique fragments includes the sequence set forth as SEQ ID NO: 123, 125, 127, 129 or 131. A unique fragment is one that is a 'signature' for the larger nucleic acid. It, for example, is long enough to assure that its precise sequence is not found in molecules outside of the nucleic acid molecules that encode the sarcoma-associated antigens defined above. Those of ordinary skill in the art may apply no more than routine procedures to determine if a fragment is unique within the human genome. In some instances the unique fragment is at least about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, 75, or 100 amino acids in length.

[0072] Unique fragments can be used as probes in Southern blot assays to identify such nucleic acid molecules, or can be used as probes in amplification assays such as those employing the polymerase chain reaction (PCR), including, but not limited to RT-PCR and RT-real-time PCR. As known to those skilled in the art, large probes such as 200 nucleotides or more are preferred for certain uses such as Southern blots, while smaller fragments will be preferred for uses such as PCR. Unique fragments also can be used to produce fusion proteins for generating antibodies or determining binding of the polypeptide fragments, or for generating immunoassay components. Likewise, unique fragments can be employed to produce nonfused fragments of the sarcoma-associated polypeptides useful, for example, in the preparation of antibodies and in immunoassays.

[0073] In screening for sarcoma-associated antigen genes, a Southern blot may be performed using the foregoing conditions, together with a detectably labeled probe (e.g., radioactive or chemiluminescent probes). After washing the membrane to which the DNA is finally transferred, the membrane can be placed against X-ray film or analyzed using a phosphorimager device to detect the radioactive or chemiluminescent signal. In screening for the expression of sarcoma-associated antigen nucleic acids, Northern blot hybridizations using the foregoing conditions can be performed on samples taken from cancer patients or subjects suspected of having a

condition characterized by abnormal cell proliferation or neoplasia. Amplification protocols such as polymerase chain reaction using primers that hybridize to the sequences presented also can be used for detection of the sarcoma-associated antigen genes or expression thereof.

[0074] Identification of related sequences can also be achieved using polymerase chain reaction (PCR) and other amplification techniques suitable for cloning related nucleic acid sequences. Preferably, PCR primers are selected to amplify portions of a nucleic acid sequence believed to be conserved (e.g., a catalytic domain, a DNA-binding domain, etc.). Again, nucleic acids are preferably amplified from a tissue-specific library (e.g., testis). One also can use expression cloning utilizing the antisera described herein to identify nucleic acids that encode related antigenic proteins in humans or other species using the SEREX procedure to screen the appropriate expression libraries. (See: Sahin et al. *Proc. Natl. Acad. Sci. USA* 92:11810-11813, 1995).

[0075] The invention also includes degenerate nucleic acids that include alternative codons to those present in the native materials. For example, serine residues are encoded by the codons TCA, AGT, TCC, TCG, TCT and AGC. Each of the six codons is equivalent for the purposes of encoding a serine residue. Thus, it will be apparent to one of ordinary skill in the art that any of the serine-encoding nucleotide triplets may be employed to direct the protein synthesis apparatus, in vitro or in vivo, to incorporate a serine residue into an elongating sarcoma-associated polypeptide. Similarly, nucleotide sequence triplets which encode other amino acid residues include, but are not limited to: CCA, CCC, CCG, and CCT (proline codons); CGA, CGC, CGG, CGT, AGA, and AGG (arginine codons); ACA, ACC, ACG, and ACT (threonine codons); AAC and AAT (asparagine codons); and ATA, ATC, and ATT (isoleucine codons). Other amino acid residues may be encoded similarly by multiple nucleotide sequences. Thus, the invention embraces degenerate nucleic acids that differ from the biologically isolated nucleic acids in codon sequence due to the degeneracy of the genetic code.

[0076] The invention also provides modified nucleic acid molecules, which include additions, substitutions and deletions of one or more nucleotides (preferably 1-20 nucleotides). In preferred embodiments, these modified nucleic acid molecules and/or the polypeptides they encode retain at least one activity or function of the unmodified nucleic acid molecule and/or the polypeptides, such as antigenicity, receptor binding, etc. In certain embodiments, the modified nucleic acid molecules encode modified polypeptides, preferably polypeptides having conservative amino acid substitutions as are described elsewhere herein. The modified nucleic acid molecules are structurally related to the unmodified nucleic acid molecules and in preferred embodiments are sufficiently structurally related to the unmodified nucleic acid molecules so that the modified and unmodified nucleic acid molecules hybridize under stringent conditions known to one of skill in the art.

[0077] For example, modified nucleic acid molecules that encode polypeptides having single amino acid changes can be prepared. Each of these nucleic acid molecules can have one, two or three nucleotide substitutions exclusive of nucleotide changes corresponding to the degeneracy of the genetic code as described herein. Likewise, modified nucleic acid molecules that encode polypeptides having two amino acid changes can be prepared which have, e.g., 2-6 nucleotide changes. Numerous modified nucleic acid molecules like

these will be readily envisioned by one of skill in the art, including for example, substitutions of nucleotides in codons encoding amino acids 2 and 3, 2 and 4, 2 and 5, 2 and 6, and so on. In the foregoing example, each combination of two amino acids is included in the set of modified nucleic acid molecules, as well as all nucleotide substitutions which code for the amino acid substitutions. Additional nucleic acid molecules that encode polypeptides having additional substitutions (i.e., 3 or more), additions or deletions (e.g., by introduction of a stop codon or a splice site(s)) also can be prepared and are embraced by the invention as readily envisioned by one of ordinary skill in the art. Any of the foregoing nucleic acids or polypeptides can be tested by routine experimentation for retention of activity or structural relation to the nucleic acids and/or polypeptides disclosed herein. As used herein the terms: "deletion", "addition", and "substitution" mean deletion, addition, and substitution changes to about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or more nucleic acids of a sequence of the invention.

[0078] According to yet another aspect of the invention, an expression vector comprising any of the isolated nucleic acid molecules of the invention, preferably operably linked to a promoter is provided. In a related aspect, host cells transformed or transfected with such expression vectors also are provided. As used herein, a "vector" may be any of a number of nucleic acid molecules into which a desired sequence may be inserted by restriction and ligation for transport between different genetic environments or for expression in a host cell. Vectors are typically composed of DNA although RNA vectors are also available. Vectors include, but are not limited to, plasmids, phagemids, and virus genomes. A cloning vector is one which is able to replicate in a host cell, and which is further characterized by one or more endonuclease restriction sites at which the vector may be cut in a determinable fashion and into which a desired DNA sequence may be ligated such that the new recombinant vector retains its ability to replicate in the host cell. In the case of plasmids, replication of the desired sequence may occur many times as the plasmid increases in copy number within the host bacterium or just a single time per host before the host reproduces by mitosis. In the case of phage, replication may occur actively during a lytic phase or passively during a lysogenic phase. An expression vector is one into which a desired DNA sequence may be inserted by restriction and ligation such that it is operably joined to regulatory sequences and may be expressed as an RNA transcript. Vectors may further contain one or more marker sequences suitable for use in the identification of cells which have or have not been transformed or transfected with the vector. Markers include, for example, genes encoding proteins which increase or decrease either resistance or sensitivity to antibiotics or other compounds, genes which encode enzymes whose activities are detectable by standard assays known in the art, e.g., -galactosidase or alkaline phosphatase, and genes which visibly affect the phenotype of transformed or transfected cells, hosts, colonies or plaques, e.g., green fluorescent protein. Preferred vectors are those capable of autonomous replication and expression of the structural gene products present in the DNA segments to which they are operably joined.

[0079] As used herein, a coding sequence and regulatory sequences are said to be "operably joined" when they are covalently linked in such a way as to place the expression or transcription of the coding sequence under the influence or

control of the regulatory sequences. As used herein, "operably joined" and "operably linked" are used interchangeably and should be construed to have the same meaning. If it is desired that the coding sequences be translated into a functional protein, two DNA sequences are said to be operably joined if induction of a promoter in the 5' regulatory sequences results in the transcription of the coding sequence and if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region to direct the transcription of the coding sequences, or (3) interfere with the ability of the corresponding RNA transcript to be translated into a protein. Thus, a promoter region is operably joined to a coding sequence if the promoter region is capable of effecting transcription of that DNA sequence such that the resulting transcript can be translated into the desired protein or polypeptide.

[0080] The precise nature of the regulatory sequences needed for gene expression may vary between species or cell types, but shall in general include, as necessary, 5' non-transcribed and 5' non-translated sequences involved with the initiation of transcription and translation respectively, such as a TATA box, capping sequence, CAAT sequence, and the like. Often, such 5' non-transcribed regulatory sequences will include a promoter region which includes a promoter sequence for transcriptional control of the operably joined gene. Regulatory sequences may also include enhancer sequences or upstream activator sequences as desired. The vectors of the invention may optionally include 5' leader or signal sequences. The choice and design of an appropriate vector is within the ability and discretion of one of ordinary skill in the art.

[0081] It will also be recognized that the invention embraces the use of the sarcoma-associated nucleic acid molecules and genomic sequences in expression vectors, as well as to transfect host cells and cell lines, be these prokaryotic, e.g., *E. coli*, or eukaryotic, e.g., CHO cells, COS cells, yeast expression systems, and recombinant baculovirus expression in insect cells. Especially useful are mammalian cells such as human, mouse, hamster, pig, goat, primate, etc. They may be of a wide variety of tissue types, including mast cells, fibroblasts, oocytes, and lymphocytes, and may be primary cells and cell lines. Specific examples include dendritic cells, peripheral blood leukocytes, bone marrow stem cells and embryonic stem cells. The expression vectors require that the pertinent sequence, i.e., those nucleic acids described supra, be operably linked to a promoter.

[0082] The invention, in one aspect, also permits the construction of sarcoma-associated antigen gene "knock-outs" and "knock-ins" in cells and in animals, providing materials for studying certain aspects of cancer and immune system responses to cancer.

[0083] Expression vectors containing all the necessary elements for expression are commercially available and known to those skilled in the art. See, e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor Laboratory Press, 1989. Cells are genetically engineered by the introduction into the cells of heterologous DNA or RNA encoding a sarcoma-associated antigen, a mutant sarcoma-associated antigen, fragments, or variants thereof. The heterologous DNA or RNA is placed under operable control of transcriptional elements to permit the expression of the heterologous DNA in the host cell.

[0084] Preferred systems for mRNA expression in mammalian cells are those such as pcDNA1.1 and pCDM8 (Invitrogen) that contain a selectable marker (which facilitates the selection of stably transfected cell lines) and contain the human cytomegalovirus (CMV) enhancer-promoter sequences. Additionally, suitable for expression in primate or canine cell lines is the pCEP4 vector (Invitrogen), which contains an Epstein Barr virus (EBV) origin of replication, facilitating the maintenance of plasmid as a multicopy extrachromosomal element. Another expression vector is the pEF-BOS plasmid containing the promoter of polypeptide Elongation Factor 1, which stimulates efficiently transcription *in vitro*. The plasmid is described by Mizushima and Nagata (Nuc. Acids Res. 18:5322, 1990), and its use in transfection experiments is disclosed by, for example, Demoulin (Mol. Cell. Biol. 16:4710-4716, 1996). Still another preferred expression vector is an adenovirus, described by Stratford-Perricaudet, which is defective for E1 and E3 proteins (J. Clin. Invest. 90:626-630, 1992). The use of the adenovirus as an Adeno.P1A recombinant is described by Warnier et al., in intradermal injection in mice for immunization against P1A (Int. J. Cancer, 67:303-310, 1996).

[0085] The invention also embraces kits termed expression kits, which allow the artisan to prepare a desired expression vector or vectors. Such expression kits include at least separate portions of each of the previously discussed coding sequences. Other components may be added, as desired, as long as the previously mentioned sequences, which are required, are included.

[0086] The invention also includes kits for amplification of a sarcoma-associated antigen nucleic acid, including at least one pair of amplification primers which hybridize to a sarcoma-associated nucleic acid. The primers preferably are about 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31 or 32 nucleotides in length and are non-overlapping to prevent formation of "primer-dimers". One of the primers will hybridize to one strand of the sarcoma-associated nucleic acid and the second primer will hybridize to the complementary strand of the sarcoma-associated nucleic acid, in an arrangement which permits amplification of the sarcoma-associated nucleic acid. Selection of appropriate primer pairs is standard in the art. For example, the selection can be made with assistance of a computer program designed for such a purpose, optionally followed by testing the primers for amplification specificity and efficiency.

[0087] The invention, in another aspect provides isolated polypeptides (including whole proteins and partial proteins) encoded by the foregoing sarcoma-associated nucleic acids. Examples of the amino acid sequences encoded by the foregoing sarcoma-associated nucleic acids are set forth as SEQ ID NOs: 46-90 and 109-120. The amino acids of the invention are also intended to encompass amino acid sequences that result from the translation of the nucleic acid sequences provided herein in a different reading frame. In one preferred embodiment of the invention a polypeptide is provided which comprises the polypeptide sequence set forth as SEQ ID NO: 55, 56, 60, 114, 116 or 120. In another preferred embodiment a polypeptide is provided which comprises the polypeptide sequence set forth as SEQ ID NO: 122. In still another preferred embodiment a polypeptide is provided which comprises the polypeptide sequence set forth as SEQ ID NO: 124. In still other embodiments polypeptides are provided which comprise the polypeptide sequence set forth as SEQ ID NO: 126, 128, 130 or 132. Such polypeptides are useful, for

example, alone or as fusion proteins to generate antibodies, and as components of an immunoassay or diagnostic assay. Immunogenic sarcoma-associated polypeptides can be isolated from biological samples including tissue or cell homogenates, and can also be expressed recombinantly in a variety of prokaryotic and eukaryotic expression systems by constructing an expression vector appropriate to the expression system, introducing the expression vector into the expression system, and isolating the recombinantly expressed protein. Fragments of the immunogenic sarcoma-associated polypeptides (including immunogenic peptides) also can be synthesized chemically using well-established methods of peptide synthesis. Thus, fragments of the disclosed polypeptides are useful for eliciting an immune response. In one embodiment fragments of a polypeptide which comprises SEQ ID NO: 55, 56, 60, 114, 116 or 120 that are at least eight amino acids in length and exhibit immunogenicity are provided. In one embodiment fragments of a polypeptide which comprises SEQ ID NO: 55 that are at least eight amino acids in length and exhibit immunogenicity are provided. In another embodiment a polypeptide is provided which comprises the polypeptide sequence set forth as SEQ ID NO: 122. In still another preferred embodiment a polypeptide is provided which comprises the polypeptide sequence set forth as SEQ ID NO: 124. In still other embodiments polypeptides are provided which comprise the polypeptide sequence set forth as SEQ ID NO: 126, 128, 130 or 132.

[0088] Fragments of a polypeptide preferably are those fragments that retain a distinct functional capability of the polypeptide. Functional capabilities that can be retained in a fragment of a polypeptide include interaction with antibodies or MHC molecules (e.g. immunogenic fragments), interaction with other polypeptides or fragments thereof, selective binding of nucleic acids or proteins, and enzymatic activity. One important activity is the ability to provoke in a subject an immune response. As will be recognized by those skilled in the art, the size of the fragment that can be used for inducing an immune response will depend upon factors such as whether the epitope recognized by an antibody is a linear epitope or a conformational epitope or the particular MHC molecule that binds to and presents the fragment (e.g. HLA class I or II). Thus, some immunogenic fragments of sarcoma-associated polypeptides will consist of longer segments while others will consist of shorter segments, (e.g. about 5, 6, 7, 8, 9, 10, 11 or 12 or more amino acids long, including each integer up to the full length of the sarcoma-associated polypeptide). Those skilled in the art are well versed in methods for selecting immunogenic fragments of polypeptides.

[0089] The invention embraces variants of the sarcoma-associated polypeptides described above. As used herein, a "variant" of a sarcoma-associated antigen polypeptide is a polypeptide which contains one or more modifications to the primary amino acid sequence of a sarcoma-associated polypeptide. Modifications which create a sarcoma-associated antigen variant can be made to a sarcoma-associated polypeptide 1) to reduce or eliminate an activity of a sarcoma-associated polypeptide; 2) to enhance a property of a sarcoma-associated polypeptide, such as protein stability in an expression system or the stability of protein-protein binding; 3) to provide a novel activity or property to a sarcoma-associated polypeptide, such as addition of an antigenic epitope or addition of a detectable moiety; or 4) to provide equivalent or better binding to a MHC molecule.

[0090] Modifications to a sarcoma-associated polypeptide are typically made to the nucleic acid which encodes the sarcoma-associated polypeptide, and can include deletions, point mutations, truncations, amino acid substitutions and additions of amino acids or non-amino acid moieties. Alternatively, modifications can be made directly to the polypeptide, such as by cleavage, addition of a linker molecule, addition of a detectable moiety, such as biotin, addition of a fatty acid, and the like. Modifications also embrace fusion proteins comprising all or part of the sarcoma-associated antigen amino acid sequence. One of skill in the art will be familiar with methods for predicting the effect on protein conformation of a change in protein sequence, and can thus “design” a variant sarcoma-associated polypeptide according to known methods. One example of such a method is described by Dahiyat and Mayo in *Science* 278:82-87, 1997, whereby proteins can be designed de novo. The method can be applied to a known protein to vary only a portion of the polypeptide sequence. By applying the computational methods of Dahiyat and Mayo, specific variants of a sarcoma-associated polypeptide can be proposed and tested to determine whether the variant retains a desired conformation.

[0091] In general, variants include sarcoma-associated polypeptides which are modified specifically to alter a feature of the polypeptide unrelated to its desired physiological activity. For example, cysteine residues can be substituted or deleted to prevent unwanted disulfide linkages. Similarly, certain amino acids can be changed to enhance expression of a sarcoma-associated polypeptide by eliminating proteolysis by proteases in an expression system (e.g., dibasic amino acid residues in yeast expression systems in which KEX2 protease activity is present).

[0092] Mutations of a nucleic acid which encode a sarcoma-associated polypeptide preferably preserve the amino acid reading frame of the coding sequence, and preferably do not create regions in the nucleic acid which are likely to hybridize to form secondary structures, such as hairpins or loops, which can be deleterious to expression of the variant polypeptide.

[0093] Mutations can be made by selecting an amino acid substitution, or by random mutagenesis of a selected site in a nucleic acid which encodes the polypeptide. Variant polypeptides are then expressed and tested for one or more activities to determine which mutation provides a variant polypeptide with the desired properties. Further mutations can be made to variants (or to non-variant sarcoma-associated polypeptides) which are silent as to the amino acid sequence of the polypeptide, but which provide preferred codons for translation in a particular host. The preferred codons for translation of a nucleic acid in, e.g., *E. coli*, are well known to those of ordinary skill in the art. Still other mutations can be made to the noncoding sequences of a sarcoma-associated antigen gene or cDNA clone to enhance expression of the polypeptide. The activity of variants of sarcoma-associated polypeptides can be tested by cloning the gene encoding the variant sarcoma-associated polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the variant sarcoma-associated polypeptide, and testing for a functional capability of the sarcoma-associated polypeptides as disclosed herein. For example, the variant sarcoma-associated polypeptide can be tested for reaction with autologous or allogeneic sera as described in the Examples. Preparation of other variant

polypeptides may favor testing of other activities, as will be known to one of ordinary skill in the art.

[0094] The skilled artisan will also realize that conservative amino acid substitutions may be made in immunogenic sarcoma-associated polypeptides to provide functionally equivalent variants, or homologs of the foregoing polypeptides, i.e., the variants retain the functional capabilities of the immunogenic sarcoma-associated polypeptides. As used herein, a “conservative amino acid substitution” refers to an amino acid substitution that does not alter the relative charge or size characteristics of the protein in which the amino acid substitution is made. Variants can be prepared according to methods for altering polypeptide sequence known to one of ordinary skill in the art such as are found in references that compile such methods, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989, or *Current Protocols in Molecular Biology*, F. M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. Exemplary functionally equivalent variants or homologs of the sarcoma-associated polypeptides include conservative amino acid substitutions of in the amino acid sequences of proteins disclosed herein. Conservative substitutions of amino acids include substitutions made amongst amino acids within the following groups: (a) M, I, L, V; (b) F, Y, W; (c) K, R, H; (d) A, G; (e) S, T; (f) Q, N; and (g) E, D. Therefore, one can make conservative amino acid substitutions to the amino acid sequence of the sarcoma-associated antigens disclosed herein and retain the specific antibody-binding characteristics of the antigens.

[0095] Likewise, upon determining that a peptide derived from a sarcoma-associated polypeptide is presented by an MHC molecule and recognized by antibodies or T lymphocytes (e.g., helper T cells or CTLs), one can make conservative amino acid substitutions to the amino acid sequence of the peptide, particularly at residues which are thought not to be direct contact points with the MHC molecule. For example, methods for identifying functional variants of HLA class II binding peptides are provided in a published PCT application of Strominger and Wucherpfennig (PCT/US96/03182). Peptides bearing one or more amino acid substitutions also can be tested for concordance with known HLA/MHC motifs prior to synthesis using, e.g. the computer program described by D’Amaro and Drijfhout (D’Amaro et al., *Human Immunol.* 43:13-18, 1995; Drijfhout et al., *Human Immunol.* 43:1-12, 1995). The substituted peptides can then be tested for binding to the MHC molecule and recognition by antibodies or T lymphocytes when bound to MHC. These variants can be tested for improved stability and are useful, inter alia, in vaccine compositions.

[0096] Conservative amino-acid substitutions in the amino acid sequence of sarcoma-associated polypeptides to produce functionally equivalent variants of sarcoma-associated polypeptides typically are made by alteration of a nucleic acid encoding a sarcoma-associated polypeptide. Such substitutions can be made by a variety of methods known to one of ordinary skill in the art. For example, amino acid substitutions may be made by PCR-directed mutation, site-directed mutagenesis according to the method of Kunkel (Kunkel, *Proc. Nat. Acad. Sci. U.S.A.* 82: 488-492, 1985), or by chemical synthesis of a gene encoding a sarcoma-associated polypeptide. Where amino acid substitutions are made to a small unique fragment of a sarcoma-associated polypeptide, such as an antigenic epitope recognized by autologous or

allogeneic sera or T lymphocytes, the substitutions can be made by directly synthesizing the peptide. The activity of functionally equivalent variants of sarcoma-associated polypeptides can be tested by cloning the gene encoding the altered sarcoma-associated polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the altered polypeptide, and testing for a functional capability of the sarcoma-associated polypeptides as disclosed herein. Peptides that are chemically synthesized can be tested directly for function, e.g., for binding to antisera recognizing associated antigens.

[0097] The invention as described herein has a number of uses, some of which are described elsewhere herein. In one aspect of the invention a method of identifying cancer-associated antigens is provided. Novel cancer-associated antigens can be identified by obtaining a biological sample from a subject, determining the reactivity of the biological sample with one or more known cancer-associated antigens, and subsequently using the reactive biological sample to screen an expression library to identify novel cancer-associated antigens as well as proteins previously known but not previously associated with cancer.

[0098] As used herein, a "subject" is preferably a human, non-human primate, cow, horse, pig, sheep, goat, dog, cat or rodent. In all embodiments, human subjects are preferred. In some embodiments, the subject is suspected of having cancer or has been diagnosed with cancer. Cancers in which the sarcoma-associated nucleic acid or polypeptide are differentially expressed include sarcoma.

[0099] As used herein, a biological sample includes, but is not limited to: tissue, cells, or body fluid (e.g. serum, blood, lymph node fluid, etc.). The fluid sample may include cells and/or fluid. The tissue and cells may be obtained from a subject or may be grown in culture (e.g. from a cell line). As used herein, a biological sample is body fluid, tissue or cells obtained from a subject using methods well-known to those of ordinary skill in the related medical arts.

[0100] The invention in another aspect permits the isolation of the cancer-associated antigens described herein. A variety of methodologies well-known to the skilled practitioner can be utilized to obtain isolated cancer-associated antigens. The proteins may be purified from cells which naturally produce the protein by chromatographic means or immunological recognition. Alternatively, an expression vector may be introduced into cells to cause production of the protein. In another method, mRNA transcripts may be microinjected or otherwise introduced into cells to cause production of the encoded protein. Translation of mRNA in cell-free extracts such as the reticulocyte lysate system also may be used to produce the protein. Those skilled in the art also can readily follow known methods for isolating cancer-associated antigens. These include, but are not limited to, chromatographic techniques such as immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography, and immune-affinity chromatography.

[0101] The invention also involves diagnosing or monitoring cancer in subjects by determining the presence of an immune response to one or more sarcoma-associated antigens of the invention. In preferred embodiments, this determination is performed by assaying a bodily fluid obtained from the subject, preferably serum, blood, or lymph node fluid for the presence of antibodies against the sarcoma-associated antigens described herein. This determination may also be performed by assaying a tissue or cells from the subject for

the presence of one or more sarcoma-associated antigens (or nucleic acid molecules that encode these antigens) described herein. In another embodiment, the presence of antibodies against at least one additional cancer antigen is determined for diagnosis of cancer. The additional antigen may be a sarcoma-associated antigen as described herein or may be some other cancer-associated antigen. This determination may also be performed by assaying a tissue or cells from the subject for the presence of the sarcoma-associated antigens described herein.

[0102] Measurement of the immune response against one of the sarcoma-associated antigens over time by sequential determinations permits monitoring of the disease and/or the effects of a course of treatment. For example, a sample, such as serum, blood, or lymph node fluid, may be obtained from a subject, tested for an immune response to one of the sarcoma-associated antigens, and at a second, subsequent time, another sample, may be obtained from the subject and similarly tested. The results of the first and second (or subsequent) tests can be compared as a measure of the onset, regression or progression of cancer, or, if cancer treatment was undertaken during the interval between obtaining the samples, the effectiveness of the treatment may be evaluated by comparing the results of the two tests. In preferred embodiments the sarcoma-associated antigens are bound to a substrate. In other preferred embodiments the immune response of the biological sample to the sarcoma-associated antigens is determined with ELISA. Other methods will be apparent to one of skill in the art.

[0103] Diagnostic methods of the invention also involve determining the aberrant expression of one or more of the sarcoma-associated antigens described herein or the nucleic acid molecules that encode them. Such determinations can be carried out via any standard nucleic acid assay, including the polymerase chain reaction or assaying with hybridization probes, which may be labeled, or by assaying biological samples with binding partners (e.g., antibodies) for sarcoma-associated antigens.

[0104] The diagnostic methods of the invention can be used to detect the presence of a disorder associated with aberrant expression of a sarcoma-associated molecule, as well as to assess the progression and/or regression of the disorder such as in response to treatment (e.g., chemotherapy, radiation). According to this aspect of the invention, the method for diagnosing a disorder characterized by aberrant expression of a sarcoma-associated molecule involve: detecting expression of a sarcoma-associated molecule in a first biological sample obtained from a subject, wherein differential expression of the sarcoma-associated molecule compared to a control sample indicates that the subject has a disorder characterized by aberrant expression of a sarcoma-associated molecule, such as cancer.

[0105] As used herein, "aberrant expression" of a sarcoma-associated antigen is intended to include any expression that is statistically significant from the expected amount of expression. For example, expression of a sarcoma-associated molecule (i.e., the sarcoma-associated antigen or the nucleic acid molecules that encode it) in a tissue that is not expected to express the sarcoma-associated molecule would be included in the definition of "aberrant expression". Likewise, expression of the sarcoma-associated molecule that is determined to be expressed at a significantly higher or lower level than expected is also included. Therefore, a determination of the level of expression of one or more of the sarcoma-asso-

ciated antigens and/or the nucleic acids that encode them is diagnostic of cancer if the level of expression is above a baseline level determined for that tissue type. The baseline level of expression can be determined using standard methods known to those of skill in the art. Such methods include, for example, assaying a number of histologically normal tissue samples from subjects that are clinically normal (i.e. do not have clinical signs of cancer in that tissue type) and determining the mean level of expression for the samples.

[0106] The level of expression of the nucleic acid molecules of the invention or the antigens they encode can indicate cancer in the tissue when the level of expression is significantly more in the tissue than in a control sample. In some embodiments, a level of expression in the tissues that is at least about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 150%, 200%, 250%, 300%, 400%, or 500% more than the level of expression in the control tissue indicates cancer in the tissue.

[0107] As used herein the term “control” means predetermined values, and also means samples of materials tested in parallel with the experimental materials. Examples include samples from control populations or control samples generated through manufacture to be tested in parallel with the experimental samples.

[0108] As used herein the term “control” includes positive and negative controls which may be a predetermined value that can take a variety of forms. The control(s) can be a single cut-off value, such as a median or mean, or can be established based upon comparative groups, such as in groups having normal amounts of sarcoma-associated molecules of the invention and groups having abnormal amounts of sarcoma-associated molecules of the invention. Another example of a comparative group is a group having a particular disease, condition and/or symptoms and a group without the disease, condition and/or symptoms. Another comparative group is a group with a family history of a particular disease and a group without such a family history of the particular disease. The predetermined control value can be arranged, for example, where a tested population is divided equally (or unequally) into groups, such as a low-risk group, a medium-risk group and a high-risk group or into quadrants or quintiles, the lowest quadrant or quintile being individuals with the lowest risk or lowest expression levels of a sarcoma-associated molecule of the invention that is up-regulated in cancer and the highest quadrant or quintile being individuals with the highest risk or highest expression levels of a sarcoma-associated molecule of the invention that is up-regulated in cancer.

[0109] The predetermined value of a control will depend upon the particular population selected. For example, an apparently healthy population will have a different “normal” sarcoma-associated molecule expression level range than will a population which is known to have a condition characterized by aberrant expression of the sarcoma-associated molecule. Accordingly, the predetermined value selected may take into account the category in which an individual falls. Appropriate ranges and categories can be selected with no more than routine experimentation by those of ordinary skill in the art. Typically the control will be based on apparently healthy individuals in an appropriate age bracket. As used herein, the term “increased expression” means a higher level of expression relative to a selected control.

[0110] The invention involves in some aspects diagnosing or monitoring cancer by determining the level of expression of one or more sarcoma-associated nucleic acid molecules

and/or determining the level of expression of one or more sarcoma-associated polypeptides they encode. In some important embodiments, this determination is performed by assaying a tissue sample from a subject for the level of expression of one or more sarcoma-associated nucleic acid molecules or for the level of expression of one or more sarcoma-associated polypeptides encoded by the nucleic acid molecules of the invention.

[0111] The expression of the molecules of the invention may be determined using routine methods known to those of ordinary skill in the art. These methods include, but are not limited to: direct RNA amplification, reverse transcription of RNA to cDNA, real-time RT-PCR, amplification of cDNA, hybridization, and immunologically based assay methods, which include, but are not limited to immunohistochemistry, antibody sandwich capture assay, ELISA, and enzyme-linked immunosorbent assay (ELISA). For example, the determination of the presence of level of nucleic acid molecules of the invention in a subject or tissue can be carried out via any standard nucleic acid determination assay, including the polymerase chain reaction, or assaying with labeled hybridization probes. Such hybridization methods include, but are not limited to microarray techniques.

[0112] These methods of determining the presence and/or level of the molecules of the invention in cells and tissues may include use of labels to monitor the presence of the molecules of the invention. Such labels may include, but are not limited to radiolabels or chemiluminescent labels, which may be utilized to determine whether a molecule of the invention is expressed in a cell or tissue, and to determine the level of expression in the cell or tissue. For example, a fluorescently labeled or radiolabeled antibody that selectively binds to a polypeptide of the invention may be contacted with a tissue or cell to visualize the polypeptide in vitro or in vivo. These and other in vitro and in vivo imaging methods for determining the presence of the nucleic acid and polypeptide molecules of the invention are well known to those of ordinary skill in the art.

[0113] The invention, therefore, also involves the use of agents such as polypeptides that bind to sarcoma-associated antigens. Such agents can be used in methods of the invention including the diagnosis and/or treatment of cancer. Such binding agents can be used, for example, in screening assays to detect the presence or absence of sarcoma-associated antigens and can be used in quantitative binding assays to determine levels of expression in biological samples and cells. Such agents also may be used to inhibit the native activity of the sarcoma-associated polypeptides, for example, by binding to such polypeptides.

[0114] According to this aspect, the binding polypeptides bind to an isolated nucleic acid or protein of the invention, including unique fragments thereof. Preferably, the binding polypeptides bind to a sarcoma-associated polypeptide, or a unique fragment thereof.

[0115] In preferred embodiments, the binding polypeptide is an antibody or antibody fragment, more preferably, an Fab or F(ab)₂ fragment of an antibody. Typically, the fragment includes a CDR3 region that is selective for the sarcoma-associated antigen. Any of the various types of antibodies can be used for this purpose, including polyclonal antibodies, monoclonal antibodies, humanized antibodies, and chimeric antibodies.

[0116] Thus, the invention provides agents which bind to sarcoma-associated antigens encoded by sarcoma-associated

nucleic acid molecules of the invention, and in certain embodiments preferably to unique fragments of the sarcoma-associated polypeptides. Such binding partners can be used in screening assays to detect the presence or absence of a sarcoma-associated antigen and in purification protocols to isolate such sarcoma-associated antigens. Likewise, such binding partners can be used to selectively target drugs, toxins or other molecules (including detectable diagnostic molecules) to cells which express sarcoma-associated antigens. In this manner, for example, cells present in solid or non-solid tumors which express sarcoma-associated proteins can be treated with cytotoxic compounds that are selective for the sarcoma-associated molecules (nucleic acids and/or antigens). Such binding agents also can be used to inhibit the native activity of the sarcoma-associated antigen, for example, to further characterize the functions of these molecules.

[0117] The antibodies of the present invention thus are prepared by any of a variety of methods, including administering a protein, fragments of a protein, cells expressing the protein or fragments thereof and the like to an animal to induce polyclonal antibodies. The present invention also provides methods of producing monoclonal antibodies to the sarcoma-associated molecules of the invention described herein. The production of monoclonal antibodies is according to techniques well known in the art. As detailed herein, such antibodies may be used for example to identify tissues expressing protein or to purify protein. Antibodies also may be coupled to specific labeling agents or imaging agents, including, but not limited to a molecule preferably selected from the group consisting of fluorescent, enzyme, radioactive, metallic, biotin, chemiluminescent, bioluminescent, chromophore, or colored, etc. In some aspects of the invention, a label may be a combination of the foregoing molecule types.

[0118] Significantly, as is well-known in the art, only a small portion of an antibody molecule, the paratope, is involved in the binding of the antibody to its epitope (see, in general, Clark, W. R. (1986) *The Experimental Foundations of Modern Immunology* Wiley & Sons, Inc., New York; Roitt, I. (1991) *Essential Immunology*, 7th Ed., Blackwell Scientific Publications, Oxford). The pFc' and Fc regions, for example, are effectors of the complement cascade but are not involved in antigen binding. An antibody from which the pFc' region has been enzymatically cleaved, or which has been produced without the pFc' region, designated an F(ab')₂ fragment, retains both of the antigen binding sites of an intact antibody. Similarly, an antibody from which the Fc region has been enzymatically cleaved, or which has been produced without the Fc region, designated an Fab fragment, retains one of the antigen binding sites of an intact antibody molecule. Fab fragments consist of a covalently bound antibody light chain and a portion of the antibody heavy chain denoted Fd. The Fd fragments are the major determinant of antibody specificity (a single Fd fragment may be associated with up to ten different light chains without altering antibody specificity) and Fd fragments retain epitope-binding ability in isolation.

[0119] Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the paratope (see, in general, Clark, 1986; Roitt, 1991). In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are

four framework regions (FR1 through FR4) separated respectively by three complementarity determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.

[0120] It is now well-established in the art that the non-CDR regions of a mammalian antibody may be replaced with similar regions of nonspecific or heterospecific antibodies while retaining the epitopic specificity of the original antibody. This is most clearly manifested in the development and use of "humanized" antibodies in which non-human CDRs are covalently joined to human FR and/or Fc/pFc' regions to produce a functional antibody. See, e.g., U.S. Pat. Nos. 4,816,567, 5,225,539, 5,585,089, 5,693,762, and 5,859,205.

[0121] Fully human monoclonal antibodies also can be prepared by immunizing mice transgenic for large portions of human immunoglobulin heavy and light chain loci. Following immunization of these mice (e.g., XenoMouse (Abgenix), HuMAb mice (Medarex/GenPharm)), monoclonal antibodies can be prepared according to standard hybridoma technology. These monoclonal antibodies will have human immunoglobulin amino acid sequences and therefore will not provoke human anti-mouse antibody (HAMA) responses when administered to humans.

[0122] Thus, as will be apparent to one of ordinary skill in the art, the present invention also provides for F(ab')₂, Fab, Fv, and Fd fragments; chimeric antibodies in which the Fc and/or FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human 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 by homologous human or non-human sequences; chimeric Fab fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; and chimeric Fd fragment antibodies in which the FR and/or CDR1 and/or CDR2 regions have been replaced by homologous human or non-human sequences. The present invention also includes so-called single chain antibodies.

[0123] Thus, the invention involves polypeptides of numerous size and type that bind specifically to sarcoma-associated antigens. These polypeptides may be derived also from sources other than antibody technology. For example, such polypeptide binding agents can be provided by degenerate peptide libraries which can be readily prepared in solution, in immobilized form or as phage display libraries. Combinatorial libraries also can be synthesized of peptides containing one or more amino acids. Libraries further can be synthesized of peptides and non-peptide synthetic moieties.

[0124] The sarcoma-associated antigens of the invention can be used to screen peptide libraries, including phage display libraries, to identify and select peptide binding partners of the sarcoma-associated antigens of the invention. Such molecules can be used, as described, for screening assays, for diagnostic assays, for purification protocols or for targeting drugs, toxins and/or labeling agents (e.g., radioisotopes, fluorescent molecules, etc.) to cells which express sarcoma-associated molecules such as cancer cells which have aberrant sarcoma-associated expression.

[0125] Phage display can be particularly effective in identifying binding peptides useful according to the invention. Briefly, one prepares a phage library (using e.g. m13, fd, or lambda phage), displaying inserts from 4 to about 80 amino

acid residues using conventional procedures. The inserts may represent, for example, a completely degenerate or biased array. One then can select phage-bearing inserts which bind to the sarcoma-associated antigen. This process can be repeated through several cycles of reselection of phage that bind to the sarcoma-associated polypeptide. Repeated rounds lead to enrichment of phage bearing particular sequences. DNA sequence analysis can be conducted to identify the sequences of the expressed polypeptides. The minimal linear portion of the sequence that binds to the sarcoma-associated polypeptide can be determined. One can repeat the procedure using a biased library containing inserts containing part or all of the minimal linear portion plus one or more additional degenerate residues upstream or downstream thereof. Yeast two-hybrid screening methods also may be used to identify polypeptides that bind to the sarcoma-associated antigens.

[0126] As detailed herein, the foregoing antibodies and other binding molecules may be used to identify tissues with normal or aberrant expression of a sarcoma-associated antigen. Antibodies also may be coupled to specific diagnostic labeling agents for imaging of cells and tissues with normal or aberrant sarcoma-associated antigen expression or to therapeutically useful agents according to standard coupling procedures. As used herein, "therapeutically useful agents" include any therapeutic molecule which desirably is targeted selectively to a cell or tissue selectively with an aberrant sarcoma-associated expression.

[0127] Diagnostic agents for in vivo use include, but are not limited to, barium sulfate, iocetamic acid, iopanoic acid, ipodate calcium, diatrizoate sodium, diatrizoate meglumine, metrizamide, tyropanoate sodium and radiodiagnostics including positron emitters such as fluorine-18 and carbon-11, gamma emitters such as iodine-123, technitium-99, iodine-131 and indium-111, and nuclides for nuclear magnetic resonance such as fluorine and gadolinium. Other diagnostic agents useful in the invention will be apparent to one of ordinary skill in the art.

[0128] The antibodies of the present invention can also be used to therapeutically target sarcoma-associated antigens. In a preferred embodiment, antibodies can be used to target antigens expressed on the cell surface, such as NY-SAR-35. These antibodies can be linked not only to a detectable marker but also an antitumor agent or an immunomodulator. Antitumor agents can include cytotoxic agents and agents that act on tumor neovasculature. Detectable markers include, for example, radioactive or fluorescent markers. Cytotoxic agents include cytotoxic radionuclides, chemical toxins and protein toxins.

[0129] The cytotoxic radionuclide or radiotherapeutic isotope preferably is an alpha-emitting isotope such as ^{225}Ac , ^{211}At , ^{212}Bi , ^{213}Bi , ^{212}Pb , ^{224}Ra or ^{223}Ra . Alternatively, the cytotoxic radionuclide may be a beta-emitting isotope such as ^{186}Rh , ^{188}Rh , ^{177}Lu , ^{90}Y , ^{131}I , ^{67}Cu , ^{64}Cu , ^{153}Sm or ^{166}Ho . Further, the cytotoxic radionuclide may emit Auger and low energy electrons and include the isotopes ^{125}I , ^{123}I or ^{77}Br .

[0130] Suitable chemical toxins or chemotherapeutic agents include members of the enediyne family of molecules, such as calicheamicin and esperamicin. Chemical toxins can also be taken from the group consisting of methotrexate, doxorubicin, melphalan, chlorambucil, ARA-C, vindesine, mitomycin C, cis-platinum, etoposide, bleomycin and 5-fluorouracil. Other antineoplastic agents that may be conjugated to the anti-PSMA antibodies of the present invention include dolastatins (U.S. Pat. Nos. 6,034,065 and 6,239,104) and

derivatives thereof. Of particular interest is dolastatin 10 (dolavaline-valine-dolaisoleuine-dolaproine-dolaphenine) and the derivatives auristatin PHE (dolavaline-valine-dolaisoleuine-dolaproine-phenylalanine-methyl ester) (Pettit, G. R. et al., *Anticancer Drug Des.* 13(4):243-277, 1998; Woyke, T. et al., *Antimicrob. Agents Chemother.* 45(12):3580-3584, 2001), and aurastatin E and the like. Toxins that are less preferred in the compositions and methods of the invention include poisonous lectins, plant toxins such as ricin, abrin, modeccin, botulina and diphtheria toxins. Of course, combinations of the various toxins could also be coupled to one antibody molecule thereby accommodating variable cytotoxicity. Other chemotherapeutic agents are known to those skilled in the art.

[0131] Agents that act on the tumor vasculature can include tubulin-binding agents such as combrestatin A4 (Griggs et al., *Lancet Oncol.* 2:82, 2001), angiostatin and endostatin (reviewed in Rosen, *Oncologist* 5:20, 2000, incorporated by reference herein) and interferon inducible protein 10 (U.S. Pat. No. 5,994,292). A number of antiangiogenic agents currently in clinical trials are also contemplated. Agents currently in clinical trials include: 2ME2, Angiostatin, Angiozyme, Anti-VEGF RhuMAb, Apra (CT-2584), Avicine, Benefin, BMS275291, Carboxyamidotriazole, CC4047, CC5013, CC7085, CDC801, CGP-41251 (PKC 412), CM101, Combretastatin A-4 Prodrug, EMD 121974, Endostatin, Flavopiridol, Genistein (GCP), Green Tea Extract, IM-862, ImmTher, Interferon alpha, Interleukin-12, Iressa (ZD1839), Marimastat, Metastat (Col-3), Neovastat, Octreotide, Paclitaxel, Penicillamine, Photofrin, Photopoint, PI-88, Prinomastat (AG-3340), PTK787 (ZK22584), R0317453, Solimastat, Squalamine, SU 101, SU 5416, SU-6668, Suradista (FCE 26644), Suramin (Metarex), Tetrathiomolybdate, Thalidomide, TNP-470 and Vitaxin. additional antiangiogenic agents are described by Kerbel, J. Clin. Oncol. 19(18s):45s-51s, 2001, which is incorporated by reference herein. Immunomodulators suitable for conjugation to the antibodies include α -interferon, γ -interferon, and tumor necrosis factor alpha (TNF α).

[0132] The coupling of one or more toxin molecules to the antibody is envisioned to include many chemical mechanisms, for instance covalent binding, affinity binding, intercalation, coordinate binding, and complexation. The toxic compounds used to prepare the immunotoxins are attached to the antibodies or antigen-binding fragments thereof by standard protocols known in the art.

[0133] In other aspects of the invention, the sarcoma-associated molecules and the antibodies and other binding molecules, as described herein, can be used for the treatment of disorders. When "disorder" is used herein, it refers to any pathological condition where the sarcoma-associated antigens are aberrantly expressed. An example of such a disorder is cancer, with sarcoma as a particular example. For human cancers, additional particular examples include synovial sarcoma, liposarcoma, neurosarcoma, chondrosarcoma, fibrosarcoma, Ewing sarcoma, leiomyosarcoma, osteosarcoma, rhabdomyosarcoma, malignant fibrous histiocytoma, DFSP, leukemia, lymphoma, gastric cancer, glioma, bladder cancer, breast cancer, ovarian cancer, renal cancer, lung cancer, colon cancer, prostate cancer, esophageal cancer, melanoma and hepatoma.

[0134] Conventional treatment for cancer may include, but is not limited to: surgical intervention, chemotherapy, radiotherapy, and adjuvant systemic therapies. In one aspect of the

invention, treatment may include administering binding polypeptides such as antibodies that specifically bind to the sarcoma-associated antigen. These binding polypeptides can be optionally linked to one or more detectable markers, anti-tumor agents or immunomodulators as described above.

[0135] Cancer treatment, in another aspect of the invention may include administering an antisense molecules or RNAi molecules to reduce expression level and/or function level of sarcoma-associated polypeptides of the invention in the subject in cancers where a sarcoma-associated molecule is up-regulated. The use of RNA interference or "RNAi" involves the use of double-stranded RNA (dsRNA) to block gene expression. (see: Sui, G, et al, Proc Natl. Acad. Sci U.S.A. 99:5515-5520, 2002). Methods of applying RNAi strategies in embodiments of the invention would be understood by one of ordinary skill in the art.

[0136] Sarcoma-associated polypeptides as described herein, can also be used in one aspect of the invention to induce or enhance an immune response. Some therapeutic approaches based upon the disclosure are premised on a response by a subject's immune system, leading to lysis of antigen presenting cells, such as cancer cells which present one or more sarcoma-associated antigens of the invention. One such approach is the administration of autologous CTLs specific to a sarcoma-associated antigen/MHC complex to a subject with abnormal cells of the phenotype at issue. It is within the ability of one of ordinary skill in the art to develop such CTLs in vitro. An example of a method for T cell differentiation is presented in International Application number PCT/US96/05607. Generally, a sample of cells taken from a subject, such as blood cells, are contacted with a cell presenting the complex and capable of provoking CTLs to proliferate. The target cell can be a transfectant, such as a COS cell. These transfectants present the desired complex of their surface and, when combined with a CTL of interest, stimulate its proliferation. COS cells are widely available, as are other suitable host cells. Specific production of CTL clones is well known in the art. The clonally expanded autologous CTLs then are administered to the subject.

[0137] Another method for selecting antigen-specific CTL clones has recently been described (Altman et al., Science 274:94-96, 1996; Dunbar et al., Curr. Biol. 8:413-416, 1998), in which fluorogenic tetramers of MHC class I molecule/peptide complexes are used to detect specific CTL clones. Briefly, soluble MHC class I molecules are folded in vitro in the presence of β_2 -microglobulin and a peptide antigen which binds the class I molecule. After purification, the MHC/peptide complex is purified and labeled with biotin. Tetramers are formed by mixing the biotinylated peptide-MHC complex with labeled avidin (e.g. phycoerythrin) at a molar ratio or 4:1. Tetramers are then contacted with a source of CTLs such as peripheral blood or lymph node. The tetramers bind CTLs which recognize the peptide antigen/MHC class I complex. Cells bound by the tetramers can be sorted by fluorescence activated cell sorting to isolate the reactive CTLs. The isolated CTLs then can be expanded in vitro for use as described herein. To detail a therapeutic methodology, 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 CTLs leading to proliferation of the CTLs specific thereto. The proliferated CTLs are then administered to a subject with a cellular abnormality which is

characterized by certain of the abnormal cells presenting the particular complex. The CTLs then lyse the abnormal cells, thereby achieving the desired therapeutic goal.

[0138] The foregoing therapy assumes that at least some of the subject's abnormal cells present the relevant HLA/cancer associated antigen complex. This can be determined very easily, as the art is very familiar with methods for identifying cells which present a particular HLA molecule, as well as how to identify cells expressing DNA of the pertinent sequences, in this case a sarcoma-associated antigen sequence. Once cells presenting the relevant complex are identified via the foregoing screening methodology, they can be combined with a sample from a patient, where the sample contains CTLs. If the complex presenting cells are lysed by the mixed CTL sample, then it can be assumed that a sarcoma-associated antigen is being presented, and the subject is an appropriate candidate for the therapeutic approaches set forth supra.

[0139] Adoptive transfer is not the only form of therapy that is available in accordance with the invention. CTLs can also be provoked in vivo, using a number of approaches. One approach is the use of non-proliferative cells expressing the complex. The cells used in this approach may be those that normally express the complex, such as irradiated tumor cells or cells transfected with one or both of the genes necessary for presentation of the complex (i.e. the antigenic peptide and the presenting MHC molecule). Chen et al. (Proc. Natl. Acad. Sci. USA 88: 110-114, 1991) exemplifies this approach, showing the use of transfected cells expressing HPV E7 peptides in a therapeutic regime. Various cell types may be used. Similarly, vectors carrying one or both of the genes of interest may be used. Viral or bacterial vectors are especially preferred. For example, nucleic acids which encode a sarcoma-associated polypeptide may be operably linked to promoter and enhancer sequences which direct expression of the sarcoma-associated antigen polypeptide in certain tissues or cell types. The nucleic acid may be incorporated into an expression vector.

[0140] Expression vectors may be unmodified extrachromosomal nucleic acids, plasmids or viral genomes constructed or modified to enable insertion of exogenous nucleic acids, such as those encoding sarcoma-associated antigen, as described elsewhere herein. Nucleic acids encoding a sarcoma-associated antigen also may be inserted into a retroviral genome, thereby facilitating integration of the nucleic acid into the genome of the target tissue or cell type. In these systems, the gene of interest is carried by a microorganism, e.g., a Vaccinia virus, pox virus, herpes simplex virus, retrovirus or adenovirus, and the materials de facto "infect" host cells. The cells which result present the complex of interest, and are recognized by autologous CTLs, which then proliferate.

[0141] A similar effect can be achieved by combining the sarcoma-associated polypeptide or a stimulatory fragment thereof with an adjuvant to facilitate incorporation into antigen presenting cells in vivo. The sarcoma-associated polypeptide is processed to yield the peptide partner of the MHC molecule while a sarcoma-associated fragment may be presented without the need for further processing. Generally, subjects can receive an intradermal injection of an effective amount of the sarcoma-associated antigen. Initial doses can be followed by booster doses, following immunization protocols standard in the art. Preferred sarcoma-associated antigens include those found to react with allogeneic cancer antisera, shown in the examples below.

[0142] The invention involves the use of various materials disclosed herein to “immunize” subjects or as “vaccines”. As used herein, “immunization” or “vaccination” means increasing or activating an immune response against an antigen. It does not require elimination or eradication of a condition but rather contemplates the clinically favorable enhancement of an immune response toward an antigen. Generally accepted animal models, can be used for testing of immunization against cancer using a sarcoma-associated nucleic acid. For example, human cancer cells can be introduced into a mouse to create a tumor, and one or more sarcoma-associated nucleic acids can be delivered by the methods described herein. The effect on the cancer cells (e.g., reduction of tumor size) can be assessed as a measure of the effectiveness of the sarcoma-associated nucleic acid immunization. Of course, testing of the foregoing animal model using more conventional methods for immunization include the administration of one or more sarcoma-associated polypeptides or fragments derived therefrom, optionally combined with one or more adjuvants and/or cytokines to boost the immune response.

[0143] Methods for immunization, including formulation of a vaccine composition and selection of doses, route of administration and the schedule of administration (e.g. primary and one or more booster doses), are well known in the art. The tests also can be performed in humans, where the end point is to test for the presence of enhanced levels of circulating CTLs against cells bearing the antigen, to test for levels of circulating antibodies against the antigen, to test for the presence of cells expressing the antigen and so forth.

[0144] As part of the immunization compositions, one or more sarcoma-associated polypeptides or immunogenic fragments thereof are administered with one or more adjuvants to induce an immune response or to increase an immune response. An adjuvant is a substance incorporated into or administered with antigen which potentiates the immune response. Adjuvants may enhance the immunological response by providing a reservoir of antigen (extracellularly or within macrophages), activating macrophages and stimulating specific sets of lymphocytes. Adjuvants of many kinds are well known in the art. Specific examples of adjuvants include monophosphoryl lipid A (MPL, SmithKline Beecham), a congener obtained after purification and acid hydrolysis of *Salmonella* minnesota Re 595 lipopolysaccharide; saponins including QS21 (SmithKline Beecham), a pure QA-21 saponin purified from *Quillja saponaria* extract; DQS21, described in PCT application WO96/33739 (SmithKline Beecham); QS-7, QS-17, QS-18, and QS-L1 (So et al., Mol. Cells 7:178-186, 1997); incomplete Freund's adjuvant; complete Freund's adjuvant; montanide; alum; CpG oligonucleotides (see e.g. Kreig et al., Nature 374:546-9, 1995); and various water-in-oil emulsions prepared from biodegradable oils such as squalene and/or tocopherol. Preferably, the antigens are administered mixed with a combination of DQS21/MPL. The ratio of DQS21 to MPL typically will be about 1:10 to 10:1, preferably about 1:5 to 5:1 and more preferably about 1:1. Typically for human administration, DQS21 and MPL will be present in a vaccine formulation in the range of about 1 µg to about 100 µg. Other adjuvants are known in the art and can be used in the invention (see, e.g. Goding, Monoclonal Antibodies: Principles and Practice, 2nd Ed., 1986). Methods for the preparation of mixtures or emulsions of polypeptide and adjuvant are well known to those of skill in the art of vaccination.

[0145] Other agents which stimulate the immune response of the subject can also be administered to the subject. For example, other cytokines are also useful in vaccination protocols as a result of their lymphocyte regulatory properties. Many other cytokines useful for such purposes will be known to one of ordinary skill in the art, including interleukin-12 (IL-12) which has been shown to enhance the protective effects of vaccines (see, e.g., Science 268: 1432-1434, 1995), GM-CSF and IL-18. Thus cytokines can be administered in conjunction with antigens and adjuvants to increase the immune response to the antigens.

[0146] There are a number of immune response potentiating compounds that can be used in vaccination protocols. These include costimulatory molecules provided in either protein or nucleic acid form. Such costimulatory molecules include the B7-1 and B7-2 (CD80 and CD86 respectively) molecules which are expressed on dendritic cells (DC) and interact with the CD28 molecule expressed on the T cell. This interaction provides costimulation (signal 2) to an antigen/MHC/TCR stimulated (signal 1) T cell, increasing T cell proliferation and effector function. B7 also interacts with CTLA4 (CD152) on T cells and studies involving CTLA4 and B7 ligands indicate that the B7-CTLA4 interaction can enhance antitumor immunity and CTL proliferation (Zheng P., et al. Proc. Natl. Acad. Sci. USA 95 (11):6284-6289 (1998)).

[0147] B7 typically is not expressed on tumor cells so they are not efficient antigen presenting cells (APCs) for T cells. Induction of B7 expression would enable the tumor cells to stimulate more efficiently CTL proliferation and effector function. A combination of B7/IL-6/IL-12 costimulation has been shown to induce IFN-gamma and a Th1 cytokine profile in the T cell population leading to further enhanced T cell activity (Gajewski et al., J. Immunol, 154:5637-5648 (1995)). Tumor cell transfection with B7 has been discussed in relation to in vitro CTL expansion for adoptive transfer immunotherapy by Wang et al., (J. Immunol., 19:1-8 (1986)). Other delivery mechanisms for the B7 molecule would include nucleic acid (naked DNA) immunization (Kim J., et al. Nat. Biotechnol., 15:7:641-646 (1997)) and recombinant viruses such as adeno and pox (Wendtner et al., Gene Ther., 4:7:726-735 (1997)). These systems are all amenable to the construction and use of expression cassettes for the coexpression of B7 with other molecules of choice such as the antigens or fragment(s) of antigens discussed herein (including polytopes) or cytokines. These delivery systems can be used for induction of the appropriate molecules in vitro and for in vivo vaccination situations. The use of anti-CD28 antibodies to directly stimulate T cells in vitro and in vivo could also be considered. Similarly, the inducible co-stimulatory molecule ICOS which induces T cell responses to foreign antigen could be modulated, for example, by use of anti-ICOS antibodies (Hutloff et al., Nature 397:263-266, 1999).

[0148] Lymphocyte function associated antigen-3 (LFA-3) is expressed on APCs and some tumor cells and interacts with CD2 expressed on T cells. This interaction induces T cell IL-2 and IFN-gamma production and can thus complement but not substitute, the B7/CD28 costimulatory interaction (Parra et al., J. Immunol., 158:637-642 (1997), Fenton et al., J. Immunother., 21:2:95-108 (1998)).

[0149] Lymphocyte function associated antigen-1 (LFA-1) is expressed on leukocytes and interacts with ICAM-1 expressed on APCs and some tumor cells. This interaction induces T cell IL-2 and IFN-gamma production and can thus

complement but not substitute, the B7/CD28 costimulatory interaction (Fenton et al., *J. Immunother.*, 21:2:95-108 (1998)). LFA-1 is thus a further example of a costimulatory molecule that could be provided in a vaccination protocol in the various ways discussed above for B7.

[0150] Complete CTL activation and effector function requires Th cell help through the interaction between the Th cell CD40L (CD40 ligand) molecule and the CD40 molecule expressed by DCs (Ridge et al., *Nature*, 393:474 (1998), Bennett et al., *Nature*, 393:478 (1998), Schoenberger et al., *Nature*, 393:480 (1998)). This mechanism of this costimulatory signal is likely to involve upregulation of B7 and associated IL-6/IL-12 production by the DC (APC). The CD40-CD40L interaction thus complements the signal 1 (antigen/MHC-TCR) and signal 2 (B7-CD28) interactions.

[0151] The use of anti-CD40 antibodies to stimulate DC cells directly, would be expected to enhance a response to tumor antigens which are normally encountered outside of an inflammatory context or are presented by non-professional APCs (tumor cells). In these situations Th help and B7 costimulation signals are not provided.

[0152] The invention contemplates delivery of nucleic acids, polypeptides or fragments thereof for vaccination. Delivery of polypeptides and fragments thereof can be accomplished according to standard vaccination protocols which are well known in the art. In another embodiment, the delivery of nucleic acid is accomplished by ex vivo methods, i.e. by removing a cell from a subject, genetically engineering the cell to include a sarcoma-associated polypeptide, and reintroducing the engineered cell into the subject. One example of such a procedure is outlined in U.S. Pat. No. 5,399,346 and in exhibits submitted in the file history of that patent, all of which are publicly available documents. In general, it involves introduction in vitro of a functional copy of a gene into a cell(s) of a subject, and returning the genetically engineered cell(s) to the subject. The functional copy of the gene is under operable control of regulatory elements which permit expression of the gene in the genetically engineered cell(s). Numerous transfection and transduction techniques as well as appropriate expression vectors are well known to those of ordinary skill in the art, some of which are described in PCT application WO95/00654. In vivo nucleic acid delivery using vectors such as viruses and targeted liposomes also is contemplated according to the invention.

[0153] A virus vector for delivering a nucleic acid encoding a sarcoma-associated polypeptide is selected from the group consisting of adenoviruses, adeno-associated viruses, poxviruses including vaccinia viruses and attenuated poxviruses, Semliki Forest virus, Venezuelan equine encephalitis virus, retroviruses, Sindbis virus, and Ty virus-like particle. Examples of viruses and virus-like particles which have been used to deliver exogenous nucleic acids include: replication-defective adenoviruses (e.g., Xiang et al., *Virology* 219:220-227, 1996; Eloit et al., *J. Virol.* 7:5375-5381, 1997; Chengalvala et al., *Vaccine* 15:335-339, 1997), a modified retrovirus (Townsend et al., *J. Virol.* 71:3365-3374, 1997), a nonreplicating retrovirus (Irwin et al., *J. Virol.* 68:5036-5044, 1994), a replication defective Semliki Forest virus (Zhao et al., *Proc. Natl. Acad. Sci. USA* 92:3009-3013, 1995), canarypox virus and highly attenuated vaccinia virus derivative (Paoletti, *Proc. Natl. Acad. Sci. USA* 93:11349-11353, 1996), non-replicative vaccinia virus (Moss, *Proc. Natl. Acad. Sci. USA* 93:11341-11348, 1996), replicative vaccinia virus (Moss, *Dev. Biol. Stand.* 82:55-63, 1994), Venezuelan equine

encephalitis virus (Davis et al., *J. Virol.* 70:3781-3787, 1996), Sindbis virus (Pugachev et al., *Virology* 212:587-594, 1995), and Ty virus-like particle (Allsopp et al., *Eur. J. Immunol* 26:1951-1959, 1996). A preferred virus vector is an adenovirus.

[0154] Preferably the foregoing nucleic acid delivery vectors: (1) contain exogenous genetic material that can be transcribed and translated in a mammalian cell and that can induce an immune response in a host, and (2) contain on a surface a ligand that selectively binds to a receptor on the surface of a target cell, such as a mammalian cell, and thereby gains entry to the target cell.

[0155] Various techniques may be employed for introducing nucleic acids of the invention into cells, depending on whether the nucleic acids are introduced in vitro or in vivo in a host. Such techniques include transfection of nucleic acid-CaPO₄ precipitates, transfection of nucleic acids associated with DEAE, transfection or infection with the foregoing viruses including the nucleic acid of interest, liposome mediated transfection, and the like. For certain uses, it is preferred to target the nucleic acid to particular cells. In such instances, a vehicle used for delivering a nucleic acid of the invention into a cell (e.g., a retrovirus, or other virus; a liposome) can have a targeting molecule attached thereto. For example, a molecule such as an antibody specific for a surface membrane protein on the target cell or a ligand for a receptor on the target cell can be bound to or incorporated within the nucleic acid delivery vehicle. Preferred antibodies include antibodies which selectively bind a sarcoma-associated antigen, alone or as a complex with a MHC molecule. Especially preferred are monoclonal antibodies. Where liposomes are employed to deliver the nucleic acids of the invention, proteins which bind to a surface membrane protein associated with endocytosis may be incorporated into the liposome formulation for targeting and/or to facilitate uptake. Such proteins include capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half life, and the like. Polymeric delivery systems also have been used successfully to deliver nucleic acids into cells, as is known by those skilled in the art. Such systems even permit oral delivery of nucleic acids.

[0156] According to a further aspect of the invention, compositions containing the nucleic acid molecules, proteins, and binding polypeptides of the invention are provided. The compositions contain any of the foregoing therapeutic agents in an optional pharmaceutically acceptable carrier. Thus, in a related aspect, the invention provides a method for forming a medicament that involves placing a therapeutically effective amount of the therapeutic agent in the pharmaceutically acceptable carrier to form one or more doses. The effectiveness of treatment or prevention methods of the invention can be determined using standard diagnostic methods described herein.

[0157] When administered, the therapeutic compositions of the present invention are administered in pharmaceutically acceptable preparations. Such preparations may routinely contain pharmaceutically acceptable concentrations of salt, buffering agents, preservatives, compatible carriers, supplementary immune potentiating agents such as adjuvants and cytokines, and optionally other therapeutic agents.

[0158] As used herein, the term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingre-

dients. The term "physiologically acceptable" refers to a non-toxic material that is compatible with a biological system such as a cell, cell culture, tissue, or organism. The characteristics of the carrier will depend on the route of administration. Physiologically and pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials which are well known in the art. The term "carrier" denotes an organic or inorganic ingredient, natural or synthetic, with which the active ingredient is combined to facilitate the application. The components of the pharmaceutical compositions also are capable of being comingled with the molecules of the present invention, and with each other, in a manner such that there is no interaction which would substantially impair the desired pharmaceutical efficacy.

[0159] The therapeutics of the invention can be administered by any conventional route, including injection or by gradual infusion over time. The administration may, for example, be oral, intravenous, intratumoral, intraperitoneal, intramuscular, intracavity, subcutaneous, or transdermal. When antibodies are used therapeutically, a preferred route of administration is by pulmonary aerosol. Techniques for preparing aerosol delivery systems containing antibodies are well known to those of skill in the art. Generally, such systems should utilize components which will not significantly impair the biological properties of the antibodies, such as the paratope binding capacity (see, for example, Sciarra and Cutie, "Aerosols," in Remington's Pharmaceutical Sciences, 18th edition, 1990, pp 1694-1712). Those of skill in the art can readily determine the various parameters and conditions for producing antibody aerosols without undue experimentation. When using antisense preparations of the invention, slow intravenous administration is preferred.

[0160] The compositions of the invention are administered in effective amounts. An "effective amount" is that amount of a sarcoma-associated polypeptide composition that alone, or together with further doses, produces the desired response, e.g. increases an immune response to the sarcoma-associated polypeptide. In the case of treating a particular disease or condition characterized by expression of one or more sarcoma-associated polypeptides, such as cancer, the desired response is inhibiting the progression of the disease. This may involve only slowing the progression of the disease temporarily, although more preferably, it involves halting the progression of the disease permanently. This can be monitored by routine methods or can be monitored according to diagnostic methods of the invention discussed herein. The desired response to treatment of the disease or condition also can be delaying the onset or even preventing the onset of the disease or condition.

[0161] Such amounts will depend, of course, on the particular condition being treated, the severity of the condition, the individual patient parameters including age, physical condition, size and weight, the duration of the treatment, the nature of concurrent therapy (if any), the specific route of administration and like factors within the knowledge and expertise of the health practitioner. These factors are well known to those of ordinary skill in the art and can be addressed with no more than routine experimentation. It is generally preferred that a maximum dose of the individual components or combinations thereof be used, that is, the highest safe dose according to sound medical judgment. It will be understood by those of ordinary skill in the art, how-

ever, that a patient may insist upon a lower dose or tolerable dose for medical reasons, psychological reasons or for virtually any other reasons.

[0162] The pharmaceutical compositions used in the foregoing methods preferably are sterile and contain an effective amount of sarcoma-associated polypeptide or nucleic acid encoding sarcoma-associated polypeptide for producing the desired response in a unit of weight or volume suitable for administration to a patient. The response can, for example, be measured by determining the immune response following administration of the sarcoma-associated polypeptide composition via a reporter system by measuring downstream effects such as gene expression, or by measuring the physiological effects of the sarcoma-associated polypeptide composition, such as regression of a tumor or decrease of disease symptoms. Other assays will be known to one of ordinary skill in the art and can be employed for measuring the level of the response.

[0163] The doses of sarcoma-associated polypeptide compositions (e.g., polypeptide, peptide, antibody, cell or nucleic acid) administered to a subject can be chosen in accordance with different parameters, in particular in accordance with the mode of administration used and the state of the subject. Other factors include the desired period of treatment. In the event that a response in a subject is insufficient at the initial doses applied, higher doses (or effectively higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits.

[0164] In general, for treatments for eliciting or increasing an immune response, doses of sarcoma-associated antigen are formulated and administered in doses between 1 ng and 1 mg, and preferably between 10 ng and 100 µg, according to any standard procedure in the art. Where nucleic acids encoding sarcoma-associated polypeptides or variants thereof are employed, doses of between 1 ng and 0.1 mg generally will be formulated and administered according to standard procedures. Other protocols for the administration of sarcoma-associated polypeptide compositions will be known to one of ordinary skill in the art, in which the dose amount, schedule of injections, sites of injections, mode of administration (e.g., intra-tumoral) and the like vary from the foregoing. Administration of sarcoma-associated polypeptide compositions to mammals other than humans, e.g. for testing purposes or veterinary therapeutic purposes, is carried out under substantially the same conditions as described above.

[0165] Where sarcoma-associated polypeptides are used for vaccination, modes of administration which effectively deliver the sarcoma-associated polypeptide and adjuvant, such that an immune response to the polypeptide is increased, can be used. For administration of a sarcoma-associated polypeptide in adjuvant, preferred methods include intradermal, intravenous, intramuscular and subcutaneous administration. Although these are preferred embodiments, the invention is not limited by the particular modes of administration disclosed herein. Standard references in the art (e.g., Remington's Pharmaceutical Sciences, 18th edition, 1990) provide modes of administration and formulations for delivery of immunogens with adjuvant or in a non-adjuvant carrier.

[0166] The pharmaceutical compositions may contain suitable buffering agents, including: acetic acid in a salt; citric acid in a salt; boric acid in a salt; and phosphoric acid in a salt.

[0167] The pharmaceutical compositions also may contain, optionally, suitable preservatives, such as: benzalkonium chloride; chlorobutanol; parabens and thimerosal.

[0168] The pharmaceutical compositions may conveniently be presented in unit dosage form and may be prepared by any of the methods well-known in the art of pharmacy. All methods include the step of bringing the active agent into association with a carrier which constitutes one or more accessory ingredients. In general, the compositions are prepared by uniformly and intimately bringing the active compound into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product.

[0169] Compositions suitable for oral administration may be presented as discrete units, such as capsules, tablets, lozenges, each containing a predetermined amount of the active compound. Other compositions include suspensions in aqueous liquids or non-aqueous liquids such as a syrup, elixir or an emulsion.

[0170] Compositions for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, and lactated Ringer's or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, and inert gases, and the like.

[0171] The pharmaceutical agents of the invention may be administered alone, in combination with each other, and/or in combination with other anti-cancer drug therapies and/or treatments. These therapies and/or treatments may include, but are not limited to: surgical intervention, chemotherapy, radiotherapy, and adjuvant systemic therapies.

[0172] The invention also provides a pharmaceutical kit comprising one or more containers comprising one or more of the pharmaceutical compounds or agents of the invention. Additional materials may be included in any or all kits of the invention, and such materials may include, but are not limited to buffers, water, enzymes, tubes, control molecules, etc. The kit may also include instructions for the use of the one or more pharmaceutical compounds or agents of the invention for the treatment of cancer.

[0173] The invention includes kits for assaying the presence of sarcoma-associated antigens and/or antibodies that specifically bind to sarcoma-associated polypeptides. An example of such a kit may include the above-mentioned polypeptides bound to a substrate, for example a dipstick, which is dipped into a blood or body fluid sample of a subject. The surface of the substrate may then be processed using procedures well known to those of skill in the art, to assess whether specific binding occurred between the polypeptides and agents (e.g. antibodies) in the subject's sample. For example, procedures may include, but are not limited to, contact with a secondary antibody, or other method that indicates the presence of specific binding.

[0174] Another example of a kit may include an antibody or antigen-binding fragment thereof, that binds specifically to a sarcoma-associated antigen. The antibody or antigen-binding fragment thereof, may be applied to a tissue or cell sample from a patient with cancer and the sample then processed to

assess whether specific binding occurs between the antibody and an antigen or other component of the sample. In addition, the antibody or antigen-binding fragment thereof, may be applied to a body fluid sample, such as serum, from a subject, either suspected of having cancer, diagnosed with cancer, or believed to be free of cancer. As will be understood by one of skill in the art, such binding assays may also be performed with a sample or object contacted with an antibody and/or sarcoma-associated antigen that is in solution, for example in a 96-well plate or applied directly to an object surface.

[0175] Another example of a kit of the invention is a kit that provides components necessary to determine the level of expression of one or more sarcoma-associated nucleic acid molecules of the invention. Such components may include primers useful for amplification of one or more sarcoma-associated nucleic acid molecules and/or other chemicals for PCR amplification.

[0176] Another example of a kit of the invention is a kit that provides components necessary to determine the level of expression of one or more sarcoma-associated nucleic acid molecules of the invention using a method of hybridization.

[0177] The foregoing kits can include instructions or other printed material on how to use the various components of the kits for diagnostic purposes.

[0178] The invention further includes nucleic acid or protein microarrays (including antibody arrays) for the analysis of expression of sarcoma-associated antigens or nucleic acids encoding such antigens. In this aspect of the invention, standard techniques of microarray technology are utilized to assess expression of the sarcoma-associated antigens and/or identify biological constituents that bind such antigens. The constituents of biological samples include antibodies, lymphocytes (particularly T lymphocytes), and the like. Microarray substrates include but are not limited to glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, or nylon. The microarray substrates may be coated with a compound to enhance synthesis of a probe (peptide or nucleic acid) on the substrate. Coupling agents or groups on the substrate can be used to covalently link the first nucleotide or amino acid to the substrate. A variety of coupling agents or groups are known to those of skill in the art. Peptide or nucleic acid probes thus can be synthesized directly on the substrate in a predetermined grid. Alternatively, peptide or nucleic acid probes can be spotted on the substrate, and in such cases the substrate may be coated with a compound to enhance binding of the probe to the substrate. In these embodiments, presynthesized probes are applied to the substrate in a precise, predetermined volume and grid pattern, preferably utilizing a computer-controlled robot to apply probe to the substrate in a contact-printing manner or in a non-contact manner such as ink jet or piezo-electric delivery. Probes may be covalently linked to the substrate. Nucleic acid probes preferably are linked using UV irradiation or heat.

[0179] Protein microarray technology, which is also known by other names including protein chip technology and solid-phase protein array technology, is well known to those of ordinary skill in the art and is based on, but not limited to, obtaining an array of identified peptides or proteins on a fixed substrate, binding target molecules or biological constituents to the peptides, and evaluating such binding. See, e.g., G. MacBeath and S. L. Schreiber, "Printing Proteins as Microarrays for High-Throughput Function Determination," *Science* 289(5485):1760-1763, 2000.

[0180] Targets are peptides or proteins and may be natural or synthetic. The tissue may be obtained from a subject or may be grown in culture (e.g. from a cell line).

[0181] In some embodiments of the invention, one or more control peptide or protein molecules are attached to the substrate. Preferably, control peptide or protein molecules allow determination of factors such as peptide or protein quality and binding characteristics, reagent quality and effectiveness, hybridization success, and analysis thresholds and success.

[0182] Nucleic acid arrays, particularly arrays that bind sarcoma-associated antigens, also can be used for diagnostic applications, such as for identifying subjects that have a condition characterized by aberrant sarcoma-associated antigen expression. Nucleic acid microarray technology, which is also known by other names including: DNA chip technology, gene chip technology, and solid-phase nucleic acid array technology, is well known to those of ordinary skill in the art and is based on, but not limited to, obtaining an array of identified nucleic acid probes on a fixed substrate, labeling target molecules with reporter molecules (e.g., radioactive, chemiluminescent, or fluorescent tags such as fluorescein, Cy3-dUTP, or Cy5-dUTP), hybridizing target nucleic acids to the probes, and evaluating target-probe hybridization. A probe with a nucleic acid sequence that perfectly matches the target sequence will, in general, result in detection of a stronger reporter-molecule signal than will probes with less perfect matches. Many components and techniques utilized in nucleic acid microarray technology are presented in *The Chipping Forecast*, *Nature Genetics*, Vol. 21, January 1999, the entire contents of which is incorporated by reference herein.

[0183] According to the invention, probes are selected from the group of nucleic acids including, but not limited to: DNA, genomic DNA, cDNA, and oligonucleotides; and may be natural or synthetic. Oligonucleotide probes preferably are 20 to 25-mer oligonucleotides and DNA/cDNA probes preferably are 500 to 5000 bases in length, although other lengths may be used. Appropriate probe length may be determined by one of ordinary skill in the art by following art-known procedures. In one embodiment, preferred probes are sets of one or more of the sarcoma-associated nucleic acid molecules as described herein. Probes may be purified to remove contaminants using standard methods known to those of ordinary skill in the art such as gel filtration or precipitation.

[0184] In one embodiment, the microarray substrate may be coated with a compound to enhance synthesis of the probe on the substrate. Such compounds include, but are not limited to, oligoethylene glycols. In another embodiment, coupling agents or groups on the substrate can be used to covalently link the first nucleotide or oligonucleotide to the substrate. These agents or groups may include, for example, amino, hydroxy, bromo, and carboxy groups. These reactive groups are preferably attached to the substrate through a hydrocarbyl radical such as an alkylene or phenylene divalent radical, one valence position occupied by the chain bonding and the remaining attached to the reactive groups. These hydrocarbyl groups may contain up to about ten carbon atoms, preferably up to about six carbon atoms. Alkylene radicals are usually preferred containing two to four carbon atoms in the principal chain. These and additional details of the process are disclosed, for example, in U.S. Pat. No. 4,458,066, which is incorporated by reference in its entirety.

[0185] In one embodiment, nucleic acid probes are synthesized directly on the substrate in a predetermined grid pattern

using methods such as light-directed chemical synthesis, photochemical deprotection, or delivery of nucleotide precursors to the substrate and subsequent probe production.

[0186] Targets for microarrays are nucleic acids selected from the group, including but not limited to: DNA, genomic DNA, cDNA, RNA, mRNA and may be natural or synthetic. In all embodiments, nucleic acid target molecules from human tissue are preferred. The tissue may be obtained from a subject or may be grown in culture (e.g. from a cell line).

[0187] In embodiments of the invention one or more control nucleic acid molecules are attached to the substrate. Preferably, control nucleic acid molecules allow determination of factors such as nucleic acid quality and binding characteristics, reagent quality and effectiveness, hybridization success, and analysis thresholds and success. Control nucleic acids may include but are not limited to expression products of genes such as housekeeping genes or fragments thereof.

Examples

Materials and Methods

Cell Lines, Tissues, Sera and RNA

[0188] SW1045, SW982, and Fuji synovial sarcoma cell lines were obtained from the cell repository of the Ludwig Institute for Cancer Research (LICR), New York Branch at the Memorial Sloan-Kettering Cancer Center. Tumor tissues and sera were obtained from Memorial Sloan-Kettering Cancer Center, Weill Medical College of Cornell University and Aichi Cancer Center Research Center, Nagoya Japan. Normal tissue RNA preparations were purchased from Clontech laboratories Incorporated (Palo Alto, Calif.) and Ambion Incorporated (Austin, Tex.). Total RNA from tumor tissues was prepared by the guanidinium thiocyanate method.

SEREX Analysis of cDNA Expression Libraries

[0189] Poly(A)⁺ RNA from two sarcoma cell lines, SW1045 and SW982, was prepared using the Fast Track mRNA Purification Kit (Invitrogen, Life Technologies, Carlsbad, Calif.). Poly(A)⁺ RNA from normal testis was purchased from CLONTECH. Separate cDNA libraries were constructed for each of these in the ZAP Express vector (Stratagene, La Jolla, Calif.) according to the manufacturer's instructions using 5 µg polyA⁺ mRNA. Libraries containing 1-2×10⁶ primary recombinants were obtained and were not amplified before immunoscreening.

[0190] To remove serum antibodies reactive with vector-related antigens, sera was absorbed against *E. coli*/bacteriophage lysates prepared in the following manner. Wild-type lambda ZAP Express bacteriophage at a concentration of 5,000 pfu (plaque-forming units) per 15 cm plate were amplified in *E. coli* XL1 Blue MRF' overnight in 100 ml NZY/0.7% agarose. 10 ml of binding buffer (0.1M NaHCO₃, pH 8.3) was then added to the plates, and the plates were gently agitated at 4° C. for 15 hours. The resultant supernatants were collected and residual *E. coli* were lysed by sonication. The lysates were then coupled to CNBr-Sepharose 4B (Amersham Pharmacia Biotech, Piscataway, N.J.) according to the manufacturer's instructions. Patient sera (1:10 dilution) were absorbed by batch absorption with an equal volume of Sepharose 4B coupled *E. coli*/phage lysates at 4° C. for 6 hours. This procedure was repeated a total of three times and was followed by a 15 hour incubation with nitrocellulose filters precoated with proteins derived from *E. coli* and *E. coli*/phage lysates. Library screenings were performed as previously described (Scanlan, M. J., et al. Characterization of human colon cancer

antigens recognized by autologous antibodies. *Int. J. Cancer* 1998; 76: 652-8. Scanlan, M. J., et al. Antigens recognized by autologous antibody in patients with renal-cell carcinoma. *Int. J. Cancer* 1999; 83: 456-64.) A total of five independent SEREX immunoscreenings of the cDNA libraries were undertaken. Sera from 2 sarcoma patients were used independently, at a dilution of 1:200, to immunoscreen the cDNA libraries. A total of $2.5\text{--}5.0 \times 10^5$ or 1.75×10^6 recombinants were screened per serum/cDNA library combination. Serum reactive phage clones were converted to plasmid forms and subjected to DNA sequencing (Cornell University DNA Services, Ithaca, N.Y.).

Determination of Serum Antibody Reactivity

[0191] Two assays were used to determine serological reactivity, an ELISA-based method and a bacteriophage expression method. With regard to CT antigens, serum antibody reactivity was determined by ELISA as previously described (Stockert E, et al. 1998. A survey of the humoral immune response of cancer patients to a panel of human tumor antigens. *J Exp Med* 187:1349-54.) Briefly, recombinant proteins (NY-ESO-1, SSX-2, MAGE-A1, MAGE-A3, MAGE-A4, MAGE-A10, CT7 and CT10) were produced in *E. coli* by transfection with pQE30 expression vectors (Qiagen, Chatsworth, Calif.) according to the manufacturer's protocol. 10 ng of recombinant protein (1 µg/ml) was absorbed to TC microwell plates (Nalge Nunc International Corp., Naperville, Ill.) for 15 hours at 4° C. After washing with PBS, plates were then blocked with 2% BSA and incubated with diluted (1:100-1:25,000) patient sera for 2 hours at room temperature. Following a PBS wash step, 10 µl of a 1:5000 dilution of alkaline phosphatase-conjugated goat anti-human IgG secondary antibody (Southern Biotechnology, Birmingham, Ala.) was added to each well and incubated for 1 hour at room temperature. Following a PBS wash step, plates were incubated with 10 ul/well Attophase substrate (JBL Scientific, San Louis Obispo, Calif.) for 25 min, and the fluorescence was then read by a Cyto-Fluor 2350 (Millipore, Bedford, Mass.).

[0192] In the case of SEREX-defined sarcoma antigens, a previously described serum antibody detection array (SADA or spot immunoassay (Scanlan M J, et al. Humoral immunity to human breast cancer: antigen definition and quantitative analysis of mRNA expression. *Cancer Immunity* 1:4 [epub]; Scanlan M J, et al. 2002. Cancer-Related Serological Recognition of Human Colon Cancer: Identification of Potential Diagnostic and Immunotherapeutic Targets. *Cancer Res.* 2002 Jul. 15; 16 (14): 4041-7.) was used to determine serological reactivity.

[0193] Preabsorbed serum samples from 39 sarcoma patients and 33 healthy blood donors were evaluated for the presence of IgG antibody reactive to a panel of SEREX-defined sarcoma antigens, identified herein, in the following manner. Precut nitrocellulose membranes (80×120 mm) were precoated with a layer (approximately 0.2 mm) of growth media (NZY/0.7% Agarose/2.5 mM isopropyl-β-D-thiogalactopyranoside) and placed on a reservoir layer of NZY/0.7% Agarose in a 86×128 mm Omni Tray (Nalge Nunc). 5.0×10^3 pfu per µl of bacteriophage encoding individual SEREX-defined tumor antigens were mixed with an equal volume of exponentially growing *E. coli* XL-1 Blue MRF⁺ and spotted (0.7 µl aliquots) on the precoated nitrocellulose membranes using a 96 pin replicator (Nalge Nunc). Membranes were incubated for 15 hours at 37° C. and then pro-

cessed as per the standard SEREX protocol (Scanlan, et al., *Int. J. Cancer* 1998; 76: 652-8; Scanlan, et al., *Int. J. Cancer* 1999; 83: 456-64). Briefly, plates were blocked in 0.5% non-fat dried milk; incubated in 10 ml of a 1:200 dilution of sera at room temperature for 15 hours; and then incubated in a 1:3000 dilution of alkaline phosphatase conjugated, Fc fragment specific, goat anti-human IgG (Jackson ImmunoResearch laboratories Inc., West Grove Pa.). Serum IgG reactivity was detected with the alkaline phosphatase substrate, 4-nitro blue tetrazolium chloride/5-bromo-4-chloro-3-indolyl-phosphate.

Reverse Transcriptase-PCR (RT-PCR) Analysis

[0194] The cDNA preparations used as templates in the RT-PCR reactions were prepared using the Superscript first strand synthesis kit (Invitrogen Life Technologies, Carlsbad, Calif.) according to the manufacturer's instructions using 2.5 µg of total RNA. For evaluation of CT antigens expression in sarcoma cell lines, PCR primers specific for NY-ESO-1, LAGE-1, MAGE-1, MAGE-3, MAGE-4, MAGE-10, SCP-1, BAGE, CT7, SSX-1, SSX-2, and SSX-4 were synthesized commercially (Invitrogen Life Technologies) using published primer sequences (van der Bruggen P, et al. 1991. A gene encoding an antigen recognized by cytolytic T lymphocytes on a human melanoma. *Science* 254:1643-47, Gaugler, B., et al. Human gene MAGE-3 codes for an antigen recognized on a melanoma by autologous cytolytic T lymphocytes. *J. Exp. Med.* 1994; 179: 921-30, Chen, Y.-T., et al. A testicular antigen aberrantly expressed in human cancers detected by autologous antibody screening. *Proc. Natl. Acad. Sci. USA.* 1997; 94: 1914-18; Boel, P., et al., and van der Bruggen, P. BAGE: a new gene encoding an antigen recognized on human melanomas by cytolytic T lymphocytes. *Immunity* 1995; 2: 167-75. (PMID: 7895173); Sahin U, et al. 1998. Expression of multiple cancer/testis antigens in breast cancer and melanoma: basis for polyvalent CT vaccine strategies. *Int J Cancer* 78:387-89, Lethe B, et al. 1998. LAGE-1, a new gene with tumor specificity. *Int. J. Cancer* 76:903-8, Türeci Ö, et al. 1998. Expression of SSX genes in human tumors. *Int J Cancer* 77:19-23, Gure A O, et al. 1997. SSX: a multigene family with several members transcribed in normal testis and human cancer. *Int J Cancer* 72:965-971). PCR primers specific for SEREX-defined antigens were also synthesized commercially (Invitrogen Life Technologies) and their sequences are as follows: NY-SAR-12 forward, TggCgCgAAAggAAAAgAAAAT (SEQ ID NO: 91); NY-SAR-12 reverse, AgAggTAgtTggCgAggATgTTAg (SEQ ID NO: 92); NY-SAR-35 forward, CTTggTgCgATCgCCTTAT (SEQ ID NO: 93); NY-SAR-35 reverse, TTgATgCATgAAAACA-gAACTC (SEQ ID NO: 94); NY-SAR-41 forward, AgAAT-TggCgAggCTCgTCATCA (SEQ ID NO: 95); NY-SAR-41 reverse, TTCCAATTTgCCTTCTCTAACTg (SEQ ID NO: 96); NY-SAR-73 forward, CCCggAgCACgTCgAggTCTAC (SEQ ID NO: 135); NY-SAR-73 reverse, ggTgAggggC-CCAggAAgC (SEQ ID NO: 136); NY-SAR-78 forward, CACAATgTATCCTgTTgAAAg (SEQ ID NO: 137); NY-SAR-78 reverse, gAgATgATACATTCTTCCAg (SEQ ID NO: 138); NY-SAR-92 forward, CTTCCgCCAACCTCTC-CTACC (SEQ ID NO: 139); NY-SAR-92 reverse, gATgC-CCgTgTCTTgTCCTT (SEQ ID NO: 140); NY-SAR-96 forward, CACTAggCTgCTgAggAAgAT (SEQ ID NO: 141); NY-SAR-96 reverse, gTTTTgTgggCgCATgAg (SEQ ID NO: 142); NY-SAR-97 forward, ggACCACCCCAAATA-gAA (SEQ ID NO: 143); NY-SAR-97 reverse, CCAC-

CAGCTCaggAAG (SEQ ID NO: 144); NY-SAR-110 forward, TCTgATggAgCggTgggATgC (SEQ ID NO: 145); NY-SAR-110 reverse, gTgTgCCTCggCTTCTTTCTTC (SEQ ID NO: 146).

[0195] RT-PCR was performed in the following manner. Twenty-five μ l PCR reaction mixtures, consisting of 2 μ l cDNA, 0.2 mM dNTP, 1.5 mM MgCl₂, 0.25 μ M gene specific forward and reverse primers, and 2.5 U Platinum Taq DNA polymerase (Invitrogen Life Technologies), were heated to 94° C. for 2 min., followed by 35 thermal cycles of 94° C. for 30 seconds, 55° C. for 30 seconds and 72° C. for 1 min., and a final cycle of 94° C. for 30 seconds, 55° C. for 30 seconds and 72° C. for 5 min. Thermal cycling was performed using a GeneAmp PCR System 9700 (Applied Biosystems, Foster City, Calif.). Resultant PCR products were analyzed in 2% Agarose/Tris-Acetate-EDTA gels.

Real-Time Quantitative Reverse Transcription (RT)-PCR

[0196] The concentration of NY-SAR-35 mRNA transcripts in normal tissues was measured by real-time RT-PCR using cDNA preparations derived from lung cancer specimens and 16 different normal tissues that had been normalized for 6 housekeeping genes (Clontech). Gene-specific TaqMan probes and PCR primers were designed using Primer Express software (PE Biosystems, Foster City, Calif.). PCR reactions were prepared using 2.5 μ l of cDNA diluted in TaqMan PCR Master Mix (PE Biosystems) supplemented with 200 nM 6-carboxy-fluorescein labeled gene-specific TaqMan probe, and a predetermined, optimum concentration of gene specific forward and reverse primers (300-900 nM). Triplicate PCR reactions were prepared for each cDNA sample. PCR consisted of 40 cycles of 95° C. denaturation (15 seconds) and 60° C. annealing/extension (60 seconds). Thermal cycling and fluorescent monitoring were performed using an ABI 7700 sequence analyzer (PE Biosystems). The point at which the PCR product is first detected above a fixed threshold, termed cycle threshold (Ct), was determined for each sample. The abundance of gene-specific transcripts in normal tissues was determined by comparison with a standard curve generated from the Ct values of known concentrations of plasmid DNA template encoding NY-SAR-35.

[0197] TaqMan primers were as follow: NY-SAR-35 forward, TggTgCgATCgCCTTATCC (SEQ ID NO: 147); NY-SAR-35 reverse, CggTTCgCTCCTCCAgAA (SEQ ID NO: 148). TaqMan probe: NY-SAR-35, TgTCTgCCCATTAT-TgCCgCTCTCT (SEQ ID NO: 149).

Northern Blot Analysis.

[0198] A Northern blot containing poly A+ RNA (2 μ g/lane) from various normal tissues was obtained commercially (Clontech). An NY-SAR-35 cDNA probe (bp 263-1029) was labeled using the Bright Star Psoralen-Biotin Kit (Ambion Inc., Austin, Tex.) and hybridized to the membrane for 15 hours at 68° C. After washing, the hybridization signal was developed using the Bright Star Bio-Detect Kit, according to the manufacturer's instructions (Ambion).

Southern Blot Analysis

[0199] Genomic DNA was extracted from normal human testis, and samples (10 μ g) were independently digested with EcoRI, HindIII, and BamHI at 37° C. overnight. The DNA was then separated on 0.7% agarose gel and blotted onto a nylon transfer membrane. An NY-SAR-35 cDNA probe (bp

252-1029) was radiolabeled with ³²P-dCTP using a random-primer DNA labeling kit (Roche Molecular Biochemicals, Indianapolis, Ind.). The blot was hybridized to a ³²P labeled probe at 68° C. After 15 hours of hybridization, the membrane was washed under high stringency conditions (0.1×SSC, 0.5% SDS at 60° C.) and exposed for autoradiography.

Example 1

Results from the First Round of Immunoscreeings by SEREX Analysis

Identification of Human Sarcoma Antigens by SEREX Analysis

[0200] Preliminary studies were carried out to determine optimum sources of target antigens and immunoreactive patient sera. Three sarcoma cell lines were typed for expression of NY-ESO-1, LAGE-1, MAGE-1, MAGE-3, MAGE-4, MAGE-10, BAGE, SCP-1, CT7, SSX-1, SSX-2, and SSX-4 transcripts by RT-PCR. As shown in Table 2, all 3 sarcoma cell lines expressed at least one of the transcripts in this panel. Specifically, the SW982 and SW1045 synovial sarcoma cell lines expressed 8 and 10 of the 12 CT antigen transcripts in the panel, respectively, while Fuji synovial sarcoma cells expressed 4/12 CT antigen transcripts.

TABLE 2

CT Antigen	Cancer/Testis antigen expression in sarcoma cell lines		
	Cell Line		
	SW982 (synovial)	SW1045 (synovial)	Fuji
NY-ESO-1	+	+	+
LAGE-1	Neg	+	+
MAGE-A1	+	+	Neg
MAGE-A3	+	+	Neg
MAGE-A4	+	+	
MAGE-A10	+	+	Neg
BAGE	+	+	Neg
SCP-1	Neg	Neg	Neg
CT7	+	+	Neg
SSX1	Neg	+	Neg
SSX2	Neg	Neg	
SSX4	+	+	Neg
Totals	8/12	10/12	4/12

[0201] In order to identify a subset of sarcoma patients that are actively mounting an immune response against tumor antigens, sera from 54 sarcoma patients (various histologies) were tested by ELISA (Stockert E, et al. 1998. A survey of the humoral immune response of cancer patients to a panel of human tumor antigens. J Exp Med 187:1349-54) for the presence of antibodies against a panel of 8 CT antigens consisting of: NY-ESO-1, SSX-2, MAGE-A1, MAGE-A3, MAGE-A4, MAGE-A10, CT7 and CT10. Only 3/4 sarcoma patients, a malignant fibrous histiocytoma (MFH) and fibrosarcoma patient (FS), had detectable serum antibodies against a CT antigen, while the remaining 52 patients lacked detectable anti-CT antigen antibodies. Both seropositive patients had antibodies to NY-ESO-1 but lacked antibodies to the other 7 CT antigens tested. Fibrosarcoma tissue from the NY-ESO-1 seropositive patient, FS, was available for CT antigen typing by RT-PCR and was found to express 11/12 different CT antigen transcripts (NY-ESO-1, LAGE-1, MAGE-A1, -A3, -A4, -A10, BAGE, CT7, SSX1, -2 and -4). Tissue from the NY-ESO-1 seropositive patient, MFH, was not available for CT antigen typing by RT-PCR.

[0202] Although it was determined that CT antigen expression is frequent in sarcoma tissue, serum antibody responses were not as frequent. This lack of immunogenicity in sarcoma may be an indication of immune escape by sarcoma cells, whereby the immune system fails to recognize CT antigens and eliminate tumor cells expressing these antigens, resulting in the expansion of a homogenous population CT antigen expressing sarcoma cells. Relevant escape mechanisms include defective antigen presentation (Garrido F, Algarra I. MHC antigens and tumor escape from immune surveillance. *Adv Cancer Res* 2001;83:117-58) and/or production of immuno-inhibitory cytokines, such as TGF- β and IL-10 (Conrad C T, et al. Differential expression of transforming growth factor beta 1 and interleukin 10 in progressing and regressing areas of primary melanoma. *J Exp Clin Cancer Res* 1999 June;18(2):225-32). It is also possible that homogenous NY-ESO-1 and MAGE expression in synovial sarcoma (Jungbluth A A, et al. 2001. Monophasic and biphasic synovial sarcomas abundantly express cancer/testis antigen NY-ESO-1 but not MAGE-A1 or CT7. *Int J Cancer* 94:252-6; Antonescu C R, et al. MAGE antigen expression in monophasic and biphasic synovial sarcoma. *Hum Pathol* 2002 February;33(2):225-9), as opposed to heterogeneous CT antigen expression observed in many other tumor types (Jungbluth A A, et al. 2001. Immunohistochemical analysis of NY-ESO-1 antigen expression in normal and malignant human tissues. *Int J Cancer* 92:856-60; Jungbluth A A, et al. 2000. Expression of MAGE-antigens in normal tissues and cancer. *Int J Cancer* 85:460-5), may also be a contributing factor to immune escape.

[0203] These 2 patients were chosen as the serum sources for SEREX immunoscreening of cDNA libraries prepared from the SW982 and SW1045 synovial sarcoma cell lines. A total of 4 SEREX immunoscreenings were performed, leading to the identification of 72 distinct sarcoma antigens, designated NY-SAR-1 through NY-SAR-72. As shown in Table 3, immunoscreening with sera from an NY-ESO-1 serum antibody positive MFH patient led to the identification of 28 antigens, including 8 overlapping antigens derived from both

the SW982 and SW1045 cDNA libraries, as well as 13 antigens derived solely from the SW982 cDNA library, and 7 antigens derived solely from the SW1045 cDNA library.

[0204] Immunoscreening with sera from an NY-ESO-1 serum antibody positive fibrosarcoma patient defined 46 antigens, including 2 overlapping antigens derived from both the SW982 and SW1045 cDNA libraries, as well as 25 antigens derived solely from the SW982 cDNA library, and 19 antigens derived solely from the SW1045 cDNA library. There was little overlap between the antigens recognized by serum antibodies from the MFH and FS patients. Only three antigens, NY-SAR-1/TMF1, NY-SAR-4/FH and NY-SAR-17/LAGE-1 were identified with both the MFH and FS sera. Because serological reactivity to NY-ESO-1 was the criteria used in selecting sera for cDNA library screening, mutual immunoreactivity to the highly homologous (84% amino acid identity) NY-SAR-17/LAGE-1 antigen was expected, and, although not intending to be bound by a particular theory, is likely to be due to shared epitopes. The 72 antigens (Tables 4-6) represent 58 known proteins and 14 uncharacterized gene products.

TABLE 3

Immunoscreening of synovial sarcoma cDNA expression libraries with allogeneic sarcoma patient sera				
Sarcoma Serum	Synovial sarcoma cDNA expression library	Number of recombinants screened	Number of different antigens identified	Total number of distinct antigens
Malignant Fibrous Histocytoma	SW982	5×10^5	21	28
Fibrosarcoma	SW1045	5×10^5	15	
Fibrosarcoma	SW982	2.5×10^5	27	46
	SW1045	2.5×10^5	21	

TABLE 4

SEREX-defined sarcoma antigens: antigens reactive with sera from multiple cancer patients				
NY-SAR-Antigen	Identity (Unigene cluster)	Reactivity with Sarcoma Sera	Source of Reactive Sera ¹	SEREX Database ID Number ² of Equivalent Isolate (Tumor Source ¹)
2	STAU (Hs.6113)	2/39	MFH (#3), OS (#2)	614 (PRC), 1273 (BC)
4	FH (Hs.75653)	5/39	MFH (#3), OS (#4, #7), ES (#1), FS (#2)	No Match
12	NESG1 (Hs.158450)	2/39	MFH (#3), LS (#4)	No Match
13	ACTN1 (Hs.119000)	1/39	MFH (#3)	855 (BC)
15	RBM6 (Hs.173993)	1/39	MFH (#3)	76 (LC)
16	FLJ12785 (Hs.192742)	1/39	MFH (#3)	756 (TALL)
17	LAGE-1a (Hs.87225)	2/39	MFH (#3), FS (#2)	1160 (BC)
18	SSSCA1 (Hs.25723)	1/39	MFH (#3)	1799 (CC)
28	MGC: 9727 (Hs.11065)	1/39	MFH (#3)	71 (BC)
30	SNK (Hs.3838)	2/39	FS (#2), RS (#1)	No Match
44	LGALS1 (Hs.227751)	1/39	FS (#2)	704 (RC)
47	MIF (Hs.73798)	1/39	FS (#2)	989 (MEL)
50	PYCR1 (Hs.79217)	3/39	FS (#2), MFH (#2, #4)	No Match
71	None (Hs.314941)	1/39	FS (#2)	1938 (GL)
72	HSPE1 (Hs.1197)	1/39	FS (#2)	882 (HC), 1202 (MEL)

Antigens did not react with sera from normal blood donors (0/33).

¹Abbreviations: BC, breast cancer; CC, colon cancer; ES, Ewing sarcoma; FS, fibrosarcoma; GC, gastric cancer; GL, glioma; HC, hepatocellular carcinoma; LC, lung cancer; LS, leiomyosarcoma; MEL, melanoma; MFH, malignant fibrous histiocytoma; OC, ovarian cancer; OS, osteosarcoma; PRC, prostate cancer; RC, renal cancer; RS, rhabdomyosarcoma; TALL, T-cell acute lymphocytic leukemia.

²SEREX database ID numbers from the LICR's SEREX database (licr.org/SEREX.html).

TABLE 5

SEREX-defined sarcoma antigens: antigens reactive with sera from both normal donors and sarcoma patients				
NY-SAR-Antigen	Identity (Unigene cluster)	SEREX Database ID Number ¹ of Equivalent Isolate (Tumor Source ²)	Reactivity with Normal Sera	Reactivity with Sarcoma Sera
1	TMF1 (Hs.267632)	246 (G), 1241 (BC)	2/33	3/39
3	KIAA1536 (Hs.156667)	89 (BR)	2/33	3/39
6	RHAMM (Hs.72550)	1513 (OC)	1/33	3/39
7	PINCH (Hs.112378)	344 (CC), 550 (GC), 1152 (RC), 1281 (BR)	16/21	14/39
10	KIAA0603 (Hs.173802)	No Match	11/33	4/39
11	U2AF1RS2 (Hs.171909)	430 (RC), 786 (HD), 1236 (BC), 1334 (GC)	6/33	17/39
14	SC65 (Hs.207251)	No Match	8/33	4/39
19	HEF1 (Hs.80261)	421 (RC)	3/33	7/39
22	NELIN (Hs.216381)	No Match	4/33	19/39
29	FLJ13441 (Hs.232146)	974 (PC)	6/33	3/39
31	HUMAUANTIG (Hs.75528)	1017 (BC), 1331 (GC), 1475 (OC)	2/33	6/39
32	PDAP1 (Hs.278426)	No Match	4/33	8/39
33	SURF6 (Hs.274430)	No Match	2/33	2/39
41	None (Hs.166670)	No Match	1/33	1/39
45	STIP1 (Hs.75612)	430 (RC)	4/33	2/39
53	FXYD5 (Hs.333418)	No Match	1/33	1/39
54	LMOD1 (Hs.79386)	No Match	7/33	13/39
55	RBM10 (Hs.154583)	No Match	1/33	1/39
58	LIP8 (Hs.348012)	No Match	1/33	3/39
61	ZNF282 (Hs.58167)	No Match	1/33	2/39
64	USP16 (Hs.99819)	No Match	2/33	2/39
65	FDF1 (Hs.48876)	No Match	2/33	1/39
66	ROCK1 (Hs.109450)	444 (RC)	1/33	1/39
68	P38IP (Hs.333500)	No Match	1/33	3/39

¹The LICR's SEREX database ID numbers from licr.org/SEREX.html.

²Abbreviations: BC, breast cancer; CC, colon cancer; HD, Hodgkins disease; GC, gastric cancer; OC, ovarian cancer; PC, pancreatic cancer; RC, renal cancer.

TABLE 6

SEREX-defined sarcoma antigens: antigens reactive with sera from a single sarcoma patient	
NY-SAR-Antigen	Gene Identity (Unigene Cluster)
5	TBC1D1(Hs.278586)
8	BIRC2 (Hs.289107)
9	ATP5B (Hs.25)
20	TCEB3 (Hs.155202)
21	GTF3C3 (Hs.90847)
23	C20orf81 (Hs.29341)
24	None (not clustered)
25	PDE4DIP (Hs.265848)
26	PIASX-BETA (Hs.111323)
27	FLJ10330(Hs.342307)
34	SEC23B (Hs.173497)
35	None (Hs.128580)
36	SSX1(Hs.194759)
37	MP1 (Hs.260116)
38	HMG20B (Hs.32317)
39	PSMD4 (Hs.148495)
40	INPP1 (Hs.32309)
42	BTG3 (Hs.77311)
43	SSX4 (Hs.278632)
46	ARNTL2 (Hs.222024)
48	MGC20533 (Hs.69280)
49	EMK1 (Hs.157199)
51	EDF1 (Hs.174050)
52	Actin (Hs.288061)
56	MLF1Hs.85195)
57	GCN5L2 (Hs.101067)

TABLE 6-continued

SEREX-defined sarcoma antigens: antigens reactive with sera from a single sarcoma patient	
NY-SAR-Antigen	Gene Identity (Unigene Cluster)
59	UPF3B (Hs.103832)
60	EGLN1 (Hs.6523)
62	AD034(Hs.281397)
63	USP19(Hs.301373)
67	LUC7L (Hs.16803)
69	ARL1 (Hs.242894)
70	RPL10A (Hs.334895)

¹Antigens reacted with sera from single sarcoma patient (1/39), but not with sera from normal individuals (0/33). The antigens listed had no matches with existing entries in the SEREX database (licr.org/SEREX.html).

[0205] The nucleotide sequences of all uncharacterized gene products (NY-SAR-3, -10, -16, -22, -23, -24, -27, -28, -29, -35, -41, -48, -62, -71) have been deposited in the GenBank database (SEQ ID NOs: 1-14, respectively). The cDNA sequences encoding the 72 sarcoma antigens were also compared to sequences deposited in the SEREX database accessible through a website of the Ludwig Institute for Cancer Research (licr.org/SEREX.html). Examination of this database revealed that 21 of the 72 sarcoma antigens defined in this study (29%) were also identified through SEREX analysis of other tumor types (Tables 4 and 5).

Reactivity Patterns of Sera from Normal Individuals and Cancer Patients with SEREX-Defined Sarcoma Antigens

[0206] To determine whether immune recognition of the isolated antigens was cancer-related, allogeneic sera samples obtained from 33 normal blood donors and 39 sarcoma patients (various histologies) were tested for reactivity against the 72 sarcoma antigens defined in the current study using serum antibody detection arrays (SADA). Twenty-four of the 72 antigens (33%) had a serological profile that was not restricted to cancer patients, as evidenced by their reactivity with normal sera. These antigens have been listed in Table 5.

[0207] Sera from two normal individuals and three sarcoma patients reacted with NY-SAR-1/TMF1, suggesting the reactivity was unrelated to cancers. With one notable exception (NY-SAR-22/NELIN), the frequency of antibody responses to 23 of the 24 antigens associated with normal sera reactivity was similar in normal blood donors and cancer patients. In the case of NY-SAR-22/NELIN (UniGene cluster Hs.216381), the frequency of antibody responses was considerably higher in cancer patients, in which $\frac{19}{39}$ (49%) of sarcoma patients and $\frac{4}{33}$ (12%) of normal individuals had a detectable antibody response. The remaining 48 antigens had a cancer-related serological profile, reacting only with sera from cancer patients.

[0208] The 48 antigens having a cancer-related serological profile could be subdivided into 4 categories; a) antigens identified by serum from only a single sarcoma patient; b) antigens that reacted with sera from a single sarcoma patient and, as determined by an analysis of the SEREX database, with sera from patients having other forms of cancer; c) antigens that reacted exclusively with sera from 2 or more sarcoma patients; and d) antigens that reacted with sera from 2 or more sarcoma patients and with sera from patients having other forms of cancer. Of the 48 antigens having a cancer-related serological profile, 33 antigens reacted with sera from a single sarcoma patient (Table 6).

[0209] As shown in Table 4, the remaining 15 antigens reacted with sera from 2 or more cancer patients, but not with sera from normal individuals. Nine antigens reacted with sera from a single sarcoma patient, and with sera from patients with other tumor types (NY-SAR-13, -15, -16, -18, -28, -44, -47, -71, -72). Four antigens reacted exclusively with sera from 2 or more sarcoma patients (NY-SAR, -4, -12, -30, -50). The remaining two antigens, NY-SAR-2/STAU and the CT antigen, NY-SAR-17/LAGE-1A, reacted with sera from 2 or more sarcoma patients and with sera from patients with other types of cancer. A cancer-related serological response to NY-SAR-4/FH occurred most frequently. In this case, serum samples from $\frac{5}{39}$ (13%) sarcoma patients were reactive with NY-SAR-4/FH, including $\frac{2}{10}$ sera samples from osteosarcoma patients, $\frac{1}{6}$ sera samples from malignant fibrous histiocytoma patients, $\frac{1}{2}$ patients sera samples from fibrosarcoma patients, and $\frac{1}{7}$ sera samples from Ewing sarcoma patients. No serological responses to NY-SAR-4/FH were detected in normal blood donors.

[0210] This serological response to NY-SAR-4/FH is of interest as germ-line mutations in the FH gene have been associated with a predisposition to uterine and cutaneous leiomyomata and also renal cell carcinoma (Tomlinson J P, et al. Germline mutations in FH predispose to dominantly inherited uterine fibroids, skin leiomyomata and papillary renal cell cancer. *Nat Genet* 2002 April;30(4):406-10) and is a target of somatic mutation in sarcoma (Kiuru, M., et al.

(2002) *Cancer Res.* 62, 4554-4557) suggesting that the immune response is directed against mutated epitopes.

Expression Patterns of mRNA Encoding Serologically Defined Sarcoma Antigens in Normal and Malignant Tissues

[0211] A preliminary in silico mRNA expression profile of all gene products identified in this study was carried out based on the tissue distribution of expressed sequence tags (ESTs) in the human EST database. Products with no EST matches, or those having EST matches limited to tumor tissue, fetal tissue, and/or less than 3 normal adult tissues were further examined by RT-PCR. Gene products with restricted EST profiles include the three well-characterized cancer-testis antigens, LAGE-1/NY-SAR-17, NY-SAR-36/SSX1, and NY-SAR-43/SSX4, which are expressed exclusively in normal testis and a range of different tumor types (Lethe B, et al. 1998. LAGE-1, a new gene with tumor specificity. *Int. J. Cancer* 76:903-8; Türeci Ö, et al. 1998. Expression of SSX genes in human tumors. *Int. J. Cancer* 77:19-23; Gure A O, et al. 1997. SSX: a multigene family with several members transcribed in normal testis and human cancer. *Int. J. Cancer* 72:965-971), and 3 putative tissue restricted antigens, including a known gene product, nasopharyngeal specific protein 1 (NESG1)/NY-SAR-12 (Li Z, Yao K, Cao Y. Molecular cloning of a novel tissue-specific gene from human nasopharyngeal epithelium. *Gene* 1999 Sep. 3;237(1):235-40), and 2 uncharacterized gene products, NY-SAR-35 (UniGene cluster Hs.128580) and NY-SAR-41 (UniGene cluster Hs.166670). With the exception of serum reactivity to NY-SAR-41 occurring in $\frac{1}{33}$ normal blood donors, these differentially expressed antigens showed a cancer-related serological profile.

[0212] As shown in FIG. 1A, mRNA expression patterns of NY-SAR-12, -35, and -41 were examined in 17 different human tissues by RT-PCR. NESG1/NY-SAR-12 mRNA was detected in normal placenta, testis, colon, lung, and ovary ($\frac{1}{12}$ other normal tissues). NY-SAR-35 mRNA was detected only in normal testis ($\frac{1}{15}$ other normal tissues), while a lower molecular weight transcript was detected in normal ovary. NY-SAR-41 was detected in normal testis, fetal brain, colon, lung, and bladder ($\frac{1}{12}$ other normal tissues). As shown in FIG. 1B, the testis restricted expression pattern of NY-SAR-35 was confirmed by real time quantitative RT-PCR at 40 amplification cycles. In these studies, NY-SAR-35 was expressed in normal testis at a level corresponding to 83.2 ag, which was more than 1000 times the level detected in the remaining 15 normal tissues.

[0213] The expression of NY-SAR-35 mRNA was also examined in 26 sarcoma specimens of various histologies, and was detected in fibrosarcoma and rhabdomyosarcoma specimens ($\frac{2}{26}$), as well as the SW1045 synovial sarcoma cell line (Table 7 and FIG. 1C). With regard to other tumor types, transcripts encoding NY-SAR-35 were detected in $\frac{1}{16}$ (6%) melanoma specimens, $\frac{5}{29}$ (21%) lung cancer specimens, and $\frac{3}{13}$ (23%) breast cancer specimens. NY-SAR-35 mRNA was not detected in small number of colon cancer specimens (%) or in small numbers of renal cancer specimens (%). Thus, on the basis of its immunogenicity in cancer patients, and its restricted mRNA expression profile, NY-SAR-35 can be considered a novel CT antigen.

TABLE 7

Expression of NY-SAR-35 in sarcoma, sarcoma cell lines and other malignant tissues	
Histology	Expression Frequency
<u>Sarcomas</u>	
Synovial sarcoma	0/8
Leiomyosarcoma	0/4
Malignant Fibrous Histocytoma	0/4
Ewing Sarcoma	0/2
Osteosarcoma	0/2
Rhabdomyosarcoma	1/1
Fibrosarcoma	1/1
Liposarcoma	0/1
Neurosarcoma	0/1
Chondrosarcoma	0/1
DFSP	0/1
SW1045 synovial sarcoma cell line	positive
SW982 synovial sarcoma cell line	negative
Fuji synovial sarcoma cell line	negative
<u>Other Malignancies</u>	
Melanoma	1/16
Lung Cancer	5/29
Colon Cancer	0/9
Breast Cancer	3/13
Renal Cancer	0/8
Esophageal Cancer	1/12
Ovarian Cancer	1/12
Gastric Cancer	5/6

The NY-SAR-35 Gene, Transcript and Putative Protein and Orthologous Gene

[0214] An analysis of the human genome database, mapped the NY-SAR-35 cDNA sequence to Xq28, approximately 5.9 Mbp downstream (3') of the CT10/MAGE-E1 gene and 6.8 Mbp upstream (5') of the NY-ESO-1 gene. The NY-SAR-35 gene is approximately 44 kb in length and spans 6 exons. Analyses of the human genome databases (NCBI GenBank, ncbi.nlm.nih.gov/genome, and Celera Genomics, Rockville, Md., celera.com) revealed no genomic sequences of high similarity, suggesting that it is a single copy gene with no additional family members. These results were verified by probing Southern blots of human genomic DNA with the NY-SAR-35 cDNA.

[0215] The present SEREX immunoscreening provided 4 overlapping NY-SAR-35 cDNA clones, ranging from 677-767 by in length, all contained identical 3' sequences originating from the poly A region. The NY-SAR-35 cDNA sequence was identical to 3 ESTs (GenBank accession nos. AA909915, AA906131, and AW593050) which were all derived from the NFL_T_GBC_S1 mixed tissue (fetal lung, testis, germinal center B cell) cDNA library and found in UniGene cluster Hs.128580 as well as 4 ESTs (GenBank accession nos. BC034320, AK098602, BG771667 and BI465380) derived from a testis cell line and found in UniGene cluster Hs.375082. As shown in FIG. 1D, Northern blot analysis revealed a single NY-SAR-35 mRNA transcript of 1.1 kb in normal testis, indicating the SEREX-defined clones and EST sequences represent partial transcripts. To obtain a full-length NY-SAR-35 transcript, 5' RACE was performed, yielding 262 by of additional 5' DNA sequence. Thus, the total length of the NY-SAR-35 transcript is 1029 by (SEQ ID NO: 10, GenBank accession no. AY211917), a size that is in

agreement with the 1.1 kb hybridization signal seen in Northern blots of testis mRNA probed with NY-SAR-35 cDNA.

[0216] The NY-SAR-35 transcript encodes an open reading frame of 255 amino acids (SEQ ID NO: 55, by 68-895) with a predicted molecular mass of 29.2kDa. It is identical to a hypothetical protein, XM098959, predicted from Genefinder analysis of human chromosome X sequences. The putative NY-SAR-35 protein has a signal peptide, a transmembrane domain and a cysteine-rich trefoil/P-domain, found in several secreted proteins of the gastrointestinal tract (Hoffmann W, Hauser F. The P-domain or trefoil motif: a role in renewal and pathology of mucous epithelial Trends Biochem Sci 1993 July;18(7):239-43). These data suggest that NY-SAR-35 is a secreted or membrane bound protein.

[0217] To identify a murine orthologue of NY-SAR-35, the putative human NY-SAR-35 protein sequence was used to search a translated nonredundant nucleotide database by using the TBLASTN tool of the NCBI (ncbi.nlm.nih.gov/blast/Blast.cgi). A hypothetical mouse protein, termed XP_150408, generated from a conceptual translation of the mouse X chromosome, was found to have 57% identity (49/85 amino acids) with NY-SAR-35. Using nucleotide primers corresponding to sequences encoding XP_150408, 5' and 3' RACE reactions were undertaken by using mouse testis cDNA. By combining 5' and 3' RACE products, a 1,202 by cDNA was identified (GenBank accession no. AY214130, SEQ ID NO: 133). This cDNA encoded a putative full length mouse protein of 238 amino acids (SEQ ID NO: 134) which is 41% identical to human NY-SAR-35, with conservation of the trefoil and transmembrane domains. This murine NY-SAR-35 (mNY-SAR-35) cDNA sequence was used to search mouse genome sequences (ncbi.nlm.nih.gov/genome/seq/MmBlast.html) yielding an identical genome sequence, NW 042622, from mouse chromosome X. Analysis of this sequence showed the mNY-SAR-35 gene is composed of approximately 42,600 nucleotides and seven exons.

Example 2

Analysis of the NY-SAR-35 Protein and its Expression

[0218] Purification of Recombinant NY-SAR-35 Protein in *E. coli* to Produce Monoclonal Antibodies and to Perform ELISA Assays

[0219] There are four ATG codons in exon 1 of the NY-SAR-35 gene. It is expected that the fourth ATG codon in the full length sequence of NY-SAR-35 is the first ATG codon of the translated NY-SAR-35 sequence. It appears then that the predicted protein has two interesting domains. The protein revealed two distinctive hydrophobic domains followed by two hydrophilic turns. One hydrophobic domain is a signal peptide, which are predicted in proteins with cleavage sites between amino acids 25 and 26 with SignalP software tool available at the website cbs.dtu.dk/services/SignalP. The other hydrophobic region is predicted to be a transmembrane domain with the TMHMM2.0 program available at the website cbs.dtu.dk/services/TMHMM/TMHMM2.0b.guide.html. Therefore, the NY-SAR-35 gene encodes a signal peptide and a transmembrane domain (FIG. 2).

[0220] Three kinds of NY-SAR-35 vectors were designed for the purification of the proteins in an *E. coli* expression system (pET System) (Novagen, Madison, Wisc.). The first encoded the largest possible NY-SAR-35 protein from the first ATG codon (SEQ ID NO: 150), the second encoded the

NY-SAR-35 protein from the fourth ATG codon (MH7) (SEQ ID NO: 152), and the third encoded the expected extracellular domain from the fourth ATG codon (SEQ ID NO: 154). An illustration of these vectors is provided below. The expected sizes of the resulting proteins are 29 kD (263 amino acids) (SEQ ID NO: 151), 22 kD (201 amino acids) (SEQ ID NO: 153) and 14.6 kD (133 amino acids) (SEQ ID NO: 155), respectively.

I. Whole protein (NY-SAR-35 from the First ATG)

[0221] Vector:pET23a(NdeI/XhoI): C-terminal His tag vector

[0222] Primer;

SAR35/NdeI:

(SEQ ID NO: 156)

CACACACACATATGTCTTCACATAGGAGGAAAGCGAAG

SAR35/XhoI:

(SEQ ID NO: 157)

CACACACCTCGAGCTCGTCACCATGTTCTCTCACGTC

(SEQ ID NO: 150)

CATATGTCTTTCACATAGGAGGAAAGCGAAGGGAGGAATAGGAGAAGTCA
CCGTGCCATGCGTGTGGCTCACTTAGAGCTGGCACTTATGAGTTGGCGG
CAACTGAGTCGAATCCCGAGAGCAGCCATCTCGGATACGAGGCCGCCATG
GCTGACAGGCCTCAGCCAGGATGGCGGGAATCTCTAAAGATGCGGGTCAG
CAAACCCCTTTGGGATGCTCATGCTCTCCATTTGGATCCTGCTGTTCTGTT
GCTACTACCTGCTCTACTACCTGTGCTCCGGTCTCTCATATTTTGTGCTT
GCAATGGACATATCCTGCCAACAGTGAAATGCTCATGGCCAACTCTCT
GGAAGAAGATTCCGCATTGGAAGCTTTGCTGAATTTTCTTCCAAACAA
CTTGCAATCTGAGGGAAATCAGGTGGCAAGCCCTTGTAATGAGCTGCAA
GATCTTAGTGAGAGTGAATGTTTGAGACACAAATGCTGTTTTTCATCATC
GGGACCACGAGCTTCAATGTTTGTCTCCATTTAGAGATGTGCTCAAC
AGATGATGCAATGTTTGGGCTTGGTGCGATCAGCCTTATCCTGGTATGT
CTGCCATTTATGCGCTCTCTTTCTGGAGGAGGCAACCGGCCGATGA
TTTACAAAGGCAGGACACAGAGTTGTAACGGGTTTGAAGAAACAAAGAA
GGAAGCGAAAGAGGAAGTCTGAAATGTTACAGAAAGCAGCAAGAGGACGT
GAGGAACATGGTGACGAGCTCGAGCACCACCACCACCACCACTGA

(SEQ ID NO: 151)

MSSHRRKAKGNRRSHRAMRVAHLELATYELAATESNPESHPGYEAMA
DRPQPGWRESLKMRVSKPFGMLMLSIIWILLFVCYYLSYYLCSGSSYFVLA
NGHTLPNSEAHGGSLEEDSALEALNFFPPTCNLRENQVAKPCNELQD
LSESECLRHKCCFSSGTTSTFKCFAPFRDVPKQMMQMFGLAISLILVCL
PIYCRSLFWRSEPADDLQRQDNRRVVTGLKKQRRKRKRKSEMLQKAARGRE
EHGDELEHHHHHH

II. Partial Protein (MH7 from the Fourth ATG)

[0223] Vector: pET23a(NdeI/XhoI)

[0224] Primer;

MH7/NdeI:

(SEQ ID NO: 158)

CACACACACATATGCGGGTCAGCAAACCCCTTTGGGA

SAR35/XhoI:

(SEQ ID NO: 159)

CACACACCTCGAGCTCGTCACCATGTTCTCTCACGTC

(SEQ ID NO: 152)

CATATGCGGGTCAGCAAACCCCTTTGGGATGCTCATGCTCTCCATTGGAT
CCTGCTGTTGCTGTGCTACTACCTGTCTACTACCTGTGCTCCGGTCTCT
CATATTTTGTGCTTGCAATGGACATATCCTGCCAACAGTGAAATGCT
CATGGCAATCTCTGGAAGAAGATTCCGCATTGGAAGCTTTGCTGAATTT
TTTCTTTCCAACTTGCAATCTGAGGGAAATCAGGTGGCAAAGCCTT
GTAATGAGCTGCAAGATCTTAGTGAGAGTGAATGTTTGAGACACAAATGC
TGTTTTTCATCATCGGGACCACGAGCTTCAATGTTTGTCTCCATTTAG
AGATGTGCTTAAACAGATGATGCAATGTTTGGGCTTGGTGCGATCAGCC
TTATCCTGGTATGTCTGCCCATTTATTGCCGCTCTCTTTCTGGAGGAGC
GAACCGGCCGATGATTTACAAAGGCAGGACACAGAGTTGTAACGGGTTT
GAAGAAACAAGAGGAAGCGAAAGAGGAAGTCTGAAATGTTACAGAAAG
CAGCAAGAGGACGTGAGGAACATGGTGACGAGCTCGAGCACCACCACCAC
CACCACCTGA

-continued

(SEQ ID NO: 153)

MRVSKPFGMLMLSIIWILLFVCYYLSYYLCSGSSYFVLANGHILPNSENAH
GQSLEEDSALEALNFFPPTCNLRENQVAKPCNELQDLSESECLRHKCC
FSSSGTTSTFKCFAPFRDVPKQMMQMFGLAISLILVCLPIYCRSLFWRSE
PADDLQRQDNRRVVTGLKKQRRKRKRKSEMLQKAARGREEHGDELEHHHHH
H

III. Expected Extracellular Domain of NY-SAR-35 from the Fourth ATG

[0225] Vector:pET23a(NdeI/XhoI)

[0226] Primer;

MH7/NdeI:

(SEQ ID NO: 160)

CACACACACATATGCGGGTCAGCAAACCCCTTTGGGA

MH7/XhoI:

(SEQ ID NO: 161)

CACACACCTCGAGCATTGTCATCATCTGTTTAGGC

(SEQ ID NO: 154)

CATATGCGGGTCAGCAAACCCCTTTGGGATGCTCATGCTCTCCATTGGAT
CCTGCTGTTGCTGTGCTACTACCTGTCTACTACCTGTGCTCCGGTCTCT
CATATTTTGTGCTTGCAATGGACATATCCTGCCAACAGTGAAATGCT
CATGGCAATCTCTGGAAGAAGATTCCGCATTGGAAGCTTTGCTGAATTT
TTTCTTTCCAACTTGCAATCTGAGGGAAATCAGGTGGCAAAGCCTT
GTAATGAGCTGCAAGATCTTAGTGAGAGTGAATGTTTGAGACACAAATGC
TGTTTTTCATCATCGGGACCACGAGCTTCAATGTTTGTCTCCATTTAG
AGATGTGCTTAAACAGATGATGCAATGCTCGAGCACCACCACCACCAC
ACTGA

(SEQ ID NO: 155)

MRVSKPFGMLMLSIIWILLFVCYYLSYYLCSGSSYFVLANGHILPNSENAH
GQSLEEDSALEALNFFPPTCNLRENQVAKPCNELQDLSESECLRHKCC
FSSSGTTSTFKCFAPFRDVPKQMMQMLEHHHHHH

[0227] Protein expression was induced in *E. coli*. Three colonies of each domain cloned plasmid were selected and cultured by IPTG induction for 4 hours. When total proteins were separated by SDS-electrophoresis and stained by Simply Blue SafeStain (Invitrogen) the highly expressed protein bands were not detected. However, when total proteins, separated by SDS-polyacrylamide gel, were immunoblotted using an anti-His epitope antibody, the His-tagged NY-SAR-35 proteins were detected. The results are shown in FIG. 3 with the expected sizes of the expressed proteins.

Functional Study of NY-SAR-35

[0228] Most cancer-testis antigens (^{11/13}) have been found to be expressed in non-malignant human kidney embryonic 293 cell while NY-SAR-35 is not. Human 293 cell and monkey Cos-1 cells were used to stably express the NY-SAR-35 gene for functional and immunolocalization studies.

[0229] The expected NY-SAR-35 open reading frame (including the 5' untranslated region) was cloned into pcDNA3.1/V5-HisA vector which had a C-terminal fusion tag (V5

epitope and 6xHis epitope). The cloned NY-SAR-35 nucleotide sequence and expected amino acid sequence are as follows:

A. Cloned NY-SAR-35 Nucleotide Sequence

[0230]

(SEQ ID NO: 162)
GAATTCCTTCTGGGCCACGGACTGCCGACCGTTGGGCTGTGAGGCAGCG
 EcoRI
 TCTCAGCGAGGCGGCACCCGGAGCC**ATG**TCTTACATAGGAGGAAAGCGA
 AGGGGAGGAATAGGAGAAGTACCGTGCC**ATG**CGTGTGGCTCACTTAGAG
 CTGGCAACT**TAT**GAGTTGGCGGCACTGAGTCGAATCCGAGAGCAGCCA
 TCCTGGATACGAGGCC**CTG**GCTGACAGGCCTCAGCCAGGATGGCGGG
 AATCTCTAAGATGCGGGTCAGCAAAACCTTTGGGATGCTCATGCTCTCC
 ATTTGGATCTGTGTTCTGTGCTACTACCTGTCTACTACCTGTGCTC
 CGGGTCCTCATATTTTGTGCTTGCAAATGGACATATCTGCCAACAGTG
 AAAATGCTCATGGCCAATCTCTGGAAGAAGATTCCGATTGGAAGCTTTG
 CTGAATTTTTCTTTTCAACAACCTGCAATCTGAGGGAAATCAGGTGGC
 AAAGCCTTGTAATGAGCTGCAAGATCTTAGTGAGAGTGAATGTTGAGAC
 ACAATGCTGTTTTTTCATCATCGGGACCACGAGCTTCAAATGTTTGTCT
 CCATTAGAGATGTGCCTAAACAGATGATGCAATGTTTGGGCTTGGTGC
 GATCAGCCTTATCTGTATGTCTGCCATTTATTGCCGCTCTCTTTCT
 GGAGGAGCGAACCAGCGGATGATTACAAAGGCAGGACAACAGAGTTGTA
 ACGGGTTTGAAGAAACAAAGAAGGAAGCGAAAGAGGAAGTCTGAAATGTT
 ACAGAAAGCAGCAAGAGGACGTGAGGAACATGGTGACGAG**CTCAG**CTCTA
 XhoI
 GAGGGCCCTTCGAA**GGTAAGCC TAT CCCTAACC CTCCTCTC**
 V5 epitope
GGTCTCGATTCTACGCGTACCGGT**CATCATCACCATCACCAT**TGA
 His tag

B. Expected Amino Acid Sequence and Expected Size of Expressed Proteins

[0231]

(SEQ ID NO: 163)
 → 31 Kd
 EFLLGHLPRWAVRQRLSEAPGAMS SHRRKAKGRNRRSHRA
 → 29 Kd → 26 Kd
 MRVAHLELATYELAATESNPESHGPGYEAMADRPQPGWRESLK
 → 24 Kd
 MRVSKPFGMLMSIWILLFVCYYLSYYLCSGSSYFVLANGHILPNSENAH
 GQSLSEDSALEALLNFFPPTCNLNRNQVAKPCNELQDLSESECLRHKCC
 FSSSGTTSFKCFAPFRDVPKQMMQMFGLGAISLILVCLPIYCRSLFWRSE
 PADDLQRQDNRVVTGLKKQRKRKRKSEMLQKAARGREEHGDLESRGPF
 EGKPIPNPLGLDSTRTGHHHHHH
 V5 epitope His tag

[0232] Human 293 cells and monkey Cos-1 cell that stably express the NY-SAR-35 gene were tested by RT-PCR and Western blotting. The cells transfected with 0.5 µg pcDNA3.1/V5/HisA/NY-SAR-35 plasmid were selected with 1 mg/ml neomycin for 14 days. Clones were picked and expanded for an additional 1 month and analyzed for NY-SAR-35 mRNA and protein expression. Three sets of NY-SAR-35 5'/3' primers were used and are provided below:

lane 1 (ORF including 5' untranslated region)
 (SEQ ID NO: 164)
 GGGAATTCATGTCTTACATAGGAGGAAAGCG/CACACACTCGAGCTCGT
 CACCATGTTCTCAGTC

lane 2 (ORF from the last ATG)
 (SEQ ID NO: 165)
 CACACACATATGTCTTACATAGGAGGAAAGCGAAG/CACACACTCGA
 GCTCGTCACCATGTTCTCAGTC

lane 3 (ORF from the fourth ATG)
 (SEQ ID NO: 166)
 CACACACATATGCGGGTCAGCAAAACCTTTGGGA/CACACACATAT
 GTCTTACATAGGAGGAAAGCGAAG

lane 4 (p53 5'/3')
 (SEQ ID NO: 167)
 TACTCCCTGCCCTCAACAAG/CTCAGGCGGCTCATAGGG

[0233] Whole cell extracts were made from the same cloned cells. Total proteins were separated by SDS-polyacrylamide gel electrophoresis and immunoblotted to detect NY-SAR-35 proteins by anti-V5 epitope monoclonal antibody (Invitrogen). The size of the stably expressed NY-SAR-35 proteins in 293 and Cos-1 cells was found to be 24 kD. This is, therefore, consistent with translation of NY-SAR-35 beginning at the fourth ATG.

Example 3

Results from the Second Round of Immunoscree- nings by SEREX Analysis

Identification of Human Sarcoma Antigens by SEREX Analysis

[0234] Serum from the two NY-ESO-1 seropositive patients (FS and MFH) were again used to immunoscreen cDNA libraries prepared from the SW982 and SW1045 synovial sarcoma cell lines, both of which were shown to express eight or more known CT antigen transcripts (Table 2). Sera from the FS patient was also used to immunoscreen a cDNA library derived from normal testis. In total, the results from Examples 1 and 3 represent five independent SEREX immunoscreenings performed, which lead to the identification of 113 distinct antigens, designated NY-SAR-1 through NY-SAR-113.

[0235] The 113 SEREX-defined antigens represent 91 known proteins and 22 uncharacterized gene products (novel, ESTs, KIAA series, FLJ series, ORFs, DKFZ series). In addition to the uncharacterized gene products described above in Example 1 (NY-SAR-3, -10, -16, -22, -23, -24, -27, -29, -35, -41, -48 and -71) additional immunoscreening identified another 11 uncharacterized gene products (NY-SAR-77, -79, -80, -84, -88, -91, -95, -97, -104, -105 and -113). All of the sequences for these uncharacterized gene products have been deposited in the GenBank database and given the sequential accession numbers AY211909-AY211931. In terms of the serum sources, 27 of the 113 antigens were identified by using sera from a MFH patient and 86 were

identified with FS sera. Of the 113 antigens identified, 95 were unique to a particular cDNA library screening and 18 antigens were identified in more than one library. This underlines the beneficial nature of incorporating multiple cDNA libraries into large-scale SEREX analyses of the cancer immunome.

Seroepidemiology of SEREX-Defined Sarcoma Antigens

[0236] The cDNA sequences encoding the 113 sarcoma antigens were compared with sequences deposited in the cancer immunome or SEREX database (licr.org/CancerImmunomeDB, formerly licr.org/SEREX.html). These comparisons are in addition to the comparisons presented above in Example 1. In a preliminary analysis, it was found that 39 of the 113 sarcoma antigens defined in this study (34%) were also identified through SEREX analysis of other tumor types (Table 8). Table 9 below provides a complete list of all 113 antigens along with their respective Unigene cluster information, if any. These results represent the information available after all rounds of immunoscreening. Contrary to the results shown, NY-SAR-39, -57, -61, -63 and -64 after the first round of immunoscreenings had not been found in the SEREX database.

TABLE 8

Immunomic analysis of sarcoma/testis antigens: Reactivity with sera from sarcoma patients, patients with other forms of cancer, and normal individuals			
NY-SAR-antigen	Gene identity (unigene cluster)	Cancer patient seroreactivity*	Normal seroreactivity
1	TMF1 (Hs.267632)	GC, BC, CC, SRC	2/33
2	STAU (Hs.6113)	PC, BC, SRC	3/30
3	KIAA1536 (Hs.156667)	BC, SRC	2/33
6	RHAMM (Hs.72550)	OC, SRC	1/33
7	PINCH (Hs.112378)	CC, GC, RC, BC HN, ESO, AML, SRC	16/21
11	U2AF1RS2 (Hs.171909)	RC, HD, BC, GC, SRC	6/33
13	ACTN1 (Hs.119000)	BC, SRC	5/30
15	RBM6 (Hs.173993)	LC, SRC	0/33
16	FLJ12785 (Hs.192742)	TALL, SRC	0/33
17	LAGE-1a (Hs.87225)	BC, SRC	0/33
18	SSSCA1 (Hs.25723)	CC, SRC	0/33
19	HEF1 (Hs.80261)	RC, SRC	3/33
28	PPIL4 (Hs.11065)	BC, SRC	0/33
29	FLJ13441 (Hs.232146)	PN, SRC	6/33
31	AUANTIG (Hs.75528)	BC, GC, OC, SRC	2/33
39	PSMD4 (Hs.148495)	MEL, SRC	0/33
44	LGALS1 (Hs.227751)	RC, SRC	0/33
45	STIP1 (Hs.75612)	RC, SRC	4/33
47	MIF (Hs.73798)	MEL, SRC	0/33
57	GCN5L2 (Hs.101067)	PC, SRC	0/33
61	ZNF282 (Hs.58167)	RC, SRC	1/33
63	USP19 (Hs.301373)	OC, SRC	0/33
64	USP16 (Hs.99819)	PN, SRC	2/33
66	ROCK1 (Hs.17820)	RC, BC, CC, SRC	1/33
74	RANBP2 (Hs.199179)	BC, GL, BC, SRC	2/33
77	KIAA0992 (Hs.194431)	PC, SRC	4/15
80	FLJ12577 (Hs.87159)	GC, SRC	0/33
81	SDS3 (Hs.20104)	GC, SRC	4/16
82	NYCO45 (Hs.160881)	CC, SRC	0/33
89	SSX2 (Hs.289105)	BC, MEL, SRC	0/33
90	UACA (Hs.49753)	BC, ESO, SRC	4/25
93	NYBR15 (Hs.178175)	BC, SRC	1/12

TABLE 8-continued

Immunomic analysis of sarcoma/testis antigens: Reactivity with sera from sarcoma patients, patients with other forms of cancer, and normal individuals			
NY-SAR-antigen	Gene identity (unigene cluster)	Cancer patient seroreactivity*	Normal seroreactivity
98	OIP2 (Hs.274170)	BC, SRC	0/33
99	SSX3 (Hs.178749)	BC, MEL, SRC	2/30
101	RANBP2L1 (Hs.179825)	GL, BC, SRC	3/33
102	RBPJK (Hs.356806)	GC, RC, BC, MEL, SRC	1/16
103	Hsp40 (Hs.94)	HN, NCC, SRC	0/33
108	EIF4G (Hs.25732)	GC, SRC	5/27
112	PMSCL1 (Hs.91728)	CC, SRC	0/33

AML, acute myelogenous leukemia; BC, breast cancer; CC, colon cancer; GC, gastric cancer; GL, glioma; HCC, hepatocellular carcinoma; HN, head and neck cancer; LC, lung cancer; MEL, melanoma; OC, ovarian cancer; PC, prostate cancer; PN, pancreatic cancer; RC, renal cancer; SRC, sarcoma; TALL, T cell acute lymphocytic leukemia.
*Determined by sequence comparisons with the SEREX database (licr.org/CancerImmunomeDB/).

TABLE 9

Sarcoma/testes antigens defined by serological analysis of cDNA expression libraries			
NY-SAR-antigen	Gene identity (Unigene Cluster)	Sera source	Library source
1	TMF1 (Hs.267632)	MFH, FS	A, T
2	STAU (Hs.6113)	MFH	A
3	KIAA1536 (Hs.156667)	MFH	A
4	FH (Hs.75653)	MFH, FS	A, B
5	TBC1D1 (Hs.278586)	MFH	A
6	RHAMM (Hs.72550)	MFH	A, B
7	PINCH (Hs.112378)	MFH	A, B
8	BIRC2 (Hs.289107)	MFH	A, B
9	ATP5B (Hs.25)	MFH	A, B
10	KIAA0603 (Hs.173802)	MFH	A
11	U2AF1RS2 (Hs.171909)	MFH	A, B
12	NESG1 (Hs.158450)	MFH	B
13	ACTN1 (Hs.119000)	MFH	A
14	SC65 (Hs.207251)	MFH	A
15	RBM6 (Hs.173993)	MFH	A
16	FLJ12785 (Hs.192742)	MFH	A
17	LAGE-1a (Hs.87225)	MFH, FS	B
18	SSSCA1 (Hs.25723)	MFH	A, B
19	HEF1 (Hs.80261)	MFH	A, B
20	TCEB3 (Hs.155202)	MFH	B
21	GTF3C3 (Hs.90847)	MFH	A
22	NELIN (Hs.216381)	MFH	A
23	C20orf81 (Hs.29341)	MFH	A
24	None (not clustered)	MFH	A
25	PDE4DIP (Hs.265848)	MFH	B
26	PIASX-BETA (Hs.111323)	MFH	B
27	FLJ10330 (Hs.342307)	MFH	B
28	PPIL4 (Hs.11065)	FS	B
29	FLJ13441 (Hs.232146)	FS	A
30	SNK (Hs.3838)	FS	A
31	HUMAUAUTIG (Hs.75528)	FS	A, B, T
32	PDAP1 (Hs.278426)	FS	A
33	SURF6 (Hs.274430)	FS	B
34	SEC23B (Hs.173497)	FS	B
35	EST (Hs.128580)	FS	B, T
36	SSX1 (Hs.194759)	FS	B, T
37	MP1 (Hs.260116)	FS	A, T
38	HMG20B (Hs.32317)	FS	A
39	PSMD4 (Hs.148495)	FS	A
40	INPP1 (Hs.32309)	FS	A
41	EST (Hs.166670)	FS	B
42	BTG3 (Hs.77311)	FS	B, T
43	SSX4 (Hs.278632)	FS	B
44	LGALS1 (Hs.227751)	FS	B
45	STIP1 (Hs.75612)	FS	A

TABLE 9-continued

NY-SAR- antigen	Sarcoma/testes antigens defined by serological analysis of cDNA expression libraries		Library source
	Gene identity (Unigene Cluster)	Sera source	
46	ARNTL2 (Hs.222024)	FS	B
47	MIF (Hs.73798)	FS	A
48	MGC20533 (Hs.69280)	FS	A
49	EMK1 (Hs.157199)	FS	A
50	PYCR1 (Hs.79217)	FS	A
51	EDF1 (Hs.174050)	FS	A
52	Actin (Hs.288061)	FS	A
53	FXYS5 (Hs.333418)	FS	A
54	LMOD1 (Hs.79386)	FS	A
55	RBM10 (Hs.154583)	FS	A
56	MLF1(Hs.85195)	FS	A, T
57	GCN5L2 (Hs.101067)	FS	A
58	LIP8 (Hs.348012)	FS	A
59	UPF3B (Hs.103832)	FS	A
60	EGLN1 (Hs.6523)	FS	A
61	ZNF282 (Hs.58167)	FS	A
62	AD034(Hs.281397)	FS	A
63	USP19(Hs.301373)	FS	A
64	USP16 (Hs.99819)	FS	B, T
65	FDF1 (Hs.48876)	FS	B
66	ROCK1 (Hs.17820)	FS	B, T
67	LUC7L (Hs.16803)	FS	B
68	P38IP (Hs.333500)	FS	B
69	ARL1 (Hs.242894)	FS	B
70	RPL10A (Hs.334895)	FS	B
71	EST (Hs.314941)	FS	B
72	HSPE1 (Hs.1197)	FS	B, T
73	PRM2 (Hs.2324)	FS	T
74	RANBP2 (Hs.199179)	FS	T
75	GKAP42 (Hs.36752)	FS	T
76	TIAL1 (Hs.182741)	FS	T
77	KIAA0992 (Hs.194431)	FS	T
78	TSP-NY (Hs.97643)	FS	T
79	Novel (not clustered)	FS	T
80	FLJ12577 (Hs.87159)	FS	T
81	SDS3 (Hs.20104)	FS	T
82	NYCO45 (Hs.160881)	FS	T
83	SOX6 (Hs.326876)	FS	T
84	DKFZp434 (Hs.131834)	FS	T
85	RAD50 (Hs.41587)	FS	T
86	EPIM (Hs.99865)	FS	T
87	SOX5 (Hs.87224)	FS	T
88	DKFZp564 (Hs.93589)	FS	T
89	SSX2 (Hs.289105)	FS	T
90	UACA (Hs.49753)	FS	T
91	FLJ11730 (Hs.17118)	FS	T
92	ESTs (Hs.368781)	FS	T
93	NYBR15 (Hs.178175)	FS	T
94	CG005 (Hs.23518)	FS	T
95	FLJ10637 (Hs.22595)	FS	T
96	MCSP (Hs.111850)	FS	T
97	EST (Hs.128836)	FS	T
98	OIP2 (Hs.274170)	FS	T
99	SSX3 (Hs.178749)	FS	T
100	PGAM2 (Hs.46039)	FS	T
101	RANBP2L1 (Hs.179825)	FS	T
102	RBPJK (Hs.356806)	FS	T
103	Hsp40 (Hs.94)	FS	T
104	DKFZp434 (Hs.131834)	FS	T
105	C11orf14 (Hs.32017)	FS	T
106	CEP11 (Hs.97437)	FS	T
107	UBE1 (Hs.2055)	FS	T
108	EIF4G (Hs.25732)	FS	T
109	SYN1 (Hs.127416)	FS	T
110	NYD-SP14 (Hs.98105)	FS	T
111	NDP52 (Hs.154230)	FS	T
112	PMSC1 (Hs.91728)	FS	T
113	KIAA0442 (Hs.32168)	FS	T

[0237] To determine whether immune recognition of these 39 antigens was cancer-related, serum samples from normal individuals (n=33) were tested for reactivity to these antigens. 23 of the 39 antigens (59%) had a serological profile that was not restricted to cancer patients, whereas the remaining 16 antigens had a cancer-related serological profile, reacting only with sera from cancer patients (sarcoma patients and serum source of SEREX database entry), and not with sera from normal individuals. 14 of these 16 antigens reacted only with sera from a single sarcoma patient when tested for reactivity with additional allogeneic sarcoma sera (n=39). The remaining 2 antigens, NY-SAR-17/LAGE-1 and NY-SAR-80/FLJ12577, reacted with 2 of 39 and 3 of 39 sarcoma sera, respectively, and not with sera from normal individuals (n=33).

[0238] NY-SAR-80/FLJ12577 is an uncharacterized member of the Mo25 protein family, an evolutionary conserved family of proteins with no known function. Analysis of the tissue distribution and frequency of EST sequences homologous to NY-SAR-80/FLJ12577 indicate widespread mRNA expression, with a preponderance of malignant tissue-derived homologous ESTs suggesting possible overexpression in cancer.

[0239] Overall, the relative infrequency of overlapping humoral immune responses among the population of sarcoma patients analyzed is contrary to previous findings for colon (Scanlan M J. et al. 2002. Cancer-Related Serological Recognition of Human Colon Cancer: Identification of Potential Diagnostic and Immunotherapeutic Targets. *Cancer Res.*, 2002; Jul. 15; 62(14), 4041-7.), breast (Scanlan M J, et al. Humoral immunity to human breast cancer: antigen definition and quantitative analysis of mRNA expression. *Cancer Immunity* 1:4 [epub]) and renal cancers (Scanlan, M. J., et al., and Old, L. J. Antigens recognized by autologous antibody in patients with renal-cell carcinoma. *Int. J. Cancer* 1999; 83: 456-64) in which a subset of antigens were mutually seroreactive in a cancer related manner. These results suggest that the immune response to sarcoma is either highly variable or that distinct sarcoma histotypes have distinct immunomes. Expression Patterns of mRNA Encoding Serologically Defined Sarcoma/Testis Antigens in Normal and Malignant Tissues

[0240] In addition to the three well-known CT antigens described in Example 1, NY-SAR-89/SSX-2 and NY-SAR-99/SSX-3 were found to have restricted EST profiles, being expressed exclusively in normal testis and a range of different tumor types (Lethe B, et al. 1998. LAGE-1, a new gene with tumor specificity. *Int. J. Cancer* 76:903-8; Türeci Ö, et al. 1998. Expression of SSX genes in human tumors. *Int J Cancer* 77:19-23; Gure A O, et al. 1997. SSX: a multigene family with several members transcribed in normal testis and human cancer. *Int J Cancer* 72:965-971). Six other putative tissue-restricted antigens were identified, including four other known gene products, NY-SAR-73/Protamine 2 (PRM2, Domenjoud, L., Fronia, C., Uhde, F. & Engel, W. (1998) *Nucleic Acids Res.* 16, 7773), NY-SAR-78/TSP-NY (UniGene cluster Hs.97643), NY-SAR-96/mitochondrial capsule selenoprotein (MCSP, Aho, H., et al. (1996) *Genomics* 32, 184-190) and NY-SAR-110/NYD-SP14 (Hs.98105) and two additional uncharacterized gene products, NY-SAR-92 (Hs. 368781) and NY-SAR-97 (not clustered).

[0241] Two of the six putative tissue restricted antigens, NY-SAR-73/PRM2 and NY-SAR-110/NYD-SP14, were ubiquitously expressed in a panel of 20 normal tissues as

determined by RT-PCR (Table 10). The remaining four genes, in addition to NY-SAR-12/nasopharyngeal specific protein 1 (NESG1, Li Z, Yao K, Cao Y. Molecular cloning of a novel tissue-specific gene from human nasopharyngeal epithelium. *Gene* 1999 Sep. 3;237(1):235-40), NY-SAR-35 and NY-SAR-41, were found to be expressed with frequencies ranging from 1 to 9 of 20 normal tissues. NY-SAR-35 and NY-SAR-78 were both testis-specific. The mRNA expression profiles of NY-SAR-35 and NY-SAR-78 were then analyzed in various malignant tissues by RT-PCR. Transcripts encoding NY-SAR-78/TSP-NY were not detected in cancer. The tumor specimens examined included, lung cancer (0 of 9), colon cancer (0 of 9), breast cancer (0 of 18), renal cancer (0 of 11), esophageal cancer (0 of 12), ovarian cancer (0 of 14), melanoma (0 of 18) and sarcoma (0 of 8). Thus, although NY-SAR-78/TSP-NY is a "virtual CT antigen" with 100% identity with ESTs derived from prostate cancer and leukemia, its expression in cancer could not be verified in our RT-PCR series.

TABLE 10

Analysis of mRNA expression by RT-PCR of 9 of the 113 sarcoma/testis antigens									
Tissue	NY-SAR antigen*								
	12	35	41	73	78	92	96	97	110
Brain	-	-	-	+	-	-	-	-	+
Kidney	-	-	-	+	-	-	-	-	+
Liver	-	-	-	+	-	-	-	-	+
Pancreas	-	-	-	+	-	-	-	-	+
Placenta	+	-	-	+	-	-	-	-	+
Testis	+	+	+	+	+	+	+	+	+
Fetal brain	-	-	+	+	-	-	+	+	+
Small intestine	-	-	-	+	-	-	-	-	+
Heart	-	-	-	+	-	-	-	-	+
Prostate	-	-	-	+	-	-	+	+	+
Adrenal	-	-	-	+	-	-	+	+	+
Spleen	+	-	-	+	-	+	+	+	+
Colon	+	-	+	+	-	-	-	-	+
Stomach	-	-	-	+	-	-	-	-	+
Lung	+	-	+	+	-	-	-	+	+
Bladder	-	-	+	+	-	-	-	+	+
Ovary	+	-	+	+	-	-	-	+	+
Breast	-	-	-	+	-	-	-	+	+
Cervix	-	-	-	+	-	-	-	-	+
Skeletal muscle	-	-	-	+	-	-	-	-	+
Total no. of positive tissues	6/20	1/20	6/20	20/20	1/20	2/20	5/20	9/20	20/20

*Unigene clusters: NY-SAR-12, Hs.158450; NY-SAR-35, Hs.128580; NY-SAR-41, Hs.166670; NY-SAR-73, Hs.2324; NY-SAR-78, Hs.97643; NY-SAR-92, Hs.368781; NY-SAR-96, Hs.111850; NY-SAR-97, Hs.128836; NY-SAR-110, Hs.98105.

[0242] The antigens presented herein are of interest for their immunotherapeutic and diagnostic potential. For example, the six known testis-restricted gene antigens (NY-SAR-17/LAGE-1, NY-SAR-36/SSX1, NY-SAR-43/SSX4, NY-SAR-78/TSP-NY, NY-SAR-89/SSX2 and NY-SAR-99/SSX3), four novel gene products that are also differentially expressed antigens (NY-SAR-35, -41, -92 and -91) and two tissue-restricted antigens (NY-SAR-12/NESG1 and NY-SAR-96/MCSP) not previously studied in relation to cancer have are potential vaccine targets and/or targets for therapeutic antibodies as well as for diagnosis of cancer, particularly by screening patient samples for antibodies that recognize the proteins.

[0243] NY-SAR-35 mRNA was detected in a variety of tumor specimens, such as melanoma (1 of 16 specimens),

sarcoma (2 of 26 specimens), lung cancer (5 of 29 specimens), breast cancer (3 of 13 specimens), bladder cancer (5 of 12 specimens), esophageal cancer (1 of 12 specimens) and ovarian cancer (1 of 12 specimens). As also shown before in Example 1, NY-SAR-35 was not detected in colon cancer (n=9) or renal cancer (n=8). The CT-restricted expression profile of NY-SAR-35 was confirmed by real-time quantitative RT-PCR at 40 amplification cycles (FIG. 4). In two of the nine non-small lung cancer specimens tested, NY-SAR-35 was expressed at levels that were 0.13 and 0.15 times the level detected in normal testis. In conformity with the proposed nomenclature for CT antigens (Chen Y T, et al. 1998. Identification of multiple cancer/testis antigens by allogeneic antibody screening of a melanoma cell line library. *Proc. Natl. Acad. Sci. USA.* 95:6919-23), NY-SAR-35 is designated CT-20.

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Equivalents

[0292] Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

[0293] All references disclosed herein are incorporated by reference in their entirety.

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<223> OTHER INFORMATION: n = a, c, g or t/u
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (994)..(995)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<220> FEATURE:
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<223> OTHER INFORMATION: n = a, c, g or t/u
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<222> LOCATION: (1033)..(1033)
<223> OTHER INFORMATION: n = a, c, g or t/u
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<220> FEATURE:
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<223> OTHER INFORMATION: n = a, c, g or t/u
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<223> OTHER INFORMATION: n = a, c, g or t/u
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<222> LOCATION: (1062)..(1062)
<223> OTHER INFORMATION: n = a, c, g or t/u
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<221> NAME/KEY: misc_feature
<222> LOCATION: (1065)..(1065)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1069)..(1069)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<222> LOCATION: (1071)..(1071)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1074)..(1074)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1077)..(1077)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1083)..(1083)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1086)..(1086)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1090)..(1090)

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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1094)..(1094)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1096)..(1096)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1099)..(1099)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1102)..(1102)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1107)..(1107)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1113)..(1113)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<222> LOCATION: (1115)..(1115)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1136)..(1137)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1139)..(1139)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1142)..(1144)
<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 1

ttnggacagg ggaactgtgt tcagaaccag ctcgatgaga gccagcaaga acggaatgac	60
ctgatgcagc tgaagctaca gctggaggga caggtgacag agctgaggag ccgagtgcag	120
gagctcgaga gggctctggc aactgccagg caggagcaca ctggagctga tggaaacagta	180
caaggggatt tccnnggtcc catggggaga tcacagaaga gagggacatc ctgagccggc	240
aacagggaga ccatgtggca cgcacctcgg agctagagga tgacatccag accatcagtg	300
agaaagtgtc gacgaaggaa gtggagcctg gacaggctta gagacacagt gaaggccctg	360
actcgggaac aagagaagct ccttgggcaa ctgaaagaag tacaagcaga caaggagcaa	420
agtgaggctg agctccaagt ggcacaacag gagaaccatc acttaaattt ggacctgaag	480
gaggcgaaga gctggcaaga ggagcanagt gtcagggtc agcgactgaa agacaaggtg	540
gcccagatga aggacacct atgccaggcc cagcagcggg tggcccagct ggagcccttg	600
aaggagcagc ttnaggggc ccaangagcc ttgncagcct caagccagca naaagccacc	660
ctttcttggg gaggagtgtg ccagcngcan cancanccag ggaccntcc atatgccgan	720
ctacaccgga gccgtcctgg aagtggctga agttaacngc aaggtggctg acctcgtttt	780
gnctttgaag ganaaaantc ccatggncca aggaccggnc anggctgntc ncaatgngga	840

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ngnncaaaag acaaannett gaactcnatg caaaatcctn tattgnaaaa gnncttngga    900
ggaaagancc aanccagtgt caaangactg gccggaaaag atnttcctng tcnattnnca    960
annaatcngg nattccaaat ttngnnnncc tgtngtnca aangaaannc gnnccctgggn   1020
naccgaatnt tancnntaaa acnaagcccn nngaagnggc anaancggnt ngtnccncac   1080
agntgngccn tngtnnatnc cncttanaca agnanccaaa atagtccctg gctgtngnga   1140
cnnntttt                                     1148

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<210> SEQ ID NO 2
<211> LENGTH: 914
<212> TYPE: DNA
<213> ORGANISM: homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (239)..(239)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (863)..(863)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (900)..(900)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (912)..(912)
<223> OTHER INFORMATION: n = a, c, g or t/u

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<400> SEQUENCE: 2

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tttcgaagac gggcacacac gttcagccac ccaccttcaa gcacaaagag aaagctgaat   180
ttgcaggatg ggagggctca ggggtgtcgt tccccctcgc tgaggcagag ctccagtcna   240
acagtgcagt gatggagaag ggagaaaaag gacctcatct acctgcagca atgagtcct    300
aagtgtggga ggaacctctg tcactcctcg ccggatctcc tggcggcagc gcattttcct   360
caggggtgct tctcccatga acaaatctcc ctccagcaatg caacagcaag atggattgga   420
caggaacgag ctgctgccac tgteccccct ctctccaacc atggaggagg aaccgctggt   480
tgtattcctg tctggggagg atgaccaga aaagattgaa gaaagaaaga aatcaaaaga   540
actgaggagc ttgtggagaa aagctataca ccaacaaatc ttgttacttc gaatggaaaa   600
agaaaaccag aaacttgaag caagcagaga tgaactccag tccagaaaag ttaaattaga   660
ctatgaagaa gttggtgcat gtcagaaaga ggtcttaata acttgggata agaagttgtt   720
aaactgcaga gctaaaatca gatgtgatat ggaagatatt catactcttc ttaagaagga   780
gttcccaaag tcgacgagga gaatttggca gtttctggct tacagtaccg actcaacaca   840
gattgcctaa taacaacagc ctntcgacta ttcttaagga ctttgagcag ctactgctan   900
cagcatgcga tntt                                     914

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<210> SEQ ID NO 3
<211> LENGTH: 891
<212> TYPE: DNA

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<213> ORGANISM: homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (677)..(677)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (775)..(775)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (785)..(785)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (807)..(807)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (847)..(847)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (858)..(858)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (879)..(879)
<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 3

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ggggcgcgtc gggcccgag gtggggaacg ctctgggcag cctggagcca ctgcgctgga      120
tgctgcgctc gcccttcgac cgcaacgtgc cggtaaacct ggagcttcag gagttgctgc      180
tggactacag cttccagcac ctgggtgtct cctcacaggg ctgtgttgat catcccatag      240
ttttgacaga agctgtgtgc aacctactgt attcacggca aatgatgtct gagcttcttt      300
ttgagtgcta cgggattccc aaggttgccct atggaataga cagcctcttc agcttctacc      360
acaataagcc aaagaactcg atgtgcagtg ggctaatacat ttcacttgga taccagtgtg      420
cgcatgtttt acccatctta gaaggagat tagatgctaa aaactgcaag cgcatcaatc      480
ttggaggaag ccaagcagct ggttacctcc agcgtctcct ccagctgaag taccctgggc      540
acctggcagc catcacccctc agccgcagtg aggagattct gcatgagcac agctacatcg      600
ctgaggatta tgtggaagaa ttacacaaat ggcgggtgtcc tgattattat gagaataatg      660
tcacacaagat gcagctncca ttttcagca agctcctggg cagcactctg acctctgagg      720
agaaacaaga aaggcggcag cagcaattgc ggcggctgca ggagctcaat gccnngcggc      780
gggangagaa gctgcagctt ggatcangag cgtctggacc gactgctata tgtgcaggaa      840
cttctanagg atggccanat ggatcagttt acaaagctnt gatgagctga t              891

<210> SEQ ID NO 4
<211> LENGTH: 880
<212> TYPE: DNA
<213> ORGANISM: homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<221> NAME/KEY: misc_feature
<222> LOCATION: (693)..(693)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (698)..(698)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (784)..(784)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (803)..(803)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (813)..(813)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (842)..(842)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (867)..(867)
<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 4

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cagaagtgtt agcggccaga gctcccagac cctaccac agccaggcgg gacgcgcaca      120
gtccctccac gcggaagaa gtacctcgc cggtcaccgg ctctgcagg gtgcaaatat      180
atacagagct tcataatcag cccaagacca catagagcaa acatgaatga tatttcccaa      240
aaggctgaga ttctgtttc ttcatctaaa cctgtcccaa aaacctatgt accaaaactt      300
ggcaagggtg atgtaaagga taagtgtgaa gccatgcaga gagccaggga agaaagaaat      360
caaaggagat ctgagagcga aaaacaaaga agaaaagaac aatatattag agagagagaa      420
tggaacagga gaaagcagga gattaaagaa atgcttgctt ctgatgatga ggaagatgta      480
tcttctaaag tagaaaaggc ttatgttcca aaattaacag gaactgtgaa gggtagattt      540
gctgaaatgg agaacaaaag acaagaggaa caaaggaaga gaacggagga ggaacgaaaa      600
cgcagaattg agcaggatat gttagaaaag aggaaaatac agcgtgaatt agcnaaaagg      660
gctgaacagg aaggagatga ttactactt atnactgnng tacctgtcaa tcatataaac      720
atctggaaaa tgaaaagaat tttagatct agaaaaagac gtgaagagaa gaaagatcca      780
gtcnaggaga taaagattag atntgagaca cgnctctct caggagcaag ggcttcttag      840
tntggtgtga ataaaaggga gcaaaanac cttctccca      880

<210> SEQ ID NO 5
<211> LENGTH: 924
<212> TYPE: DNA
<213> ORGANISM: homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (754)..(754)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (772)..(772)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (783)..(783)
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (799)..(799)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (873)..(875)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (898)..(898)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (918)..(918)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (920)..(920)
<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 5

ctggagctcg cgcgctcgca ggtcgacact agtggatcca aagaattcgg cacgaggctc      60
actgctcaca gctgcccagc tgaaagccaa gggggagctg agctttgaac aggaccagct      120
ggtggtggg ggcagctgg gcgagctgca caacgggaca cagtatcgtg aggtccgcca      180
gttctgctcg ggcctctggcc accaccttgt gcgctttctac ttctctactc gtgtttactc      240
cgagtacctt gaggatgttc tggaagagct gacatatgga cctgccccgg acctggtgat      300
catcaactcc tgctctctggg atctctccag atatggtcgc tgctcaatgg agagctaccg      360
ggagaacctg gagcgggtgt ttgtgcgcat ggaccaagta ttgccagact cctgcctgct      420
gggtgtggaac atggcgatgc cctcgggga acgtatcact ggggggtttcc tctgcccaga      480
gctccagccc ctggcaggct cctcgggcg ggatgtggtt gaagggaact tctacagtgc      540
tacgctggcc ggggaccact gctttgatgt cctagacctc cactttcact tccggcatgc      600
agtacagcac cgtcatcggg atggtgtcca ctgggaccag catgcacacc gccacctctc      660
acacctgctt ctgacctatg tggctgacgc ctggggcgtg gagctgcccc agcgtggcta      720
tccccctgac ccgtggattg aggactgggc aganatgaat catccattcc anggaagcca      780
tangcagacc caaacttcng ggagacctgg gccttgctcc accccacttc ttcttgctct      840
ccatgccttt tctaccgggt tctaggcctg cannttctt tttccacctt gccagganac      900
ccttttccag gcagcctnch ccca                                           924

<210> SEQ ID NO 6
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<212> TYPE: DNA
<213> ORGANISM: homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (640)..(640)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (672)..(672)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (715)..(715)
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<220> FEATURE:
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = a, c, g or t/u
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<223> OTHER INFORMATION: n = a, c, g or t/u
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<222> LOCATION: (820)..(820)
<223> OTHER INFORMATION: n = a, c, g or t/u
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<223> OTHER INFORMATION: n = a, c, g or t/u
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<221> NAME/KEY: misc_feature
<222> LOCATION: (846)..(846)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (849)..(849)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (852)..(852)
<223> OTHER INFORMATION: n = a, c, g or t/u
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<222> LOCATION: (873)..(873)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (875)..(875)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (887)..(887)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<222> LOCATION: (909)..(909)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<222> LOCATION: (928)..(928)
<223> OTHER INFORMATION: n = a, c, g or t/u

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gaaggaaaata agggaaaagtt tgaaaaacag ttaagaaga aatctgaaga ggtatattgt 120
ttacagaaag agctaaagat aaaaaatcac agtcttcaag agacttctga gcaaacgtt 180
attctacagc atactcttca gcaacagcag caaatgttac aacaagagac aattagaaat 240
ggagagctag aagatactca aactaaactt gaaaaacagg tgtcaaaact ggaacaagaa 300
cttcaaaaac aaagggaaaag ttcagctgaa aagttgagaa aaatggagga gaaatgtgaa 360
tcagctgcac atgaagcaga tttgaaaagg caaaaagtga ttgagcttac tggcactgcc 420
aggcaagtaa agattgagat ggatcagtag aaagaagagc tgtctaaaat ggaaaaggaa 480
ataatgcacc taaaacgaga tggagaaaat aaagcaatgc acctctctca attagatatg 540
atcttagatc agacaaagac agagctagaa aagaaaacca atgctgtaaa ggagttagaa 600
aagttacagc acagtactga aactgaacta acagaagccn tgcaaacagg gaagtacttg 660
agactgacta cnaaatgtct atgggagatt taaaaagtac tttagacaa ctccnggaat 720
tggngagatg tactacagaa ggctccattht tcattagagg aaaatacnct actataagga 780
tncccccgtt ggacntaaan aatgcaagat ggnattgnan acaaaancng gagctcctgn 840
aatggncng cnccttaagag anaattggga ctnangcaaa aacagcncng gtaccctttg 900
ganttgctnt tcnggacccg agggaaaang 929

<210> SEQ ID NO 7
<211> LENGTH: 935
<212> TYPE: DNA
<213> ORGANISM: homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (792)..(792)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (799)..(799)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (820)..(820)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (856)..(856)

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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (872)..(872)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (875)..(875)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (886)..(886)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (899)..(899)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (904)..(904)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (906)..(906)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (922)..(922)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (926)..(927)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (935)..(935)
<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 7

ngctggagct cgcgcgcctg caggtcgaca ctagtggatc caaagaattc ggacacgaggg	60
aaacataaag aagacaaga tgataggcgg cacagagatg acaaaagaga ttccaagaaa	120
gagaaaaaac acagtagaag cagaagcaga gaaaggaaac acagaagtag gagtccaagt	180
agaaatgcag ggaacgaag tagaagtaga agcaaagaga aatcaagtaa acataaaaaat	240
gaaagtaaag aaaaatcaaa taaacgaagt cgaagtggca gtcaaggaag aactgacagt	300
gttgaaaaat caaaaaaacg ggaacatagt cccagcaaag aaaaatctag aaagcgtagt	360
agaagcaaag aacgttccca caaacgagat cacagtgata gtaaggacca gtcagacaaa	420
catgatcgtc gaaggagcca aagtatagaa caagagagcc aagaaaaaca gcataaaaaac	480
aaagatgaga ctgtgtgaaa atattttgta aaagtggatc acattgaatc ctataaatga	540
ttaaatctgc ttttttcccc cactgtgaga ttgtgcagta gttcgactc ctcaagctct	600
ccctgtaggc tgcattttca tttctctttt cgtgtaggga agtgcccttg taattccatt	660
tattgcattg gtgttttcac ccaattgtta agtttgatac atgatgcaca gattggtctt	720
gcatttttat tgttttggtt tgaatgtaca gtctgtacta tgctctgaaa tggttttatc	780
ctttggcatg gntgcctgnt ggttaatttg tataggcatn aactgcccta tctaaaaaaa	840
aaaaaaaaaa ctcgangtct ttaaagcggc gnggnccctg atttenccg gggggaccng	900
taangnccca tcccccttag gngcgnntaa atccn	935

<210> SEQ ID NO 8
<211> LENGTH: 943
<212> TYPE: DNA

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<213> ORGANISM: homo sapiens
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<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (741)..(741)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (796)..(796)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (823)..(823)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (842)..(842)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (857)..(857)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (869)..(869)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (873)..(873)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (898)..(898)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (911)..(911)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (915)..(915)
<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 8

aaangctgga gctcgcgcg ctcgaggtcg acactagtgg atccaaagaa ttcggcacga      60
ggcaagagtg atttcaagga gtatgaaaaa gaacaggata aaccacctaa ttggttctg      120
aaagataaag taaagcccaa acaggatata aaatacgatc ttatattaga tgagcaggcc      180
gaagactcaa aatcaagtca ctacacaca agtaaaaaac acaagaagaa aacccatcac      240
tgttctgaag agaaagaaga tgaggactac atgccaatca aaaatactaa tcaggatata      300
tatagagaaa tgggggtttg tcactatgaa gaagaagaaa gctgttggga gaaacaaaag      360
agtgaaaaga gagaccgaac tcagaaccga agtcgtagcc gatctcgaga gagggatggc      420
cattatagta atagtcataa atcaaaatac caaacagatc tttatgaaag agaaaggagt      480
aaaaagagag accgaagcag aagtccaaag aagtccaaag ataagaaaa atctaagtat      540
agatgaaaga tgaagaggca gaattgagag gctaacatat ttactcttgt ctaacttaag      600
agtgccagga aagcagatgc ttagattttg tgtcaaagct tggtattttt ttcatactag      660
gattatggtc tttagattaa tactgattat atagagcagc gaaagataaa gaattgacat      720
tttctttgta tactttttac nctaattttt atggtatata taatggtagt cttcattttt      780
gaagtcttca ttttctctct ttttttatgg agtattttcta ctncaaaatc cttaacgttt      840
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tntaagggtga ataataatgaat atctgggtcnc tcncaacttag atacgtgtgc gacttttnag 900

tccctaggcc ncccnccaa aatatttga tttgggtggc ttg 943

<210> SEQ ID NO 9
<211> LENGTH: 910
<212> TYPE: DNA
<213> ORGANISM: homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (584)..(584)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (626)..(626)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (723)..(723)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (751)..(751)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (756)..(756)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (775)..(775)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (784)..(784)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (796)..(796)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (833)..(833)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
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<222> LOCATION: (844)..(844)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (870)..(870)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (884)..(884)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (894)..(894)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (903)..(903)
<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 9

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gggcgagctc ggcaacctcg gcgcagcgag cgcgggcggc cagccagggc cagggggcgg 120

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tggcggccaa ggtccgaccg ggtgccagct gttcccagcc cccgcctcgg gcccgccgce	180
ggcgccgcca tgggcaagaa gcacaagaag cacaaggccg agtggcgctc gtcctacgag	240
gattatgccg acaagccctt ggagaagcct ctaaagctag tctgaaggt cggaggaagt	300
gaagtgactg aactctcagg atccggccac gactccagtt actatgatga caggtcagac	360
catgagcgag agaggcaca aaaaagaaa aagaagaaga agaagaagtc cgagaaggag	420
aagcatctgg acgatgagga aagaaggaa cgaaaggaa agaagaagcg gaagcgagag	480
agggagcact gtgacacgga gggagaggct gacgactttg atcctgggaa gaaggtggag	540
gtggagccgc ccccgatcgc gccagtcgga gcgtgccgga cacngccagc cgaatatgag	600
agcacaccta ttcagcaact cctggnaaca cttcctccgc cagcttcaga gaaaagatcc	660
ccatggattt tttgcttttc ctgtcacgga tgcaattgct cctgggatat tccatgataa	720
tanaacctcc catggatttt ggcaccatga nagacnaaat tgtagctaat gaatncaagt	780
cagntacgga atttanggca attccacgct gatgtgtgat atgcatggac ttncataggc	840
cagntccgtg tactacagtt ggcaagagan cttcccgag cttnaagatg atgngcaacc	900
gcngctcttt	910

<210> SEQ ID NO 10

<211> LENGTH: 1029

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 10

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cggagccatg tcttcacata ggaggaaagc gaaggggagg aataggagaa gtcaccgtgc	120
catgcgtgtg gctcacttag agctggcaac ttatgagttg gcggcaactg agtcgaatcc	180
cgagagcagc catcctggat acgaggccgc catggctgac aggcctcagc caggatggcg	240
ggaatctcta aagatgcggg tcagcaaac ctttgggatg ctcatgctct ccatttggat	300
cctgctgttc gtgtgctact acctgtccta ctacctgtgc tccgggtcct catattttgt	360
gcttgcaaat ggacatatcc tgccaacag tgaaaatgct catggccaat ctctggaaga	420
agattccgca ttggaagctt tgctgaattt tttctttcca acaacttgca atctgaggga	480
aaatcagggt gcaaaagcctt gtaatgagct gcaagatctt agtgagagtg aatgtttgag	540
acacaaatgc tgtttttcat catcggggac cagcagcttc aaatgttttg ctccatttag	600
agatgtgcct aaacagatga tgcaaatggt tgggcttggc gcgatcagcc ttatcctggt	660
atgtctgccc atttattgct gctctctttt ctggaggagc gaaccggccg atgatttaca	720
aaggcaggac aacagagttg taacgggttt gaagaaacaa agaaggaaagc gaaagaggaa	780
gtctgaaatg ttacagaaaag cagcaagagg acgtgaggaa catggtgacg agtagcaaga	840
gaccaaagca ttattttccc ctcaagacaa cagaaacat tcagagcaga ggggactgtc	900
tcagccatgc aaacctcatg gagcattttg gaaagttaaa attgattctt atttttgtca	960
tgtttacttt caaacatgaa ataaaattga gttctgtttt catgcatcaa aaaaaaaaaa	1020
aaaaaaaaa	1029

<210> SEQ ID NO 11

<211> LENGTH: 924

<212> TYPE: DNA

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<213> ORGANISM: homo sapiens
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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (204)..(204)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (752)..(752)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (754)..(754)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (756)..(759)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (761)..(761)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (765)..(765)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (770)..(770)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (773)..(775)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (777)..(779)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (781)..(781)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (802)..(802)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (812)..(812)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (829)..(829)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (833)..(833)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (849)..(849)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (866)..(866)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (873)..(873)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (879)..(880)

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<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (886)..(886)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (901)..(901)
<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 11

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aatngctgga gctcgcgcgc ctgcaggtcg acactagtgg atccaaagaa ttcggcacga      60
gggagaaaaa gagtttataa tgctacaaaa tgaacaggag ataagtcaac tgaaaaaaga      120
aattgaaaga acacaacaaa ggatgaaaga aatggagagt gttatgaaag agcaagaaca      180
gtacattgcc actcagtaca aggnggccat agatttgggg caagaattga ggctgacccg      240
ggagcaggtg cagaactctc atacagaatt ggcagaggct cgtcatcagc aagtccaagc      300
acagagagaa atagaaaggc tctctagtga actggaggat atgaagcaac tctctaaaga      360
gaaagatgct catggaaacc atttagctga agaactgggg gcttctaaag tacgtgaagc      420
tcatttagaa gcaagaatgc aagcagaaat caagaaattg tcagcagaag tagaatctct      480
caaagaagct tatcatatgg agatgatttc acatcaagag aaccatgcaa agtgggaagat      540
ttctgctgac tctcaaaagt cttctgttca gcaactaaac gaacagttag agaaggcaaa      600
attggaatta gaagaagctc aggatactgt aagcaatttg catcaacaag tccaagatag      660
gaatgaagta attgaagctg caaatgaagc attacttact aaagtaagta aacatataaa      720
agtattaaag catatctatg aaaacaaaac cncncnnnnc ngcctcccn cennnnnnnc      780
ntctcgagag tactttctaaa gnggcgcggg gncectccga tttccccng gngggggtag      840
caggtaagng tacccaattc cccctntag agncgtatnn aattenctgg ccgccgttta      900
ncacctcgtg ctgggaaaaa ctgg                                           924
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<210> SEQ ID NO 12
<211> LENGTH: 917
<212> TYPE: DNA
<213> ORGANISM: homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (745)..(745)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (784)..(784)
<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 12

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ttctagcagt gccaaagaaga aggataaaag agttcaaggt ggaagagtga ttgagtcccg      180
gtatctgcag tatgaaaaa agacaaccca aaaggctcct gcaggagatg ggtcacagac      240
ccgaggggaag atgtctgaag gtggaaggaa atccagcctg ctccagaaaa gcaaagcaga      300
tagcagtggg gtcggaaaagg gtgacctgca gtccacgttg ctggaagggc atggcacagc      360
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tccacctgac ctggatctct ctgctattaa tgacaaaagc atcgtaaaaa agacgccaca	420
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gagcccgat ttatctgaag caatggaaat gatggagtct cagacactac tgctgacgct	540
actatccgta aagatggaga acaatcttgc tgagtttgaa agaagggcag aaaagaattt	600
attaataatg tgtaaggaga aggagaagct acagaaaaag gccacgagc tgaagcgag	660
gcttctctc tctcagagga agcgggagct ggcagatgtc ctggatgcc agatcgagat	720
gctcagcccc cttcagaggca gtggnacac gttcaagga gcaatacagg acattcgcca	780
cggnccttg acactaccag gcacgagctg cccgtgaggt ccataccct ggaggagat	840
gggcagcagc tcttagacgc cctgcagcat gactggtgac cctcagcgcc tctgggaaa	900
cttgatgttg gtgatcg	917

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<210> SEQ ID NO 13
<211> LENGTH: 921
<212> TYPE: DNA
<213> ORGANISM: homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (742)..(742)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (808)..(808)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (822)..(822)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (842)..(842)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (858)..(858)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (895)..(895)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (912)..(912)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (918)..(918)
<223> OTHER INFORMATION: n = a, c, g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (920)..(920)
<223> OTHER INFORMATION: n = a, c, g or t/u

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<400> SEQUENCE: 13

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gcacgtgggt gccactgttg gcttctgaat ggtttgcaag gggatatcc acgccaaggc	180
ctttggtatg gccgtgggta caccgtctg agccgttctc ttccatcgca gagcggcgcc	240

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ctccggcggc gctctccagt catggactac cggcggcttc tcatgagccg ggtgggtccc	300
gggcaattcg acgacgcgga ctctcttgac agtgaaaaca gagacttgaa gacagtcaaa	360
gagaaggatg acattctgtt tgaagacctt caagacaatg tgaatgagaa tggtaagggt	420
gaaatagaag atgaggagga ggaggggttat gacgatgatg atgatgactg ggactgggat	480
gaaggagtgt gaaaactcgc caaggggttat gtctggaatg gaggaagcaa cccacaggca	540
aatcgacaga cctccgacag cagttcagcc aaaatgtcta ctccagcaga caaggtctta	600
cggaaaattt gagaataaaa ttaatttaga taagctaaat gttactgatt ccgtcataaa	660
taaagtcacc gaaaagtcta gacaaaagga agcagatatg tatcgcatca aagataaggc	720
agacagagca actgtagaac angtgttgga tcccagacca agaagattt tattcaagat	780
gttgactaga ggaatcataa cagagatnaa tggctgcatt anccaggaaa aaagctaattg	840
tnaccatgct acccagcnaa tggagagagc agaccatcaa atttataaac ttctntttgg	900
ggttcaagat cnggatantn t	921

<210> SEQ ID NO 14
 <211> LENGTH: 901
 <212> TYPE: DNA
 <213> ORGANISM: homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (836)..(836)
 <223> OTHER INFORMATION: n = a, c, g or t/u
 <220> FEATURE:
 <221> NAME/KEY: misc_feature
 <222> LOCATION: (892)..(892)
 <223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 14

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attttcctta tctgcttcct agtcctgtat gcccttttcc taacactcac aacaaaacta	180
actaatacta acatctcaga cgctcaggaa atagaaaccg tctgaactat cctgcccgcc	240
atcactctag tctcctcgc cctcccatcc ctacgcctcc tttacataac agacgaggtc	300
aacgatccct cctttaccat caaatcaatt ggccaccaat ggtactgaac ctacgagtac	360
accgactacg gcggactaat cttcaactcc tacatacttc cccattatt cctagaacca	420
ggcgacctgc gactccttga cggtgacaat cgagtagtac tcccgattga agccccatt	480
cgtataataa ttacatcaca agacgtcttg cactcatgag ctgtcccac attaggctta	540
aaaacagatg caattcccgc acgtctaaac caaaccactt tcaccgtac acgaccgggg	600
gtatactacg gtcaatgctc tgaaatctgt ggagcaaacc acagtttcat gcccatcgtc	660
ctagaattaa tccccctaaa aatctttgaa ataggaccgc tatttaccct atagcacccc	720
ctctaccccc tctagagcca aaaaaaaaaa aaaaaaactc gagactagtt ctctccggac	780
attcagactg agcgtgccta ccaaaagcag ccgaccatct ttcaaaaca gaaganggtc	840
ctgctgggag aactggcaag gagaagctcc gcggtactac aagaacatcg gnetgggctt	900
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<210> SEQ ID NO 15
 <211> LENGTH: 1850
 <212> TYPE: DNA

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<213> ORGANISM: homo sapiens

<400> SEQUENCE: 15

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cgctatcgga ccaaaagccgt gagctctgag gtggatgaga gcctcttttg agatatcaag    180
tccccagccc agggccagag cgacagcccc attgtgctgc tccagataa gcataccctt    240
caaaaaactc tctactgcttt gggcttggat cgcaagccag agaccatcca gctcatcacc    300
cgggacatgg tccgagaact cattgttccc acagaggatc cctccgggga gtccctaacc    360
atcagccctg aggagtttga gcgaatcaaa tgggcatccc atgtctgac cagagaagaa    420
cttgaggcca gggaccaggc cttcaagaag gagaaggaa ccaccatgga tgcagtgatg    480
acacgaaaga agatcatgaa acagaaggag atggtgtgga acaacaacaa gaagctcagt    540
gacctggagg aggtggccaa ggaacgggac cagaacctcc tgcagagagc caacaagctg    600
cggatggagc aggaggagga gctcaaggac atgagcaaga ttatctcaa tgctaagtgc    660
catgccatcc gggatgcccc aatcctggag aagcagcaga tccaaaaga actggacaca    720
gaagagaagc ggttggatca gatgatgga gtggagcggc agaataccat tcaaaaggcag    780
gaggaactgg agaggaagag gagggaggaa agaattagag gaaggcggca aattgtggaa    840
cagatggaaa agaaccagga ggagcgatcg ctgcttgctg agcagcggga gcaggagaag    900
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aaacagaaag cagaactgct ggctcaggag aagctggcag accagatggt gatggagttt    1080
accaagaaga agatggctcg agaagcagag tttaggctg agcaggagag aatccggagg    1140
gagaaagaga aggagatcgc acgcttgagg gccatgcagg agaaggccca ggattaccag    1200
gcagaacagg atgccttgcg ggccaagcgc aaccaggagg ttgcagacag agagtggcgc    1260
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agaaccagca gaaggaagtg cagaaccgga ttgccacctt tgaggggggc cggcgccctca    1560
aagaggaggc ccagaaacgc cgtgagcgca tcgatgagat caagaggaaa aagcttgaag    1620
agctgagagc cactggcctt ccgagaagt actgcattga agctgagcgc aaagctaaca    1680
tcctgccagc tacctctgtg aactgagggg agccttcgtg gccctcagga tgccttcggg    1740
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ttacagatta aatctacttg actaaaaaaaa aaaaaaaaaa aaaaaaaaaa    1850

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<210> SEQ ID NO 16

<211> LENGTH: 1791

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 16

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tccgataga atatgatac tttggtgaac taaagtgcc aatgataag tattatggcg	240
cccagaccgt gagatctacg atgaacttta agattggagg tgtgacagaa cgcagccaa	300
cccagttat taaagctttt ggcaccttga agcagcggc cgctgaagta aaccaggatt	360
atggtcttga tccaaagatt gctaatagca taatgaaggc agcagatgag gtagctgaag	420
gtaaattaaa tgatcatctt cctctcgtgg tatggcagac tggatcagga actcagacaa	480
atatgaatgt aatgaagtc attagcaata gagcaattga aatgttagga ggtgaacttg	540
gcagcaagat acctgtgcat cccaacgac atgttaataa aagccagagc tcaaatgata	600
cttttccac agcaatgcac attgctgctg caatagaagt tcataagta ctgttaccag	660
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gcaagggtga cctactcag tgtgaagcaa tgaccatggt tgcagcccaa gtcagggga	1200
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gctatctcac agcagagcag tttagcgaat gggtaaaacc taaggacatg ctgggtccaa	1560
agtgatttac ataaatttat aatgaaaata aacatgtata aaatttaaaa aaacagactc	1620
ccatttctta aaaacggata agtttgaag gaaactgcta ttgaacttaa gcatctctag	1680
cagagcaatt tgatcagtat ataaaacct aggatgtgct aggtctaaga tggattaaac	1740
aagtataaaa taaaatacat ttataaaata aaaaggaaaa cagacttaaa a	1791

<210> SEQ ID NO 17

<211> LENGTH: 3258

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 17

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tgccgcgccc acaggagacc aggagcctgt gcgcaggccc atgcgcaagt ccttctccca	180
gcccggcctg cgtcgcctgg cctttaggaa ggagctgcag gatgggggcc tccgaagcag	240
cggcttcttc agctccttcg aggagagcga cattgagaac cacctcatta gcggacacaa	300

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tattgtgcag	cccacagata	togaggaaaa	togaactatg	ctcttcacga	ttggccagtc	360
tgaagtttac	ctcatcagtc	ctgacaccaa	aaaaatagca	ttggagaaaa	attttaagga	420
gatactcttt	tgtctcagg	gcacagaca	cgtggaccac	tttgggttta	tctgtcggga	480
gtcttccgga	gggtggcgct	ttcattttgt	ctgttacgtg	tttcagtgc	caaagaggc	540
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gacagctaag	gcgccagccc	agctgtgtga	gggctgcccc	ctgcaaagcc	tgcacaagct	660
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tccaacttgc aattcagggg gcattgtcca gtgttttttt tgtgttttt agatactaaa 3180
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aatgcaact tatgtttt 3258

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<210> SEQ ID NO 18

<211> LENGTH: 3496

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 18

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gtacaatatt ttgttaggcg tttctgataa cactagaaag gacaagtttt atcttgtgat 180
aaattgatta atgttttaca catgactgat aattatagct gaatagtcct taaatgatga 240
acaggttatt tagtttttaa atgcagtgtg aaaagtgtgc tgtggaaatt ttatggctaa 300
ctaagtttat ggagaaaata ccttcagttg atcaagaata atagtgggtat acaaagttag 360
gaagaaagtc aacatgatgc tgcaggaaat ggaacaaat acaaatgata tttaacaaag 420
atagagttta cagtttttga actttaagcc aaattcattt gacatcaagc actatagcag 480
gcacaggttc aacaaagctt gtgggtattg acttccccca aaagttgtca gctgaagtaa 540
tttagcccac ttaagtaaat actatgatga taagctgtgt gaacttagct tttaaatagt 600
gtgaccatat gaaggtttta attacttttg ttatttgtaa taaaatgaga ttttttgggt 660
tgtcatgtta aagtgttat agggaaagaa gcctgcataa aattttttac cttgtggcat 720
aatcagtaat tggctgttta ttcaggcttc atagcttgta accaaatata aataaaaggc 780
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<210> SEQ ID NO 19

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<211> LENGTH: 1807

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 19

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gcaggcgccg ccaccggcg catcgtggcg gtcattggcg cagtgggtga cgtccagttt      300
gatgagggac taccaccaat tctaaatgcc ctggaagtgc aaggcaggga gaccagactg      360
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gttggtcctg agactttggg cagaatcatg aatgtcattg gagaacctat tgatgaaaga      540
gggtccatca aaaccaaaac atttgcctcc attcatgctg aggtccaga gttcatggaa      600
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tgtacttgtc tctctccttg ccctaaacct aaaaagcttc atttttctat ataggctgca      1740
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<210> SEQ ID NO 20

<211> LENGTH: 2676

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 20

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<211> LENGTH: 2961

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 21

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<211> LENGTH: 5676

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

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ctacactgga atgaactttt tacattaggg catttgtatt tccctcaca tacttgccac	5400
attacttggc ataggagaga tgcttagtgt aattataagt taacaagcct ttggatcagg	5460
gcttgactca tgaatagaaa agtatatgcc tgctggatgg aagaatctct tgggcgagca	5520
ccatttttct tcccatcacc ttcccttgaa aatatatctt cagctttggg taggaggaat	5580
cttggtgtat gaaatcattg caaatttact tcatcttttc tggagtgtga agttgtgact	5640
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<210> SEQ ID NO 23

<211> LENGTH: 1866

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 23

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gcgctgcatt tattgaagag cggctgcagc cctgcggttc agattaaaat ccgagaattg	180
tatagacgcc gatattccac aactcttgaa ggactttctg atttatccac aatcaaatca	240
tcggttttca gtttggatgg tggctcatca cctgtagaac ctgacttggc cgtggctgga	300
atccactcgt tgccttcac ttcagttaca cctcactcac catcctctcc tgttggttct	360
gtgctgcttc aagatactaa gccacattt gagatgcagc agccatctcc cccaattcct	420
cctgtccatc ctgatgtgca gttaaaaaat ctgccctttt atgatgtcct tgatgttctc	480
atcaagccca cgagtttagt tcaaacgagt attcagcgat ttcaagagaa gttttttatt	540
tttgctttga cacctcaaca agttagagag atatgcatat ccagggattht ttgcccaggt	600
ggtaggagag attatacagt ccaagttcag ttgagacttt gctgggcaga gacaagttgc	660
cctcaagaag ataactatcc aaatagtcta tgtataaaag taaatgggaa gctatttcct	720
ttgcctggct atgcaccacc gccataaaat gggattgaac agaagcgccc tggacgcccc	780
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tgggcatcag aaattgggaa gaattactct atgtctgtat atcttgtacg gcagettaca	900
tcagccatgt tattacagag attaaaaatg aaaggtatta gaaaccctga tcattccaga	960
gcactaatta aagaaaaact tactgcagat cctgatagtg aaattgctac aactagcctt	1020
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cccacctgga tttgtcctgt gtgtgacaaa aaagctgcct atgaaagtct aatattagat	1200
gggcttttta tggaaattct caatgactgt tctgatgtag atgagatcaa attccaagaa	1260
gatggttcct ggtgtccaat gagaccgaag aaagaagcta tgaaagtatc cagccaaccg	1320
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gaggcaagca agaagaaagt agatgttatt gatcttaca tagaaagctc ttctgacgaa	1440
gaggaagacc ctctgcca aaggaaatgc atctttatgt cagaaacaca aagcagccca	1500
accaaagggg ttctcatgta tcagccatct tctgtaaggg tgcccagtggt gacttcgggt	1560

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ccccagtact gtccctcctat gtttttggat agtctcacct cacccttaac agcaagcagt	1740
acgtctgtca ccaccaccag ctcccatgaa agcagtactc atgttagttc atccagcagc	1800
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gactaa	1866

<210> SEQ ID NO 24

<211> LENGTH: 2972

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 24

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tccgccccct tccgcctcc ccgtatataa gacttcgccc agcactctca ctgcacaaag	180
tggaccgggg tgttgggtgc tagtcggcac cagaggcaag ggtgcgagga ccacggcccg	240
ctcggacgtg tgaccgcgcc taggggggtg cagcgggcag tgcggggcgg caaggcgacc	300
atggarcttt tgcggactat cactaccag ccagccgcca gcacaaaat gtgcgagcag	360
gcgctgggca aggggtgcgg aggggactcg aagaagaagc ggccgcgcga gcccccgag	420
gaatcgagc cactcagtc ccaggcgcaa gtgcccccg cgccccctca ccaccatcac	480
caccattcgc actcggggcc ggagatctcg cggattatcg tcgacccac gactgggaag	540
cgctactgcc ggggcaaaag gctgggaaag ggtggctttg caaaatgtta cgagatgaca	600
gatttgacaa ataacaaagt ctacgccgca aaaattatc ctcacagcag agtagctaaa	660
cctcatcaaa gggaaaagat tgacaaagaa atagagcttc acagaattct tcatcataag	720
catgtagtgc agttttacca ctacttcgag gacaaagaaa acatttacat tctcttgga	780
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gttggggact tcggtctggc agccaggcta gaacccttgg aacacagaag gagaacgata	1020
tgtggtaccc caaattatct ctctctgaa gtctcaaca aacaaggaca tggctgtgaa	1080
tcagacatct gggccctggg ctgtgtaatg tatacaatgt tactaggag gccccattt	1140
gaaactacaa atctcaaga aacttatagg tgcataagg aagcaaggta tacaatgccg	1200
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gatactccca gtttggatga catcattcga catgactttt ttttgaggg ctteactccg	1320
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aagaatttct ttaagaaagc agctgctgct ctttttgggt gcaaaaaaga caaagcaaga	1440
tatatgaca cacataatag agtgtctaaa gaagatgaag acatctacaa gcttaggcat	1500
gatttgaaaa agacttcaat aactcagcaa ccagcaaac acaggacaga tgaggagctc	1560
cagccaccta ccaccacagt tgccaggctt ggaacacccg cagtagaaaa caagcagcag	1620
attggggatg ctattcggat gatagtcaga gggactcttg gcagctgtag cagcagcagt	1680

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gaatgccttg aagacagtag catgggaagt gttgcagaca cagtggaag ggttcttcgg	1740
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tttcagtggg tcaccaaatg ggttgattac tctaacaat atggcttttg gtaccagctc	1860
tcagaccaca ccgtcggtgt ccttttcaac aatggtgctc acatgagcct ccttcagac	1920
aaaaaacag ttcactatta cgcagagctt ggccaatgct cagttttccc agcaacagat	1980
gctcctgagc aatttattag tcaagtgaag gtgctgaaat acttttctca ttacatggag	2040
gagaacctca tggatggtgg agatctgctt agtggtactg atattcgaag acctcggtc	2100
tacctcttc agtggctaaa atctgataag gccctaatga tgctctttaa tgatggcacc	2160
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taccttctca cctacatcaa tgaggatagg atatctacaa ctttcaggct gacaactctg	2280
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ggtggtacga aaacaattcc cctgtggcct gctggactgg gtggaacca gaaccaggct	2520
aaggcataca gttcttgact ttggacaatc ccaagagtga accagaatgc agttttcctt	2580
gagatacctg ttttaaaagg tttttcagac aattttgcag aaaggtgcat tgattcttaa	2640
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tggctgcgta actgtgaact atggccatat ataatttttt ttcattaatt ttggaagata	2820
cttggtgctg gaaaagtgca ttccttgcta ataaactttt tatttattac agcccaaaga	2880
gcagtattta ttatcaaaat gtcttttttt ttatgttgac cattttaaac cgttggcaat	2940
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<210> SEQ ID NO 25

<211> LENGTH: 2805

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 25

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gttcacccag cagaatgaag aacgggatgg tgtgcgtttt agttggaacg tgtggccttc	180
cagccggctg gaggtacaaa gaatggttgt acccctggct tgtctcctta ctcccttgaa	240
agaacgtcca gacctacctc ctgtacaata tgaacctgtg ctttcagca ggccaacttg	300
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tttctgtttt caaagaaatc agtttctcc agcttatgga ggcatactg aggtgaatca	420
acctgccgaa ttgatcccc agttttctac aattgagtac gtgatacagc gaggtgctca	480
gtccctctg atctttctct atgtggttga cacatgcctg gaggaagatg acctcaagc	540
actcaaagag tccctgcaga tgcctctgag tcttctctcc ccagatgctc tgggtgggtct	600
gatcacattt ggaaggatgg tgcaggttca tgagctaagc tgtgaaggaa tctccaaaag	660
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tgaattaaag attcctattc	1080
gaaaaaggca accaagcact	1140
cattgatatt tatgcttgtg	1200
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gacattccaa agaattctta	1320
tactttggac gtaaagacct	1380
atctctgaat gtgaaaggac	1440
tcagtggaaa atctgtggcc	1500
caatcagcac aacaccccca	1560
ttatcagcac tccagacccc	1620
agatgtacag agtcagctca	1680
gttgatggca cggcttgggg	1740
gtggctggac cgacaactca	1800
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ctcttactcc tttcatgggc	2040
tgacagaatt ttgctgatgg	2100
agcccagtgg cgtaaagctg	2160
tctgcaggca ccaactggatg	2220
ttacatcaac acggagcatg	2280
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tgatgatgtt agcctgcagg	2400
ctgttaagct gaggatacaa	2460
agaaaggctt gataacatto	2520
atcttatatg taactcttta	2580
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aggtgagaat cttaatgatc	2760
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<210> SEQ ID NO 26

<211> LENGTH: 766

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

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<400> SEQUENCE: 26

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accacgggat gatgctaaag catcagagaa gagaagcaag gcctttgatg atattgccac    180
atacttctct aagaaagagt ggaaaaagat gaaatactcg gagaaaatca gctatgtgta    240
tatgaagaga aactataagg ccatgactaa actaggtttc aaagtcaccc tcccaccttt    300
catgtgtaat aaacaggcca cagacttcca ggggaatgat tttgataatg accataaccg    360
caggattcag gttgaacatc ctcatgatgc ttctggcagg ctccacagaa tcatcccgaa    420
gatcatgccc aagaagccag cagaggacga aaatgattcg aagggagtgt cagaagcatc    480
tgccccacaa aacgatggga aacaactgca cccccagga aaagcaaata tttctgagaa    540
gattaataag agatctggac ccaaaagggg gaaacatgcc tggaccacac gactgctgta    600
gagaaagcag ctgggtgattt atgaagagat cagtgaccct gaggaagatg acgagtaact    660
ccctggggg atacgacaca tgcccttgat gagaagcaga acgtggtgac ctttcacgaa    720
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<210> SEQ ID NO 27

<211> LENGTH: 3432

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: (2741)..(2741)

<223> OTHER INFORMATION: n = a, c, g or t/u

<400> SEQUENCE: 27

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ggctctgcag tataaactag gagacaagat ccatggatcc accgtaaac aggtgacatc    180
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gcatacagaa attcgagaaa aaggcgggtg ttatggtgga ngcgcaaac tcagccacaa	2760
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tgggaaggct gtcgactggg ctaagtctgg aaaattcaca cagcaagaca tcgacgaagc	2880
caaaactttt gtctttctca ccgtagatgc tctgtcgtc ccttcagaca aaggaatgga	2940
ccactttctg tacggcctct cggatgagat gaagcaggcc cacagagagc agctctttgc	3000
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catccgatga gcagccgtgg cgctcgactg cacaggagcc cgagacaata cactccaag	3180
ctgaatatga aaagtcagaa atgctactgc tttttccaag aatattatgt cattgagtgt	3240
cgccaaagcc cttgactggc gagtcaaaaa ctcagatcta tottaagagt gaccaggaag	3300
aggttcattg aaataatcat gcatgaagcg ccaaagatgc accatgtaga attttcaactt	3360

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tgtactggca ggctcgtttt acctgattct agaatattta agaactctaaa aataaagggc	3420
aactctgact ta	3432

<210> SEQ ID NO 28
 <211> LENGTH: 1232
 <212> TYPE: DNA
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 28

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taccagcagt ctgaagccta taagatgtgc acggagaaga tccaggagaa gaagatcaag	180
aaagaagact cgagctctgg gctcatgaac actctcctga atggacacaa gggtagggac	240
tgcgatggct tctccacctt cgatgttccc atcttctctg aagagtcttt ggacccaaac	300
aaagcgcgtg aggcggagct tcggcgcttg cggaagatga atgtggcctt cgaggagcag	360
aacgcggtac tgcagaggca aaacgcagag catgagcagc gcgcgcgagc gtctggagca	420
ggagctggcg ctggaggagc ggaggacgct ggcgctgcag cagcagctcc aggccgtgcg	480
ccaggcgctc accgccagct tcgcctcact gccggtgcgc ggcacgggag aaacggccac	540
gctgggcact ctggacttct acatggcccg gcttcacgga gccatcgagc gcgaccccg	600
ccagcagcag aagctcatcg tccgcatcaa ggaaatcctg gccaggtcgc ccagcgagca	660
cctgtgagga gtgggagggc ccacgatgca gaggagaagc tgtgggagcg gccctgccac	720
acccaccccc gtggagcaga ggctgggggt ccacccttg gggcctggc ccatcctgca	780
cctttggggg ctccagcccc cctaaaatta aatttctgca gcaccccttt agctttcaat	840
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gggtgtcccc gcatacctgt accccagatg ggtgggggac ggtttgccc atcctgctct	1140
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<210> SEQ ID NO 29
 <211> LENGTH: 1313
 <212> TYPE: DNA
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 29

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acttcttacc caccaggctg caggcccagc aggatgctgt caacatagtt tgtcattcaa	180
agacccgcag caaccctgag aacaacgtgg gccttatcac actggctaact gactgtgaag	240
tgctgaccac actcaccaca gacactggcc gtatcctgtc caagctacat actgtccaac	300
ccaagggcaa gatcaccttc tgcacgggca tccgcgtggc coactgtgct ctgaagcacc	360
gacaaggcaa gaatcacaaag atgcgcatca ttgcctttgt gggaagccca gtggaggaca	420

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atgagaagga tctggtgaaa ctggctaacc gcctcaagaa ggagaaagta aatgttgaca	480
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tgaatggcaa agatggaacc ggttctcatc tggtagacgt gcctcctggg cccagtttgg	600
ctgatgctct catcagttct ccgatttttg ctggtgaagg tggtgccatg ctgggtcttg	660
gtgccagtga ctttgaattt ggagtagatc ccagtgcctg tctgagctg gccttgcccc	720
ttcgtgtatc tatggaagag cagcggcagc ggcaggagga ggaggcccg cgggcagctg	780
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agaacctccc aggtgtggat cccaacaatg aagccattcg aaatgctatg ggctccctgg	1140
cctcccaggc caccaaggac ggcaagaagg acaagaagga ggaagacaag aagtgaagact	1200
ggagggaaag ggtagctgag tctgcttagg ggactgcatg ggaagcacgg aatatagggt	1260
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<210> SEQ ID NO 30

<211> LENGTH: 1682

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 30

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cccagcggcc ctgcctaac ctccgcggg gccgcgcctc ctccctctcc tgcctccgcc	180
cgtctccgtt tctcgaggga aaggtgctg cctcctgctc tgtcctcatc cccggcttag	240
ctgacggccc agaggtgggt gccaatcca ccagcagctg caactgaaaa gcaaggttca	300
gaaatgtcag atatctccg ggagctgctc tgtgtctctg agaaggtgc taacattgcc	360
cgggcgtgca gacagcagga agcctcttc cagctgctga tcgaagaaaa gaaagaggga	420
gaaaagaaca agaagtttgc agttgacttc aagactctgg ctgatgtact ggtacaggaa	480
gttataaaac agaatatgga gaacaagttt ccaggcttgg aaaaaatat ttttgagaa	540
gaatccaatg agtttactaa tgactggggg gaaaagatta ccttgagggt gtgttcaaca	600
gaggaagaaa cagcagagct tottagcaaa gtccctcaatg gtaacaaggt agcatctgaa	660
gcattagcca gggttgttca tcaggatgtt gcctttactg acccaactct ggattccaca	720
gagatcaatg ttccacagga catcttggga atttgggtgg accccataga ttcaacttat	780
cagtatataa aaggttctgc tgacattaaa tccaaccagg gaatcttccc ctgtggactt	840
cagtgtgtca ccattttaat tgggtgtctat gacatacaga caggggttcc cctgatggga	900
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tattggggcc tttcttacat ggggaccaac atgcattcac tacagctcac catctctaga	1020
agaaacggca gtgaaacaca cactggaaac accggctctg aggcagcatt ctccccagt	1080
tttccagccg taattagtac aagtgaaaag gagactatca aagctgcatt gtcacgtgtg	1140

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gc	1682

<210> SEQ ID NO 31
 <211> LENGTH: 1511
 <212> TYPE: DNA
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 31

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gccgaagagc ggccggcgga gccggcgga aaaaatgaag aatgaaattg ctgccgttgt	180
cttctttttc acaaggctag ttcgaaaaca tgataagttg aaaaaagagg cagttgagag	240
gtttgctgag aaattgacct taatacttca agaaaaatat aaaaatcact ggtatccaga	300
aaaaccatcg aaaggacagg cctacagatg tattcgtgtc aataaatttc agagagttga	360
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accatgttgg ccagactgct ctcaaaactc tgacctcgtg atccgccgcg cttggcctcc	540
caaagcgtg gattacaggc gtgagccact gcgccgggc tctcctttt tgattatgta	600
tggagagaaa aacaatgcat tcattgttgc cagctttgaa aataaagatg agaacaagga	660
tgagatctcc aggaaagtta ccagggccct tgataaggtt acctctgatt atcattcagg	720
atcctcttct tcagatgaag aaacaagtaa ggaaatggaa gtgaaaccca gttcgggtgac	780
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aaaaaaaaa a 1511
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<210> SEQ ID NO 32
<211> LENGTH: 1250
<212> TYPE: DNA
<213> ORGANISM: homo sapiens
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<400> SEQUENCE: 32
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acgaaaggcc ttcatgata ttgccaata cttctctaag aaagagtggg aaaagatgaa 180
atcctcggag aaaatcgtct atgtgtatat gaagctaaac tatgaggtca tgactaaact 240
aggtttcaag gtcaccctcc cacctttcat gcgtagtaaa cgggctgcag acttccacgg 300
gaatgatttt ggtaacgatc gaaaccacag gaatcagggt gaacgtctc agatgacttt 360
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tggtttgaag gaagtgccag aggcattctg ccacaaaaat gatgggaaac agctgtgccc 480
cccgggaaat ccaagtacct tggagaagat caacaagaca tctggacca aaagggggaa 540
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aagcagaacg tggtgacctt tcacgaacat gggcatggct gcggaccct cgtcatcagg 720
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tgtgccaaga gttecatgtt ggcgtttccg ctgtatttcc ttgagtggtg ccattctgtt 840
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<210> SEQ ID NO 33
<211> LENGTH: 6792
<212> TYPE: DNA
<213> ORGANISM: homo sapiens
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<400> SEQUENCE: 33
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cctgtccag agccgcgccc tgggcggggg cagggcgggc cgggggctcc tccatgtgtc 180
cagccgcgg gctgcggagc cgaccaagtg gctcctgcga tggcggcgga agaggaggct 240
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cgctgtgagc cagggacaag accaacagct atggggtctt tcagtcaca catgacagag 360
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ccaggcactc tccccactcc actacattac tgtagtggta attcttaggg ttaaaaaaag	5340
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gaagtagacc aaagtattata ccataaggat atttttcctt aaataccatg tttgaagaac	5760
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tattcttgag tttagatttg tcttttatac aatttttagc tcttttccag ttcacttggtg	6660
ctcgtctgta tattggtatt tttaaathtt tgtggtaaat aatgaaaaga gtgaaattat	6720
attttataat tactcatttg tagttttttt ttttaattta ataaacttcc tccaaaaagt	6780
gctcccttaa aa	6792

<210> SEQ ID NO 34

<211> LENGTH: 2946

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 34

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tttgtccctg ttgctctctt tgccaaaacc agtctctctg ctagtgggtg tttcggttgc	120
gacaccgtcc aggttcccag gcaggaaccg ctgggcctgg ctgcttagct acttttcaat	180

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gaggaggtgg	tggaaggtgt	cgctgtctct	ggctgagtaa	gggtggctgg	ctgagccggc	240
agcccccgcc	ctaggcctgg	ctcttcccg	cctctgtact	ttgcctcgc	tgctgacag	300
gttctgtgt	gggtctgtgt	gaatggaagt	cgctggtagt	cctttccct	ttctccagtc	360
ggccacctt	gggacacctt	gactccaagc	ccagcagtaa	gtccaacatg	attcggggccc	420
gcaactcagc	cacctctgct	gatgagcagc	cccacattgg	aaactaccgg	ctcctcaaga	480
ccattggcaa	gggtaatttt	gccaaagtga	agttggcccg	acacatcctg	actgggaaaag	540
aggtagctgt	gaagatcatt	gacaagactc	aactgaactc	ctccagcctc	cagaaactat	600
tcccggaagt	aagaataatg	aagggtttga	atcatcccaa	catagttaaa	ttatttgaag	660
tgattgagac	tgagaaaacg	ctctaccttg	tcatggagta	cgctagtggc	ggagaggat	720
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cagaactctt	ccagggcaaa	aaatatgatg	gacccgaggt	ggatgtgtgg	agcctaggag	1020
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atgagaagta catgctgctg tgcctgcacg gcacgccggg ccacgaggac ttctgtcagt	2520
gggagatgga ggtgtgcaaa ctgccgcggc tctctctcaa cgggggtcga ttttagcgga	2580
tatcgggcac ctccatggcc ttcaaaaaca ttgcctccaa aatagccaac gagctgaagc	2640
tttaacaggc tgccaggagc gggggcggcg ggggcgggcc agctggacgg gctgccggcc	2700
gtgcgccgcc ccacctgggc gagactgcag cgatggattg gtgtgtctcc ctgctggcac	2760
ttctcccctc cctggccctt ctcatgtttc tcccacattc acccctgccc agagattccc	2820
ccttctcttc tcccctactg gaggcaaagg aaggggaggg tggatggggg ggcagggttc	2880
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aaaaga	2946

<210> SEQ ID NO 35

<211> LENGTH: 1792

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 35

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tggacctggc cacagtthct gctctcagga agatgggggt gaagttgaca cccacaaca	180
aggagacggt gcagcacagt gatgtgctct tcttggtgt gaagccacac atcatccct	240
tcatcctgga tgaataggc gccgacattg aggacagaca cattgtggtg tctgcgcgg	300
cggcgctcac catcagctcc attgagaaga agctgtcagc gtttcggcca gccccaggg	360
tcatccgtg catgaccaac actccagtcg tggcgcgga gggggccacc gtgtatgcca	420
caggcacgca cggccagggt gaggacggga ggctcatgga gcagctgctg agcacggtgg	480
gcttctgcac ggaggtgga gaggacctga ttgatgccgt cacggggctc agtggcagcg	540
gccccgccta cgcattcaca gccctggatg ccctggctga tgggggtgtg aagatgggac	600
ttccaaggcg cctggcagtc cgcctcgggg cccaggccct cctgggggct gccaaatgc	660
tgctgcactc agaacagcac ccaggccagc tcaaggacaa cgtcagctct cctggtgggg	720
ccaccatcca tgcttgcctg gtgctggaga gtgggggctt ccgctccctg ctcatcaacg	780
ctgtggaggc ctctctgcat cgcacacggg agctgcagtc catggctgac caggagcagg	840
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gccagccagg gacatagcca gggagggggc acatcacttc cactggaaa tctctgtgt	1140
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tctgtcccca aacctgtgca ggaccacctt cctctagagc tcgggagccc ggagggtctt	1260
caccactcc tactccagta tcagctggca cgggctcctt cctgagagca aaggteaagg	1320
acccctctg tgaaggctca gcagaggtgg gatccacgc cccctcccg cccctccctg	1380
ccctccattc agggagaaac ctctcttcc cgtgtgagaa gggccaggg gtccaggcat	1440
cccaagtcca gcgtgaaggg ccacagcccc tcttggtctc caagcacgca gatcccatgg	1500

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acatttgggg aaagggtccc ttgggctgct ggtgaacttc tgtggccacc acctcctgct	1560
cctgacctcc ctggggaggt gctatcagtt ctgtcctggc cctttcagtt ttataagttg	1620
gtttccagcc cccagtgctc tgacttctgt ctgccacatg aggaggaggg cctgcctgt	1680
gtgggagggg ggttactgtg ggtggaatag tggaggcctt caactgatta gacaaggccc	1740
gcccacatct tggagggcct ctgccttact gattaaaatg tcaatgtaat ct	1792

<210> SEQ ID NO 36
 <211> LENGTH: 639
 <212> TYPE: DNA
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 36

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ctgcgcaaga agggccctac ggccgcccag gccaaatcca agcaggctat cttagcggca	120
cagagacgag gagaagatgt ggagacttcc aagaaatggg ctgctggcca gaacaacaa	180
cattctatta ccaagaacac ggccaagctg gaccgggaga cagaggagct gcaccatgac	240
aggggtgacc tggaggtggg caaggtgatc cagcaaggtc ggcagagcaa ggggcttacg	300
cagaaggacc tggccacgaa aatcaatgag aagccacagg tgatcgcgga ctatgagagc	360
ggacgggcca taccataaa ccaggtgctt ggcaaatcg agcgggccc tggcctcaag	420
ctccggggaa aggacattgg aaagcccatc gagaaggggc ctaggcgcaa atgaacacaa	480
agcctcgaaa tcagtgcgct ccagctgatc tcgttcgccc ggttcccctt ggccgcccag	540
tccgttctcc tcacggggcg aacggaacaa ggggtccagc ttgcggggga cctccccag	600
ccattcctg ctgtcaaaaca aacaaaacct tgcaaagcg	639

<210> SEQ ID NO 37
 <211> LENGTH: 1793
 <212> TYPE: DNA
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 37

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gtgcaaggcc ggttcgcggg gcgacgatgc cccccgggccc gtcttcccct ccatcgtggg	180
gcgccccagg caccagggcg tgatgggtggg catgggtcag aaggattcct atgtgggcga	240
cgaggcccag agcaagagag gcacacctcacc cctgaagtac cccatcgagc acggcatcgt	300
caccaactgg gacgacatgg agaaaatctg gcaccacacc ttctacaatg agctgcgtgt	360
ggctcccag gacgaccccg tgctgctgac cgaggccccc ctgaacccca aggccaaaccg	420
cgagaagatg acccagatca tgtttgagac cttaacacc ccagccatgt acgttgctat	480
ccaggctgtg ctatccctgt acgcctctgg ccgtaccact ggcacgtga tggactccgg	540
tgacgggggc acccactctg tgcccactca cgagggggtat gccctcccc atgccatcct	600
gcgtctggac ctggctggcc gggacctgac tgactacctc atgaagatcc tcaccgagcg	660
cggctacagc ttcaccacca cggccgagcg ggaaatcgtg cgtgacatta aggagaagct	720
gtgctacgct gccctggact tcgagcaaga gatggccacg gctgcttcca gtcctccct	780
ggagaagagc tacgagctgc ctgacggcca ggtcatcacc attggcaatg agcggttccg	840

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ctgccctgag gcaactcttc agccttcctt cctgggcatg gagtctgtg gcatccacga	900
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cacagtgtg tctggcgga ccaccatgta cctggcatt gccgacagga tgcagaagga	1020
gatcactgcc ctggcaccca gcacaatgaa gatcaagatc attgctctc ctgagcgcaa	1080
gtactccgtg tggatcggtg gctccatcct ggctcgctg tccaccttc agcagatgtg	1140
gatcagcaag caggagtatg acgagtcggg cccctccatc gtccaccgca aatgcttcta	1200
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ccacccact tctctctaag gagaatggcc cagtctctc ccaagtcac acaggggagg	1560
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gtcccccaac ttgagatgta tgaaggcttt tggctcctt gggagtgggt ggaggcagcc	1740
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<210> SEQ ID NO 38

<211> LENGTH: 1116

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 38

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ctgaacagca gttttgagga tgaccccttc ttctctgagt ccattcttgc acaccgagaa	180
aatatgcgac agatgataag aagttttctt gaacccttg gaagagactt gctcagtatc	240
tctgatggta gagggagagc tcataatcgt agaggacata atgatggtga agattcttgc	300
actcatacag atgtcagctc ttccagacc atggacaaa tgggtgcaaa tatgagaaac	360
tatatgcaga aattagaaag aaacttcggt caactttcag tggatccaaa tggacattca	420
ttttgttctt cctcagttat gacttattcc aaaataggag atgaaccgcc aaaggttttt	480
caggcctcaa ctcaaaactc tcgagctoca ggaggaataa aggaaccag gaaagcaatg	540
agagattctg acagtggact agaaaaatg gctattggtc atcatatcca tgaccgagct	600
catgtcatta aaaagtcaaa gaacaagaag actggagatg aagaggtaaa ccaggagtgc	660
atcaatatga atgaaagcga tgctcatgct tttgatgagg agtggcaaaag tgaggttttg	720
aagtacaaac caggacgaca caatctagga aacactagaa tgagaagtgt tggccatgag	780
aatcctggct cccgagaact taaaagaagg gagaaacctc aacaaagtcc agccattgaa	840
catggaagga gatcaaatgt tttgggggac aaactccaca tcaaaggctc atctgtgaaa	900
agcaacaaaa aataaatagc catgcatttg atttgtttag ttttgattgt ttaacagtt	960
agtaatggtg ctgggttaata agcataagac caatctcttg ctgttaaatc agttctgtcc	1020
ttggcaactt tcttctgata tctgaatggt catgaaggtc ctgcttttat attgtccctc	1080

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<210> SEQ ID NO 39

<211> LENGTH: 3074

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 39

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 agccccgctt cagccccgat tccgactccc accccggcac cagccccctgc cccagctgca 180
 gccccagccg gcagcacagg gactgggggg cccggggtag gaagtggggg gcccgggagc 240
 gggggggatc cggtctggcc tggcctgagc cagcagcagc gcgccagtca gaggaaggcg 300
 caagtccggg ggctgccccg cgccaagaag cttgagaagc taggggtctt ctcggcttgc 360
 aaggccaatg gaacctgtaa tgtaatggc tggaaaaacc ccaagcccc cactgcaccc 420
 cgcatagatc tgcagcagcc agctgccaac ctgagtgagc tgtgccgcag ttgtgagcac 480
 cccttggtcg accacgtatc ccacttgagc aatgtgtcag aggatgagat aaaccgactg 540
 ctggggatgg tgggtgatgt ggagaatctc ttcattgtct ttcacaagga agaggacaca 600
 gacaccaagc aggtctatct ctacctcttc aagctactgc ggaaatgcat cctgcagatg 660
 acccggcctg tgggtgaggg gtccttgagg agccctccat ttgagaaacc taatattgag 720
 cagggtgtgc tgaactttgt gcagtacaag tttagtcacc tggctccccg ggagcggcag 780
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 aagaggacgc tcccagagaa cctgaccctg gaggatgcca agcggctccg tgtgatgggt 1380
 gacatcccca tggagctggc caatgaggtc atgctgacca tcaactgacc tgetgcatg 1440
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 gaggagcgcc gcggcatcat cgagttccat gtcacggcca actcactgac gcccaggcc 1560
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tgtgagctga atccccgcgt cccctacacg gagctgtccc acatcatcaa gaagcagaaa	2040
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ctcagctgct tcaagggagg cgtgaggcag atccctgtgg agagcgttcc tggcattcga	2160
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ctctacacaa cctcaaaaa cctgctggcc caaatcaagt ctacccccag tgcttgcccc	2280
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<211> LENGTH: 2381

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 40

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<212> TYPE: DNA

<213> ORGANISM: homo sapiens

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gtcctttatt	gctgaatgtg	atcggagaac	tgagctcgcc	aagaagcggc	tggcagaaac	420
acaggaggaa	atcagtgcgg	aagtttctgc	aaaggcagaa	aaagtacatg	agttaaatga	480
agaaatagga	aaactccttg	ctaaagccga	acagctaggg	gctgaaggta	atgtggatga	540
atcccagaag	attcttatgg	aagtggaaaa	agttcgtgcg	aagaaaaaag	aagctgagga	600
agaatacaga	aattccatgc	ctgcatccag	ttttcagcag	caaaagctgc	gtgtctgcga	660
ggctctgttc	gctaccttg	gtctccatga	caatgaccgt	cgctggcag	accacttcgg	720
tggaagtta	cacttggggg	tcattcagat	ccgagagaag	cttgatcagt	tgaggaaaac	780
tgctcgctga	aagcaggaga	agagaaatca	ggatcgcttg	aggaggagag	aggagaggga	840
acgggaggag	cgtctgagca	ggaggctcgg	atcaagaacc	agagatcgca	ggaggtcacg	900
ctcccgggat	cgcgctcgga	ggcggtaaac	atctacctcc	cgagagcgac	ggaattgtc	960
ccggtcccg	tcctcgagata	gacatcgggc	ccaccgcagc	cgttcccga	gccacagccg	1020
gggacatcgt	cgggcttccc	gggaccgaag	tcgaaatac	aagtaactac	tctgactcct	1080
tcggtagctg	caaccaggag	tgagcccttc	tctgtgttcc	cagggtctgc	tgagggccgt	1140
gtctggtggg	gatggggctg	ggctcaccct	caggagtagg	gotggggagt	cgtgaacggg	1200
actcaggtgt	gggaagaggc	gagagggtctg	tgaggagct	cgcacggcgc	cagggtgatgg	1260
gtgcacagg	cactgtcccc	tgctgctgc	ctggggcctg	tgcaactgtt	cgtecatgct	1320
cagagtggct	gagacttgtg	tcctgaccag	gcctgctta	cctctgtttt	ggtttttgtt	1380
tttgatattt	ttttttccat	tgtgttttta	cgtagtgtca	tgttctgtgc	atatagtgtt	1440
gtattctcct	ttgcactgtt	tatgttacag	tgaaggctct	ccttattaaa	aatcttcgca	1500
aaggtcaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aa		1542

<210> SEQ ID NO 44
 <211> LENGTH: 968
 <212> TYPE: DNA

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<213> ORGANISM: homo sapiens

<400> SEQUENCE: 44

```

gggggaagtt gctggctgac tgggcttgcg aggaaaccgc ctcggagctg cagcgaaggc    60
caaggaatca ctgaagatcg gcgagggagg acaggggggtt catcatgggt ggctttttct    120
caagtatatt ttccagtctg tttggaactc gggaaatgag aattttaatt ttgggattag    180
atggagcagg aaaaaccaca atttgtaca gattacaagt gggagaagtt gttactacta    240
tacctacat tggaattaat gtagagacgg tgacgtacaa aaaccttaaa ttccaagtct    300
gggatttagg aggacagaca agtatcaggc catactggag atgttactat tcaaacacag    360
atgcagtcac ttatgtagta gacagttgtg accgagaccg aattggcatt tccaaatcag    420
agttagtgtc catgttggag gaagaagagc tgagaaaagc cattttagtg gtgtttgcaa    480
ataaacagga catggaacag gccatgactt cctcagagat ggcaaattca cttgggttac    540
ctgccttgaa ggaccgaaaa tggcagatat tcaaacgcgc agcaacccaa ggcaccggcc    600
ttgatgaggc aatggaatgg ttagttgaaa cattaaaaag cagacagtaa ttcagtccat    660
tcttctcccc tgaatgaag actacatcac ctctctccct ttggaaacag tcaagtgtac    720
ttcacactac tagatgttaa aactatatga ttattggcat atactgactg actgcaatat    780
ttgtagtaaa tagggaaaat aagtatttag ttggagggat aatttgatcg aatcacctga    840
atgttctatg taatgtaaaa tattcttttc ttgctttctt gtgttaaggt atatattcta    900
tttgtatgga attcttattc aaatacagtt gtattaaaga gtatactcct attggatgaa    960
aaaaacct                                         968

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<210> SEQ ID NO 45

<211> LENGTH: 700

<212> TYPE: DNA

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 45

```

gcggcgtgag aagccatgag cagcaaagtc tctcgcgaca ccctgtacga ggcggtgcgg    60
gaagtctctc acgggaacca gcgcaagcgc cgcaagttcc tggagacggg ggagttgcag    120
atcagcttga agaactatga tcccagaag gacaagcgct tctcgggcac cgtcaggctt    180
aagtcactc cccgccttaa gttctctgtg tgtgtcctgg gggaccagca gcactgtgac    240
gaggctaagg ccgtggatat ccccacatg gacatcgagg cgctgaaaaa actcaacaag    300
aataaaaaac tggtaagaa gctggccaag aagtatgatg cgtttttggc ctcagagtct    360
ctgatcaagc agattccacg aatcctcggc ccaggtttaa ataaggcagg aaagttccct    420
tccctgctca cacacaacga aaacatgggt gccaaagtgg atgaggtgaa gtccacaatc    480
aagttccaaa tgaagaaggt gttatgtctg gctgtagctg ttggtcacgt gaagatgaca    540
gacgatgagc ttgtgtataa cattcacctg gctgtcaact tcttgggtgc attgctcaag    600
aaaaactggc agaattgccg ggcccttatat atcaagagca ccattgggcaa gccccagcgc    660
ctatattaag gcacatttga ataaattcta ttaccagttc                                         700

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<210> SEQ ID NO 46

<211> LENGTH: 145

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<220> FEATURE:

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<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (65)..(65)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (101)..(101)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (105)..(105)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (108)..(108)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (113)..(113)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (125)..(128)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (132)..(132)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (136)..(136)
<223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 46

Arg Arg Lys Trp Ser Leu Asp Arg Leu Arg Asp Thr Val Lys Ala Leu
1          5          10          15

Thr Arg Glu Gln Glu Lys Leu Leu Gly Gln Leu Lys Glu Val Gln Ala
20          25          30

Asp Lys Glu Gln Ser Glu Ala Glu Leu Gln Val Ala Gln Gln Glu Asn
35          40          45

His His Leu Asn Leu Asp Leu Lys Glu Ala Lys Ser Trp Gln Glu Glu
50          55          60

Xaa Ser Ala Gln Ala Gln Arg Leu Lys Asp Lys Val Ala Gln Met Lys
65          70          75          80

Asp Thr Leu Cys Gln Ala Gln Gln Arg Val Ala Gln Leu Glu Pro Leu
85          90          95

Lys Glu Gln Leu Xaa Gly Ala Gln Xaa Ala Leu Xaa Ala Ser Ser Gln
100         105         110

Xaa Lys Ala Thr Leu Ser Trp Gly Gly Val Cys Gln Xaa Xaa Xaa Xaa
115         120         125

Pro Gly Thr Xaa Pro Tyr Ala Xaa Leu His Arg Ser Arg Pro Gly Ser
130         135         140

Gly
145

<210> SEQ ID NO 47
<211> LENGTH: 208
<212> TYPE: PRT
<213> ORGANISM: homosapiens
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 47
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-continued

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

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<210> SEQ ID NO 48
<211> LENGTH: 256
<212> TYPE: PRT
<213> ORGANISM: homosapiens
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (186)..(186)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (219)..(219)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (222)..(222)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (230)..(230)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (243)..(243)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (247)..(247)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (254)..(254)
<223> OTHER INFORMATION: Xaa = any amino acid

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<400> SEQUENCE: 48

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Met Leu Arg Ser Pro Phe Asp Arg Asn Val Pro Val Asn Leu Glu Leu

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-continued

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

<210> SEQ ID NO 49
 <211> LENGTH: 205
 <212> TYPE: PRT
 <213> ORGANISM: homosapiens
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (144)..(144)
 <223> OTHER INFORMATION: Xaa = any amino acid
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (157)..(157)
 <223> OTHER INFORMATION: Xaa = any amino acid
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (159)..(159)
 <223> OTHER INFORMATION: Xaa = any amino acid
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (188)..(188)
 <223> OTHER INFORMATION: Xaa = any amino acid
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (194)..(194)
 <223> OTHER INFORMATION: Xaa = any amino acid
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (197)..(197)
 <223> OTHER INFORMATION: Xaa = any amino acid

-continued

<400> SEQUENCE: 49

```

Met Asn Asp Ile Ser Gln Lys Ala Glu Ile Leu Leu Ser Ser Ser Lys
1           5           10           15

Pro Val Pro Lys Thr Tyr Val Pro Lys Leu Gly Lys Gly Asp Val Lys
          20           25           30

Asp Lys Phe Glu Ala Met Gln Arg Ala Arg Glu Glu Arg Asn Gln Arg
          35           40           45

Arg Ser Arg Asp Glu Lys Gln Arg Arg Lys Glu Gln Tyr Ile Arg Glu
          50           55           60

Arg Glu Trp Asn Arg Arg Lys Gln Glu Ile Lys Glu Met Leu Ala Ser
65           70           75           80

Asp Asp Glu Glu Asp Val Ser Ser Lys Val Glu Lys Ala Tyr Val Pro
          85           90           95

Lys Leu Thr Gly Thr Val Lys Gly Arg Phe Ala Glu Met Glu Lys Gln
          100          105          110

Arg Gln Glu Glu Gln Arg Lys Arg Thr Glu Glu Glu Arg Lys Arg Arg
          115          120          125

Ile Glu Gln Asp Met Leu Glu Lys Arg Lys Ile Gln Arg Glu Leu Xaa
          130          135          140

Lys Arg Ala Glu Gln Glu Gly Asp Asp Ser Leu Leu Xaa Thr Xaa Val
145          150          155          160

Pro Val Asn His Ile Asn Ile Trp Lys Met Lys Arg Ile Leu Arg Ser
          165          170          175

Arg Lys Arg Arg Glu Glu Lys Lys Asp Pro Val Xaa Glu Ile Lys Ile
          180          185          190

Arg Xaa Glu Thr Xaa Pro Leu Ser Gly Ala Arg Ala Ser
          195          200          205

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<210> SEQ ID NO 50

<211> LENGTH: 172

<212> TYPE: PRT

<213> ORGANISM: homosapiens

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (136)..(136)

<223> OTHER INFORMATION: Xaa = any amino acid

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (142)..(142)

<223> OTHER INFORMATION: Xaa = any amino acid

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (146)..(146)

<223> OTHER INFORMATION: Xaa = any amino acid

<220> FEATURE:

<221> NAME/KEY: MISC_FEATURE

<222> LOCATION: (151)..(151)

<223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 50

```

Met Glu Ser Tyr Arg Glu Asn Leu Glu Arg Val Phe Val Arg Met Asp
1           5           10           15

Gln Val Leu Pro Asp Ser Cys Leu Leu Val Trp Asn Met Ala Met Pro
          20           25           30

Leu Gly Glu Arg Ile Thr Gly Gly Phe Leu Leu Pro Glu Leu Gln Pro
          35           40           45

Leu Ala Gly Ser Leu Arg Arg Asp Val Val Glu Gly Asn Phe Tyr Ser

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-continued

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

<210> SEQ ID NO 51
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: homosapiens
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (143)..(143)
 <223> OTHER INFORMATION: Xaa = any amino acid
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (153)..(153)
 <223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 51

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

<210> SEQ ID NO 52
 <211> LENGTH: 122
 <212> TYPE: PRT
 <213> ORGANISM: homosapiens
 <400> SEQUENCE: 52

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Met Ile Gly Gly Thr Glu Met Thr Lys Glu Ile Pro Arg Lys Arg Lys
1           5           10           15
Asn Thr Val Glu Ala Glu Ala Glu Lys Gly Asn Thr Glu Val Gly Val
20           25           30
Glu Val Glu Met Gln Gly Asn Glu Val Glu Val Glu Ala Lys Arg Asn
35           40           45
Gln Val Asn Ile Lys Met Lys Val Lys Lys Asn Gln Ile Asn Glu Val
50           55           60
Glu Val Ala Val Lys Glu Glu Leu Thr Val Leu Lys Asn Gln Lys Asn
65           70           75           80
Gly Asn Ile Val Pro Ala Lys Lys Asn Leu Glu Ser Val Val Glu Ala
85           90           95
Lys Asn Val Pro Thr Asn Glu Ile Thr Val Ile Val Arg Thr Ser Gln
100          105          110
Thr Asn Met Ile Val Glu Gly Ala Lys Val
115          120

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<210> SEQ ID NO 53
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: homosapiens

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<400> SEQUENCE: 53

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

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<210> SEQ ID NO 54
<211> LENGTH: 175
<212> TYPE: PRT
<213> ORGANISM: homosapiens
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (132)..(132)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (146)..(146)
<223> OTHER INFORMATION: Xaa = any amino acid

```

```

<400> SEQUENCE: 54

```

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

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-continued

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

<210> SEQ ID NO 55

<211> LENGTH: 255

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 55

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

-continued

Trp Arg Ser Glu Pro Ala Asp Asp Leu Gln Arg Gln Asp Asn Arg Val
 210 215 220

Val Thr Gly Leu Lys Lys Gln Arg Arg Lys Arg Lys Arg Lys Ser Glu
 225 230 235 240

Met Leu Gln Lys Ala Ala Arg Gly Arg Glu Glu His Gly Asp Glu
 245 250 255

<210> SEQ ID NO 56
 <211> LENGTH: 239
 <212> TYPE: PRT
 <213> ORGANISM: homosapiens
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (42)..(42)
 <223> OTHER INFORMATION: Xaa = any amino acid
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (225)..(229)
 <223> OTHER INFORMATION: Xaa = any amino acid
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (231)..(234)
 <223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 56

Met Leu Gln Asn Glu Gln Glu Ile Ser Gln Leu Lys Lys Glu Ile Glu
 1 5 10 15

Arg Thr Gln Gln Arg Met Lys Glu Met Glu Ser Val Met Lys Glu Gln
 20 25 30

Glu Gln Tyr Ile Ala Thr Gln Tyr Lys Xaa Ala Ile Asp Leu Gly Gln
 35 40 45

Glu Leu Arg Leu Thr Arg Glu Gln Val Gln Asn Ser His Thr Glu Leu
 50 55 60

Ala Glu Ala Arg His Gln Gln Val Gln Ala Gln Arg Glu Ile Glu Arg
 65 70 75 80

Leu Ser Ser Glu Leu Glu Asp Met Lys Gln Leu Ser Lys Glu Lys Asp
 85 90 95

Ala His Gly Asn His Leu Ala Glu Glu Leu Gly Ala Ser Lys Val Arg
 100 105 110

Glu Ala His Leu Glu Ala Arg Met Gln Ala Glu Ile Lys Lys Leu Ser
 115 120 125

Ala Glu Val Glu Ser Leu Lys Glu Ala Tyr His Met Glu Met Ile Ser
 130 135 140

His Gln Glu Asn His Ala Lys Trp Lys Ile Ser Ala Asp Ser Gln Lys
 145 150 155 160

Ser Ser Val Gln Gln Leu Asn Glu Gln Leu Glu Lys Ala Lys Leu Glu
 165 170 175

Leu Glu Glu Ala Gln Asp Thr Val Ser Asn Leu His Gln Gln Val Gln
 180 185 190

Asp Arg Asn Glu Val Ile Glu Ala Ala Asn Glu Ala Leu Leu Thr Lys
 195 200 205

Val Ser Lys His Ile Lys Val Leu Lys His Ile Tyr Glu Asn Lys Thr
 210 215 220

Xaa Xaa Xaa Xaa Xaa Pro Xaa Xaa Xaa Xaa Ser Arg Glu Tyr Phe
 225 230 235

-continued

<210> SEQ ID NO 57
<211> LENGTH: 249
<212> TYPE: PRT
<213> ORGANISM: homosapiens
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (226) .. (226)
<223> OTHER INFORMATION: Xaa = any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (239) .. (239)
<223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 57

Met Ala Asp Ser Ser Gly Arg Gly Ala Gly Lys Pro Ala Thr Gly Pro
1 5 10 15

Thr Asn Ser Ser Ser Ala Lys Lys Lys Asp Lys Arg Val Gln Gly Gly
20 25 30

Arg Val Ile Glu Ser Arg Tyr Leu Gln Tyr Glu Lys Lys Thr Thr Gln
35 40 45

Lys Ala Pro Ala Gly Asp Gly Ser Gln Thr Arg Gly Lys Met Ser Glu
50 55 60

Gly Gly Arg Lys Ser Ser Leu Leu Gln Lys Ser Lys Ala Asp Ser Ser
65 70 75 80

Gly Val Gly Lys Gly Asp Leu Gln Ser Thr Leu Leu Glu Gly His Gly
85 90 95

Thr Ala Pro Pro Asp Leu Asp Leu Ser Ala Ile Asn Asp Lys Ser Ile
100 105 110

Val Lys Lys Thr Pro Gln Leu Ala Lys Thr Ile Ser Lys Lys Pro Glu
115 120 125

Ser Thr Ser Phe Ser Ala Pro Arg Lys Lys Ser Pro Asp Leu Ser Glu
130 135 140

Ala Met Glu Met Met Glu Ser Gln Thr Leu Leu Leu Thr Leu Leu Ser
145 150 155 160

Val Lys Met Glu Asn Asn Leu Ala Glu Phe Glu Arg Arg Ala Glu Lys
165 170 175

Asn Leu Leu Ile Met Cys Lys Glu Lys Glu Lys Leu Gln Lys Lys Ala
180 185 190

His Glu Leu Lys Arg Arg Leu Leu Leu Ser Gln Arg Lys Arg Glu Leu
195 200 205

Ala Asp Val Leu Asp Ala Gln Ile Glu Met Leu Ser Pro Leu Arg Gly
210 215 220

Ser Xaa His Thr Leu Gln Gly Ala Ile Gln Asp Ile Arg His Xaa Pro
225 230 235 240

Trp Thr Leu Pro Gly Thr Ser Cys Pro
245

<210> SEQ ID NO 58
<211> LENGTH: 116
<212> TYPE: PRT
<213> ORGANISM: homosapiens

<400> SEQUENCE: 58

Met Asp Tyr Arg Arg Leu Leu Met Ser Arg Val Val Pro Gly Gln Phe
1 5 10 15

Asp Asp Ala Asp Ser Ser Asp Ser Glu Asn Arg Asp Leu Lys Thr Val
20 25 30

-continued

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

<210> SEQ ID NO 59
<211> LENGTH: 225
<212> TYPE: PRT
<213> ORGANISM: homo sapiens

<400> SEQUENCE: 59

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

<210> SEQ ID NO 60
<211> LENGTH: 384
<212> TYPE: PRT

-continued

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 60

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

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<210> SEQ ID NO 61
<211> LENGTH: 510
<212> TYPE: PRT
<213> ORGANISM: homo sapiens

<400> SEQUENCE: 61

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

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Pro Gly Lys Val Asn Pro Thr Gln Cys Glu Ala Met Thr Met Val Ala
 370                               375                               380

Ala Gln Val Met Gly Asn His Val Ala Val Thr Val Gly Gly Ser Asn
385                               390                               395                               400

Gly His Phe Glu Leu Asn Val Phe Lys Pro Met Met Ile Lys Asn Val
                               405                               410                               415

Leu His Ser Ala Arg Leu Leu Gly Asp Ala Ser Val Ser Phe Thr Glu
                               420                               425                               430

Asn Cys Val Val Gly Ile Gln Ala Asn Thr Glu Arg Ile Asn Lys Leu
                               435                               440                               445

Met Asn Glu Ser Leu Met Leu Val Thr Ala Leu Asn Pro His Ile Gly
450                               455                               460

Tyr Asp Lys Ala Ala Lys Ile Ala Lys Thr Ala His Lys Asn Gly Ser
465                               470                               475                               480

Thr Leu Lys Glu Thr Ala Ile Glu Leu Gly Tyr Leu Thr Ala Glu Gln
                               485                               490                               495

Phe Asp Glu Trp Val Lys Pro Lys Asp Met Leu Gly Pro Lys
500                               505                               510

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<210> SEQ ID NO 62

<211> LENGTH: 937

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 62

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Met Arg Lys Ser Phe Ser Gln Pro Gly Leu Arg Ser Leu Ala Phe Arg
1      5      10      15

Lys Glu Leu Gln Asp Gly Gly Leu Arg Ser Ser Gly Phe Phe Ser Ser
20     25     30

Phe Glu Glu Ser Asp Ile Glu Asn His Leu Ile Ser Gly His Asn Ile
35     40     45

Val Gln Pro Thr Asp Ile Glu Glu Asn Arg Thr Met Leu Phe Thr Ile
50     55     60

Gly Gln Ser Glu Val Tyr Leu Ile Ser Pro Asp Thr Lys Lys Ile Ala
65     70     75     80

Leu Glu Lys Asn Phe Lys Glu Ile Ser Phe Cys Ser Gln Gly Ile Arg
85     90     95

His Val Asp His Phe Gly Phe Ile Cys Arg Glu Ser Ser Gly Gly Gly
100    105    110

Gly Phe His Phe Val Cys Tyr Val Phe Gln Cys Thr Asn Glu Ala Leu
115    120    125

Val Asp Glu Ile Met Met Thr Leu Lys Gln Ala Phe Thr Val Ala Ala
130    135    140

Val Gln Gln Thr Ala Lys Ala Pro Ala Gln Leu Cys Glu Gly Cys Pro
145    150    155    160

Leu Gln Ser Leu His Lys Leu Cys Glu Arg Ile Glu Gly Met Asn Ser
165    170    175

Ser Lys Thr Lys Leu Glu Leu Gln Lys His Leu Thr Thr Leu Thr Asn
180    185    190

Gln Glu Gln Ala Thr Ile Phe Glu Glu Val Gln Lys Leu Arg Pro Arg
195    200    205

Asn Glu Gln Arg Glu Asn Glu Leu Ile Ile Ser Phe Leu Arg Cys Leu

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210	215	220
Tyr Glu Glu Lys Gln Lys Glu His Ile His Ile Gly Glu Met Lys Gln 225 230 235 240		
Thr Ser Gln Met Ala Ala Glu Asn Ile Gly Ser Glu Leu Pro Pro Ser 245 250 255		
Ala Thr Arg Phe Arg Leu Asp Met Leu Lys Asn Lys Ala Lys Arg Ser 260 265 270		
Leu Thr Glu Ser Leu Glu Ser Ile Leu Ser Arg Gly Asn Lys Ala Arg 275 280 285		
Gly Leu Gln Glu His Ser Ile Ser Val Asp Leu Asp Ser Ser Leu Ser 290 295 300		
Ser Thr Leu Ser Asn Thr Ser Lys Glu Pro Ser Val Cys Glu Lys Glu 305 310 315 320		
Ala Leu Pro Ile Ser Glu Ser Ser Phe Lys Leu Leu Gly Ser Ser Glu 325 330 335		
Asp Leu Ser Ser Asp Ser Glu Ser His Leu Pro Glu Glu Pro Ala Pro 340 345 350		
Leu Ser Pro Gln Gln Ala Phe Arg Arg Arg Ala Asn Thr Leu Ser His 355 360 365		
Phe Pro Ile Glu Cys Gln Glu Pro Pro Gln Pro Ala Arg Gly Ser Pro 370 375 380		
Gly Val Ser Gln Arg Lys Leu Met Arg Tyr His Ser Val Ser Thr Glu 385 390 395 400		
Thr Pro His Glu Arg Lys Asp Phe Glu Ser Lys Ala Asn His Leu Gly 405 410 415		
Asp Ser Gly Gly Thr Pro Val Lys Thr Arg Arg His Ser Trp Arg Gln 420 425 430		
Gln Ile Phe Leu Arg Val Ala Thr Pro Gln Lys Ala Cys Asp Ser Ser 435 440 445		
Ser Arg Tyr Glu Asp Tyr Ser Glu Leu Gly Glu Leu Pro Pro Arg Ser 450 455 460		
Pro Leu Glu Pro Val Cys Glu Asp Gly Pro Phe Gly Pro Pro Pro Glu 465 470 475 480		
Glu Lys Lys Arg Thr Ser Arg Glu Leu Arg Glu Leu Trp Gln Lys Ala 485 490 495		
Ile Leu Gln Gln Ile Leu Leu Leu Arg Met Glu Lys Glu Asn Gln Lys 500 505 510		
Leu Gln Ala Ser Glu Asn Asp Leu Leu Asn Lys Arg Leu Lys Leu Asp 515 520 525		
Tyr Glu Glu Ile Thr Pro Cys Leu Lys Glu Val Thr Val Trp Glu 530 535 540		
Lys Met Leu Ser Thr Pro Gly Arg Ser Lys Ile Lys Phe Asp Met Glu 545 550 555 560		
Lys Met His Ser Ala Val Gly Gln Gly Val Pro Arg His His Arg Gly 565 570 575		
Glu Ile Trp Lys Phe Leu Ala Glu Gln Phe His Leu Lys His Gln Phe 580 585 590		
Pro Ser Lys Gln Gln Pro Lys Asp Val Pro Tyr Lys Glu Leu Leu Lys 595 600 605		
Gln Leu Thr Ser Gln Gln His Ala Ile Leu Ile Asp Leu Gly Arg Thr 610 615 620		

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Phe Pro Thr His Pro Tyr Phe Ser Ala Gln Leu Gly Ala Gly Gln Leu
625                      630                      635                      640

Ser Leu Tyr Asn Ile Leu Lys Ala Tyr Ser Leu Leu Asp Gln Glu Val
                      645                      650                      655

Gly Tyr Cys Gln Gly Leu Ser Phe Val Ala Gly Ile Leu Leu Leu His
                      660                      665                      670

Met Ser Glu Glu Glu Ala Phe Lys Met Leu Lys Phe Leu Met Phe Asp
                      675                      680                      685

Met Gly Leu Arg Lys Gln Tyr Arg Pro Asp Met Ile Ile Leu Gln Ile
690                      695                      700

Gln Met Tyr Gln Leu Ser Arg Leu Leu His Asp Tyr His Arg Asp Leu
705                      710                      715                      720

Tyr Asn His Leu Glu Glu His Glu Ile Gly Pro Ser Leu Tyr Ala Ala
725                      730                      735

Pro Trp Phe Leu Thr Met Phe Ala Ser Gln Phe Pro Leu Gly Phe Val
740                      745                      750

Ala Arg Val Phe Asp Met Ile Phe Leu Gln Gly Thr Glu Val Ile Phe
755                      760                      765

Lys Val Ala Leu Ser Leu Leu Gly Ser His Lys Pro Leu Ile Leu Gln
770                      775                      780

His Glu Asn Leu Glu Thr Ile Val Asp Phe Ile Lys Ser Thr Leu Pro
785                      790                      795                      800

Asn Leu Gly Leu Val Gln Met Glu Lys Thr Ile Asn Gln Val Phe Glu
805                      810                      815

Met Asp Ile Ala Lys Gln Leu Gln Ala Tyr Glu Val Glu Tyr His Val
820                      825                      830

Leu Gln Glu Glu Leu Ile Asp Ser Ser Pro Leu Ser Asp Asn Gln Arg
835                      840                      845

Met Asp Lys Leu Glu Lys Thr Asn Ser Ser Leu Arg Lys Gln Asn Leu
850                      855                      860

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

Glu Ala Thr Ile Glu Lys Leu Leu Ser Ser Glu Ser Lys Leu Lys Gln
885                      890                      895

Ala Met Leu Thr Leu Glu Leu Glu Arg Ser Ala Leu Leu Gln Thr Val
900                      905                      910

Glu Glu Leu Arg Arg Arg Ser Ala Glu Pro Ser Asp Arg Glu Pro Glu
915                      920                      925

Cys Thr Gln Pro Glu Pro Thr Gly Asp
930                      935

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<210> SEQ ID NO 63

<211> LENGTH: 618

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 63

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Met His Lys Thr Ala Ser Gln Arg Leu Phe Pro Gly Pro Ser Tyr Gln
1          5          10          15

Asn Ile Lys Ser Ile Met Glu Asp Ser Thr Ile Leu Ser Asp Trp Thr
20         25         30

Asn Ser Asn Lys Gln Lys Met Lys Tyr Asp Phe Ser Cys Glu Leu Tyr

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

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Gln Ala Glu Glu Met Ala Ser Asp Asp Leu Ser Leu Ile Arg Lys Asn
 450 455 460
 Arg Met Ala Leu Phe Gln Gln Leu Thr Cys Val Leu Pro Ile Leu Asp
 465 470 475 480
 Asn Leu Leu Lys Ala Asn Val Ile Asn Lys Gln Glu His Asp Ile Ile
 485 490 495
 Lys Gln Lys Thr Gln Ile Pro Leu Gln Ala Arg Glu Leu Ile Asp Thr
 500 505 510
 Ile Leu Val Lys Gly Asn Ala Ala Ala Asn Ile Phe Lys Asn Cys Leu
 515 520 525
 Lys Glu Ile Asp Ser Thr Leu Tyr Lys Asn Leu Phe Val Asp Lys Asn
 530 535 540
 Met Lys Tyr Ile Pro Thr Glu Asp Val Ser Gly Leu Ser Leu Glu Glu
 545 550 555 560
 Gln Leu Arg Arg Leu Gln Glu Glu Arg Thr Cys Lys Val Cys Met Asp
 565 570 575
 Lys Glu Val Ser Val Val Phe Ile Pro Cys Gly His Leu Val Val Cys
 580 585 590
 Gln Glu Cys Ala Pro Ser Leu Arg Lys Cys Pro Ile Cys Arg Gly Ile
 595 600 605
 Ile Lys Gly Thr Val Arg Thr Phe Leu Ser
 610 615

<210> SEQ ID NO 64
 <211> LENGTH: 539
 <212> TYPE: PRT
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 64

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

-continued

180				185				190							
Leu	Val	Thr	Gly	Ile	Lys	Val	Val	Asp	Leu	Leu	Ala	Pro	Tyr	Ala	Lys
	195						200					205			
Gly	Gly	Lys	Ile	Gly	Leu	Phe	Gly	Gly	Ala	Gly	Val	Gly	Lys	Thr	Val
	210					215					220				
Leu	Ile	Met	Glu	Leu	Ile	Asn	Asn	Val	Ala	Lys	Ala	His	Gly	Gly	Tyr
	225				230					235					240
Ser	Val	Phe	Ala	Gly	Val	Gly	Glu	Arg	Thr	Arg	Glu	Gly	Asn	Asp	Leu
			245						250					255	
Tyr	His	Glu	Met	Ile	Glu	Ser	Gly	Val	Ile	Asn	Leu	Lys	Asp	Ala	Thr
		260						265					270		
Ser	Lys	Val	Ala	Leu	Val	Tyr	Gly	Gln	Met	Asn	Gln	Pro	Pro	Gly	Ala
		275					280					285			
Arg	Ala	Arg	Val	Ala	Leu	Thr	Gly	Leu	Thr	Val	Ala	Glu	Tyr	Phe	Arg
		290				295					300				
Asp	Gln	Glu	Gly	Gln	Asp	Val	Leu	Leu	Phe	Ile	Asp	Asn	Ile	Phe	Arg
	305				310					315					320
Phe	Thr	Gln	Ala	Gly	Ser	Glu	Val	Ser	Ala	Leu	Leu	Gly	Arg	Ile	Pro
			325						330					335	
Ser	Ala	Val	Gly	Tyr	Gln	Pro	Thr	Leu	Ala	Thr	Asp	Met	Gly	Thr	Met
		340						345					350		
Gln	Glu	Arg	Ile	Thr	Thr	Thr	Lys	Lys	Gly	Ser	Ile	Thr	Ser	Val	Gln
		355					360					365			
Ala	Ile	Tyr	Val	Pro	Ala	Asp	Asp	Leu	Thr	Asp	Pro	Ala	Pro	Ala	Thr
	370					375					380				
Thr	Phe	Ala	His	Leu	Asp	Ala	Thr	Thr	Val	Leu	Ser	Arg	Ala	Ile	Ala
	385				390					395					400
Glu	Leu	Gly	Ile	Tyr	Pro	Ala	Val	Asp	Pro	Leu	Asp	Ser	Thr	Ser	Arg
			405					410						415	
Ile	Met	Asp	Pro	Asn	Ile	Val	Gly	Ser	Glu	His	Tyr	Asp	Val	Ala	Arg
		420						425					430		
Gly	Val	Gln	Lys	Ile	Leu	Gln	Asp	Tyr	Lys	Ser	Leu	Gln	Asp	Ile	Ile
		435					440					445			
Ala	Ile	Leu	Gly	Met	Asp	Glu	Leu	Ser	Glu	Glu	Asp	Lys	Leu	Thr	Val
	450				455						460				
Ser	Arg	Ala	Arg	Lys	Ile	Gln	Arg	Phe	Leu	Ser	Gln	Pro	Phe	Gln	Val
	465				470					475					480
Ala	Glu	Val	Phe	Thr	Gly	His	Met	Gly	Lys	Leu	Val	Pro	Leu	Lys	Glu
			485					490						495	
Thr	Ile	Lys	Gly	Phe	Gln	Gln	Ile	Leu	Ala	Gly	Glu	Tyr	Asp	His	Leu
			500					505					510		
Pro	Glu	Gln	Ala	Phe	Tyr	Met	Val	Gly	Pro	Ile	Glu	Glu	Ala	Val	Ala
		515					520					525			
Lys	Ala	Asp	Lys	Leu	Ala	Glu	Glu	His	Ser	Ser					
	530					535									

<210> SEQ ID NO 65

<211> LENGTH: 772

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 65

-continued

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

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405					410					415					
Arg	Lys	Lys	Lys	Lys	Lys	Ile	Val	Lys	Thr	Ser	Ala	Thr	Ala	Leu	Gly
			420					425					430		
Asp	Lys	Gly	Leu	Lys	Lys	Asn	Asp	Ser	Lys	Ser	Thr	Gly	Lys	Asn	Leu
		435					440					445			
Asp	Ser	Val	Gln	Lys	Leu	Pro	Lys	Val	Asn	Lys	Thr	Lys	Ser	Glu	Lys
	450					455					460				
Pro	Ala	Gly	Ala	Asp	Leu	Ala	Lys	Leu	Arg	Lys	Val	Pro	Asp	Val	Leu
465					470					475					480
Pro	Val	Leu	Pro	Asp	Leu	Pro	Leu	Pro	Ala	Ile	Gln	Ala	Asn	Tyr	Arg
			485						490					495	
Pro	Leu	Pro	Ser	Leu	Glu	Leu	Ile	Ser	Ser	Phe	Gln	Pro	Lys	Arg	Lys
			500					505					510		
Ala	Phe	Ser	Ser	Pro	Gln	Glu	Glu	Glu	Glu	Ala	Gly	Phe	Thr	Gly	Arg
		515					520					525			
Arg	Met	Asn	Ser	Lys	Met	Gln	Val	Tyr	Ser	Gly	Ser	Lys	Cys	Ala	Tyr
	530					535					540				
Leu	Pro	Lys	Met	Met	Thr	Leu	His	Gln	Gln	Cys	Ile	Arg	Val	Leu	Lys
545					550					555					560
Asn	Asn	Ile	Asp	Ser	Ile	Phe	Glu	Val	Gly	Gly	Val	Pro	Tyr	Ser	Val
			565						570					575	
Leu	Glu	Pro	Val	Leu	Glu	Arg	Cys	Thr	Pro	Asp	Gln	Leu	Tyr	Arg	Ile
			580					585					590		
Glu	Glu	Tyr	Asn	His	Val	Leu	Ile	Glu	Glu	Thr	Asp	Gln	Leu	Trp	Lys
		595					600					605			
Val	His	Cys	His	Arg	Asp	Phe	Lys	Glu	Glu	Arg	Pro	Glu	Glu	Tyr	Glu
	610					615					620				
Ser	Trp	Arg	Glu	Met	Tyr	Leu	Arg	Leu	Gln	Asp	Ala	Arg	Glu	Gln	Arg
625				630						635					640
Leu	Arg	Val	Leu	Thr	Lys	Asn	Ile	Gln	Phe	Ala	His	Ala	Asn	Lys	Pro
			645					650						655	
Lys	Gly	Arg	Gln	Ala	Lys	Met	Ala	Phe	Val	Asn	Ser	Val	Ala	Lys	Pro
			660					665					670		
Pro	Arg	Asp	Val	Arg	Arg	Arg	Gln	Glu	Lys	Phe	Gly	Thr	Gly	Gly	Ala
		675					680					685			
Ala	Val	Pro	Glu	Lys	Ile	Lys	Ile	Lys	Pro	Ala	Pro	Tyr	Pro	Met	Gly
	690					695					700				
Ser	Ser	His	Ala	Ser	Ala	Ser	Ser	Ile	Ser	Phe	Asn	Pro	Ser	Pro	Glu
705				710						715					720
Glu	Pro	Ala	Tyr	Asp	Gly	Pro	Ser	Thr	Ser	Ser	Ala	His	Leu	Ala	Pro
			725					730					735		
Val	Val	Ser	Ser	Thr	Val	Ser	Tyr	Asp	Pro	Arg	Lys	Pro	Thr	Val	Lys
			740					745					750		
Lys	Ile	Ala	Pro	Met	Met	Ala	Lys	Thr	Ile	Lys	Ala	Phe	Lys	Asn	Arg
	755						760					765			
Phe	Ser	Arg	Arg												
	770														

<210> SEQ ID NO 66

<211> LENGTH: 886

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

-continued

<400> SEQUENCE: 66

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Met Ser Gly Phe Ser Pro Glu Leu Ile Asp Tyr Leu Glu Gly Lys Ile
1      5      10      15

Ser Phe Glu Glu Phe Glu Arg Arg Arg Glu Glu Arg Lys Thr Arg Glu
20      25      30

Lys Lys Ser Leu Gln Glu Lys Gly Lys Leu Ser Ala Glu Glu Asn Pro
35      40      45

Asp Asp Ser Glu Val Pro Ser Ser Ser Gly Ile Asn Ser Thr Lys Ser
50      55      60

Gln Asp Lys Asp Val Asn Glu Gly Glu Thr Ser Asp Gly Val Arg Lys
65      70      75      80

Ser Val His Lys Val Phe Ala Ser Met Leu Gly Glu Asn Glu Asp Asp
85      90      95

Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Thr
100      105      110

Pro Glu Gln Pro Thr Ala Gly Asp Val Phe Val Leu Glu Met Val Leu
115      120      125

Asn Arg Glu Thr Lys Lys Met Met Lys Glu Lys Arg Pro Arg Ser Lys
130      135      140

Leu Pro Arg Ala Leu Arg Gly Leu Met Gly Glu Ala Asn Ile Arg Phe
145      150      155      160

Ala Arg Gly Glu Arg Glu Glu Ala Ile Leu Met Cys Met Glu Ile Ile
165      170      175

Arg Gln Ala Pro Leu Ala Tyr Glu Pro Phe Ser Thr Leu Ala Met Ile
180      185      190

Tyr Glu Asp Gln Gly Asp Met Glu Lys Ser Leu Gln Phe Glu Leu Ile
195      200      205

Ala Ala His Leu Asn Pro Ser Asp Thr Glu Glu Trp Val Arg Leu Ala
210      215      220

Glu Met Ser Leu Glu Gln Asp Asn Ile Lys Gln Ala Ile Phe Cys Tyr
225      230      235      240

Thr Lys Ala Leu Lys Tyr Glu Pro Thr Asn Val Arg Tyr Leu Trp Glu
245      250      255

Arg Ser Ser Leu Tyr Glu Gln Met Gly Asp His Lys Met Ala Met Asp
260      265      270

Gly Tyr Arg Arg Ile Leu Asn Leu Leu Ser Pro Ser Asp Gly Glu Arg
275      280      285

Phe Met Gln Leu Ala Arg Asp Met Ala Lys Ser Tyr Tyr Glu Ala Asn
290      295      300

Asp Val Thr Ser Ala Ile Asn Ile Ile Asp Glu Ala Phe Ser Lys His
305      310      315      320

Gln Gly Leu Val Ser Met Glu Asp Val Asn Ile Ala Ala Glu Leu Tyr
325      330      335

Ile Ser Asn Lys Gln Tyr Asp Lys Ala Leu Glu Ile Ile Thr Asp Phe
340      345      350

Ser Gly Ile Val Leu Glu Lys Lys Thr Ser Glu Glu Gly Thr Ser Glu
355      360      365

Glu Asn Lys Ala Pro Glu Asn Val Thr Cys Thr Ile Pro Asp Gly Val
370      375      380

Pro Ile Asp Ile Thr Val Lys Leu Met Val Cys Leu Val His Leu Asn

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385	390	395	400
Ile Leu Glu Pro	Leu Asn Pro	Leu Leu Thr Thr	Leu Val Glu Gln Asn
	405	410	415
Pro Glu Asp Met	Gly Asp Leu Tyr	Leu Asp Val Ala	Glu Ala Phe Leu
	420	425	430
Asp Val Gly Glu	Tyr Asn Ser	Ala Leu Pro Leu Leu	Ser Ala Leu Val
	435	440	445
Cys Ser Glu Arg	Tyr Asn Leu Ala	Val Val Trp	Leu Arg His Ala Glu
	450	455	460
Cys Leu Lys Ala	Leu Gly Tyr Met	Glu Arg Ala Ala	Glu Ser Tyr Gly
	465	470	475
Lys Val Val Asp	Leu Ala Pro Leu	His Leu Asp Ala	Arg Ile Ser Leu
	485	490	495
Ser Thr Leu Gln	Gln Gln Leu Gly	Gln Pro Glu Lys	Ala Leu Glu Ala
	500	505	510
Leu Glu Pro Met	Tyr Asp Pro Asp	Thr Leu Ala Gln	Asp Ala Asn Ala
	515	520	525
Ala Gln Gln Glu	Leu Lys Leu Leu	Leu His Arg Ser	Thr Leu Leu Phe
	530	535	540
Ser Gln Gly Lys	Met Tyr Gly Tyr	Val Asp Thr Leu	Leu Thr Met Leu
	545	550	555
Ala Met Leu Leu	Lys Val Ala Met	Asn Arg Ala Gln	Val Cys Leu Ile
	565	570	575
Ser Ser Ser Lys	Ser Gly Glu Arg	His Leu Tyr Leu	Ile Lys Val Ser
	580	585	590
Arg Asp Lys Ile	Ser Asp Ser Asn	Asp Gln Glu Ser	Ala Asn Cys Asp
	595	600	605
Ala Lys Ala Ile	Phe Ala Val Leu	Thr Ser Val Leu	Thr Lys Asp Asp
	610	615	620
Trp Trp Asn Leu	Leu Leu Lys Ala	Ile Tyr Ser Leu	Cys Asp Leu Ser
	625	630	635
Arg Phe Gln Glu	Ala Glu Leu Leu	Val Asp Ser Ser	Leu Glu Tyr Tyr
	645	650	655
Ser Phe Tyr Asp	Asp Arg Gln Lys	Arg Lys Glu Leu	Glu Tyr Phe Gly
	660	665	670
Leu Ser Ala Ala	Ile Leu Asp Lys	Asn Phe Arg Lys	Ala Tyr Asn Tyr
	675	680	685
Ile Arg Ile Met	Val Met Glu Asn	Val Asn Lys Pro	Gln Leu Trp Asn
	690	695	700
Ile Phe Asn Gln	Val Thr Met His	Ser Gln Asp Val	Arg His His Arg
	705	710	715
Phe Cys Leu Arg	Leu Met Leu Lys	Asn Pro Glu Asn	His Ala Leu Cys
	725	730	735
Val Leu Asn Gly	His Asn Ala Phe	Val Ser Gly Ser	Phe Lys His Ala
	740	745	750
Leu Gly Gln Tyr	Val Gln Ala Phe	Arg Thr His Pro	Asp Glu Pro Leu
	755	760	765
Tyr Ser Phe Cys	Ile Gly Leu Thr	Phe Ile His Met	Ala Ser Gln Lys
	770	775	780
Tyr Val Leu Arg	Arg His Ala Leu	Ile Val Gln Gly	Phe Ser Phe Leu
	785	790	795
			800

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Asn Arg Tyr Leu Ser Leu Arg Gly Pro Cys Gln Glu Ser Phe Tyr Asn
      805                      810                      815

Leu Gly Arg Gly Leu His Gln Leu Gly Leu Ile His Leu Ala Ile His
      820                      825                      830

Tyr Tyr Gln Lys Ala Leu Glu Leu Pro Pro Leu Val Val Glu Gly Ile
      835                      840                      845

Glu Leu Asp Gln Leu Asp Leu Arg Arg Asp Ile Ala Tyr Asn Leu Ser
      850                      855                      860

Leu Ile Tyr Gln Ser Ser Gly Asn Thr Gly Met Ala Gln Thr Leu Leu
      865                      870                      875                      880

Tyr Thr Tyr Cys Ser Ile
      885

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<210> SEQ ID NO 67
<211> LENGTH: 1130
<212> TYPE: PRT
<213> ORGANISM: homo sapiens

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<400> SEQUENCE: 67

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Met Lys Glu Ile Cys Arg Ile Cys Ala Arg Glu Leu Cys Gly Asn Gln
1      5      10      15

Arg Arg Trp Ile Phe His Thr Ala Ser Lys Leu Asn Leu Gln Val Leu
20      25      30

Leu Ser His Val Leu Gly Lys Asp Val Pro Arg Asp Gly Lys Ala Glu
35      40      45

Phe Ala Cys Ser Lys Cys Ala Phe Met Leu Asp Arg Ile Tyr Arg Phe
50      55      60

Asp Thr Val Ile Ala Arg Ile Glu Ala Leu Ser Ile Glu Arg Leu Gln
65      70      75      80

Lys Leu Leu Leu Glu Lys Asp Arg Leu Lys Phe Cys Ile Ala Ser Met
85      90      95

Tyr Arg Lys Asn Asn Asp Asp Ser Gly Ala Glu Ile Lys Ala Gly Asn
100     105     110

Gly Thr Val Asp Met Ser Val Leu Pro Asp Ala Arg Tyr Ser Ala Leu
115     120     125

Leu Gln Glu Asp Phe Ala Tyr Ser Gly Phe Glu Cys Trp Val Glu Asn
130     135     140

Glu Asp Gln Ile Gln Glu Pro His Ser Cys His Gly Ser Glu Gly Pro
145     150     155     160

Gly Asn Arg Pro Arg Arg Cys Arg Gly Cys Ala Ala Leu Arg Val Ala
165     170     175

Asp Ser Asp Tyr Glu Ala Ile Cys Lys Val Pro Arg Lys Val Ala Arg
180     185     190

Ser Ile Ser Cys Gly Pro Ser Ser Arg Trp Ser Thr Ser Ile Cys Thr
195     200     205

Glu Glu Pro Ala Leu Ser Glu Val Gly Pro Pro Asp Leu Ala Ser Thr
210     215     220

Lys Val Pro Pro Asp Gly Glu Ser Met Glu Glu Glu Thr Pro Gly Ser
225     230     235     240

Ser Val Glu Ser Leu Asp Ala Ser Val Gln Ala Ser Pro Pro Gln Gln
245     250     255

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

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260				265				270			
Cys	Cys	Ser	Asp	Asp	Gln	Ala	Pro	Gln	His	Gly	Cys
	275						280				285
Glu	Leu	Ala	Leu	Ser	Met	Ile	Lys	Gly	Leu	Asp	Tyr
	290					295				300	
Ser	Pro	Arg	Gly	Ser	Arg	Leu	Pro	Ile	Pro	Val	Lys
305				310						315	
Gly	Ala	Lys	Pro	Gly	Pro	Ser	Met	Thr	Asp	Gly	Val
			325					330			
Leu	Asn	Arg	Ser	Leu	Lys	Pro	Leu	Tyr	Lys	Thr	Pro
		340						345			350
Leu	Glu	Leu	Ser	Asp	Leu	Gln	Glu	Leu	Trp	Asp	Asp
	355					360				365	
Tyr	Leu	Pro	Leu	Arg	Val	Gln	Pro	Met	Thr	Glu	Glu
	370					375				380	
Gln	Lys	Leu	Asn	Ser	His	Glu	Thr	Thr	Ile	Thr	Gln
385					390					395	
Asp	Ser	His	Leu	Ala	Glu	Leu	Gln	Glu	Lys	Ile	Gln
			405						410		
Thr	Asn	Lys	Ile	Leu	Gln	Glu	Lys	Leu	Asn	Glu	Met
		420						425			
Lys	Cys	Ala	Gln	Glu	Ser	Ser	Gln	Lys	Gln	Asp	Gly
	435						440				445
Leu	Lys	Glu	Thr	Leu	Lys	Ser	Arg	Glu	Arg	Glu	Thr
	450					455				460	
Gln	Val	Ile	Glu	Gly	Gln	Asn	Asp	Thr	Met	Ala	Lys
465					470					475	
Leu	His	Gln	Ser	Gln	Leu	Gly	Gln	Leu	His	Ser	Ser
			485						490		
Pro	Ala	Gln	Gln	Gln	Val	Ala	Leu	Leu	Asp	Leu	Gln
			500					505			510
Cys	Ser	Gln	Leu	Glu	Ile	Gln	Lys	Leu	Gln	Arg	Val
	515						520				525
Glu	Arg	Gln	Leu	Ala	Asp	Ala	Lys	Gln	Cys	Val	Gln
	530					535				540	
Ala	Ala	His	Glu	Ser	Glu	Gln	Gln	Lys	Glu	Ala	Ser
545					550					555	
Gln	Glu	Leu	Arg	Lys	Ala	Leu	Gln	Gln	Leu	Glu	Glu
			565					570			
Lys	Ser	Gln	Gln	Leu	Arg	Ala	Trp	Glu	Ala	Glu	Lys
			580					585			
Arg	Thr	Gln	Glu	Gln	Asn	Ile	Gln	His	Leu	Asn	His
		595					600				605
Lys	Glu	Gln	Leu	Leu	Gln	Glu	Phe	Arg	Glu	Leu	Leu
	610					615				620	
Asn	Ser	Asp	Lys	Thr	Leu	Glu	Ala	Asn	Glu	Met	Leu
625					630					635	
Arg	Gln	Arg	Ile	His	Asp	Lys	Ala	Val	Ala	Leu	Glu
			645						650		
Glu	Lys	Phe	Ser	Ala	Leu	Glu	Glu	Lys	Glu	Lys	Glu
		660						665			670

Arg	Leu	Ala	Val	Arg	Glu	Arg	Asp	His	Asp	Leu	Glu	Arg	Leu	Arg	Asp
675															
Val	Leu	Ser	Ser	Asn	Glu	Ala	Thr	Met	Gln	Ser	Met	Glu	Ser	Leu	Leu
690															
Arg	Ala	Lys	Gly	Leu	Glu	Val	Glu	Gln	Leu	Ser	Thr	Thr	Cys	Gln	Asn
705															
Leu	Gln	Trp	Leu	Lys	Glu	Glu	Met	Lys	Phe	Ser	Arg	Trp	Gln	Lys	Glu
725															
Gln	Glu	Ser	Ile	Gln	Gln	Leu	Gln	Thr	Ser	Leu	His	Asp	Arg	Asn	
740															
Lys	Glu	Val	Glu	Asp	Leu	Ser	Ala	Thr	Leu	Leu	Cys	Lys	Leu	Gly	Pro
755															
Gly	Gln	Ser	Glu	Ile	Ala	Glu	Glu	Leu	Cys	Gln	Arg	Leu	Gln	Arg	Lys
770															
Glu	Arg	Met	Leu	Gln	Asp	Leu	Leu	Ser	Asp	Arg	Asn	Lys	Gln	Val	Leu
785															
Glu	His	Glu	Met	Glu	Ile	Gln	Gly	Leu	Leu	Gln	Ser	Val	Ser	Thr	Arg
805															
Glu	Gln	Glu	Ser	Gln	Ala	Ala	Ala	Glu	Lys	Leu	Val	Gln	Ala	Leu	Met
820															
Glu	Arg	Asn	Ser	Glu	Leu	Gln	Ala	Leu	Arg	Gln	Tyr	Leu	Gly	Gly	Arg
835															
Asp	Ser	Leu	Met	Ser	Gln	Ala	Pro	Ile	Ser	Asn	Gln	Gln	Ala	Glu	Val
850															
Thr	Pro	Thr	Gly	Arg	Leu	Gly	Lys	Gln	Thr	Asp	Gln	Gly	Ser	Met	Gln
865															
Ile	Pro	Ser	Arg	Asp	Asp	Ser	Thr	Ser	Leu	Thr	Ala	Lys	Glu	Asp	Val
885															
Ser	Ile	Pro	Arg	Ser	Thr	Leu	Gly	Asp	Leu	Asp	Thr	Val	Ala	Gly	Leu
900															
Glu	Lys	Glu	Leu	Ser	Asn	Ala	Lys	Glu	Glu	Leu	Glu	Leu	Met	Ala	Lys
915															
Lys	Glu	Arg	Glu	Ser	Gln	Met	Glu	Leu	Ser	Ala	Leu	Gln	Ser	Met	Met
930															
Ala	Val	Gln	Glu	Glu	Glu	Leu	Gln	Val	Gln	Ala	Ala	Asp	Met	Glu	Ser
945															
Leu	Thr	Arg	Asn	Ile	Gln	Ile	Lys	Glu	Asp	Leu	Ile	Lys	Asp	Leu	Gln
965															
Met	Gln	Leu	Val	Asp	Pro	Glu	Asp	Ile	Pro	Ala	Met	Glu	Arg	Leu	Thr
980															
Gln	Glu	Val	Leu	Leu	Leu	Arg	Glu	Lys	Val	Ala	Ser	Val	Glu	Ser	Gln
995															
Gly	Gln	Glu	Ile	Ser	Gly	Asn	Arg	Arg	Gln	Gln	Leu	Leu	Leu	Met	
1010															
Leu	Glu	Gly	Leu	Val	Asp	Glu	Arg	Ser	Arg	Leu	Asn	Glu	Ala	Leu	
1025															
Gln	Ala	Glu	Arg	Gln	Leu	Tyr	Ser	Ser	Leu	Val	Lys	Phe	His	Ala	
1040															
His	Pro	Glu	Ser	Ser	Glu	Arg	Asp	Arg	Thr	Leu	Gln	Val	Glu	Leu	
1055															

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Glu Gly Ala Gln Val Leu Arg Ser Arg Leu Glu Glu Val Leu Gly
 1070 1075 1080

Arg Ser Leu Glu Arg Leu Asn Arg Leu Glu Thr Leu Ala Ala Ile
 1085 1090 1095

Gly Gly Ala Ala Ala Gly Asp Asp Thr Glu Asp Thr Ser Thr Glu
 1100 1105 1110

Phe Thr Asp Ser Ile Glu Glu Glu Ala Ala His His Ser His Gln
 1115 1120 1125

Gln Leu
 1130

<210> SEQ ID NO 68
 <211> LENGTH: 621
 <212> TYPE: PRT
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 68

Met Ala Asp Phe Glu Glu Leu Arg Asn Met Val Ser Ser Phe Arg Val
 1 5 10 15

Ser Glu Leu Gln Val Leu Leu Gly Phe Ala Gly Arg Asn Lys Ser Gly
 20 25 30

Arg Lys His Asp Leu Leu Met Arg Ala Leu His Leu Leu Lys Ser Gly
 35 40 45

Cys Ser Pro Ala Val Gln Ile Lys Ile Arg Glu Leu Tyr Arg Arg Arg
 50 55 60

Tyr Pro Arg Thr Leu Glu Gly Leu Ser Asp Leu Ser Thr Ile Lys Ser
 65 70 75 80

Ser Val Phe Ser Leu Asp Gly Gly Ser Ser Pro Val Glu Pro Asp Leu
 85 90 95

Ala Val Ala Gly Ile His Ser Leu Pro Ser Thr Ser Val Thr Pro His
 100 105 110

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

Thr Phe Glu Met Gln Gln Pro Ser Pro Pro Ile Pro Pro Val His Pro
 130 135 140

Asp Val Gln Leu Lys Asn Leu Pro Phe Tyr Asp Val Leu Asp Val Leu
 145 150 155 160

Ile Lys Pro Thr Ser Leu Val Gln Ser Ser Ile Gln Arg Phe Gln Glu
 165 170 175

Lys Phe Phe Ile Phe Ala Leu Thr Pro Gln Gln Val Arg Glu Ile Cys
 180 185 190

Ile Ser Arg Asp Phe Leu Pro Gly Gly Arg Arg Asp Tyr Thr Val Gln
 195 200 205

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

Asn Tyr Pro Asn Ser Leu Cys Ile Lys Val Asn Gly Lys Leu Phe Pro
 225 230 235 240

Leu Pro Gly Tyr Ala Pro Pro Pro Lys Asn Gly Ile Glu Gln Lys Arg
 245 250 255

Pro Gly Arg Pro Leu Asn Ile Thr Ser Leu Val Arg Leu Ser Ser Ala
 260 265 270

Val Pro Asn Gln Ile Ser Ile Ser Trp Ala Ser Glu Ile Gly Lys Asn
 275 280 285

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Tyr Ser Met Ser Val Tyr Leu Val Arg Gln Leu Thr Ser Ala Met Leu
 290 295 300
 Leu Gln Arg Leu Lys Met Lys Gly Ile Arg Asn Pro Asp His Ser Arg
 305 310 315 320
 Ala Leu Ile Lys Glu Lys Leu Thr Ala Asp Pro Asp Ser Glu Ile Ala
 325 330 335
 Thr Thr Ser Leu Arg Val Ser Leu Met Cys Pro Leu Gly Lys Met Arg
 340 345 350
 Leu Thr Ile Pro Cys Arg Ala Val Thr Cys Thr His Leu Gln Cys Phe
 355 360 365
 Asp Ala Ala Leu Tyr Leu Gln Met Asn Glu Lys Lys Pro Thr Trp Ile
 370 375 380
 Cys Pro Val Cys Asp Lys Lys Ala Ala Tyr Glu Ser Leu Ile Leu Asp
 385 390 395 400
 Gly Leu Phe Met Glu Ile Leu Asn Asp Cys Ser Asp Val Asp Glu Ile
 405 410 415
 Lys Phe Gln Glu Asp Gly Ser Trp Cys Pro Met Arg Pro Lys Lys Glu
 420 425 430
 Ala Met Lys Val Ser Ser Gln Pro Cys Thr Lys Ile Glu Ser Ser Ser
 435 440 445
 Val Leu Ser Lys Pro Cys Ser Val Thr Val Ala Ser Glu Ala Ser Lys
 450 455 460
 Lys Lys Val Asp Val Ile Asp Leu Thr Ile Glu Ser Ser Ser Asp Glu
 465 470 475 480
 Glu Glu Asp Pro Pro Ala Lys Arg Lys Cys Ile Phe Met Ser Glu Thr
 485 490 495
 Gln Ser Ser Pro Thr Lys Gly Val Leu Met Tyr Gln Pro Ser Ser Val
 500 505 510
 Arg Val Pro Ser Val Thr Ser Val Asp Pro Ala Ala Ile Pro Pro Ser
 515 520 525
 Leu Thr Asp Tyr Ser Val Pro Phe His His Thr Pro Ile Ser Ser Met
 530 535 540
 Ser Ser Asp Leu Pro Gly Leu Asp Phe Leu Ser Leu Ile Pro Val Asp
 545 550 555 560
 Pro Gln Tyr Cys Pro Pro Met Phe Leu Asp Ser Leu Thr Ser Pro Leu
 565 570 575
 Thr Ala Ser Ser Thr Ser Val Thr Thr Thr Ser Ser His Glu Ser Ser
 580 585 590
 Thr His Val Ser Ser Ser Ser Arg Ser Glu Thr Gly Val Ile Thr
 595 600 605
 Ser Ser Gly Ser Asn Ile Pro Glu Ile Ile Ser Leu Asp
 610 615 620

<210> SEQ ID NO 69

<211> LENGTH: 685

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 69

Met Glu Leu Leu Arg Thr Ile Thr Tyr Gln Pro Ala Ala Ser Thr Lys
 1 5 10 15
 Met Cys Glu Gln Ala Leu Gly Lys Gly Cys Gly Gly Asp Ser Lys Lys

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

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Pro Ala Val Glu Asn Lys Gln Gln Ile Gly Asp Ala Ile Arg Met Ile
  435                      440                      445

Val Arg Gly Thr Leu Gly Ser Cys Ser Ser Ser Ser Glu Cys Leu Glu
  450                      455                      460

Asp Ser Thr Met Gly Ser Val Ala Asp Thr Val Ala Arg Val Leu Arg
  465                      470                      475                      480

Gly Cys Leu Glu Asn Met Pro Glu Ala Asp Cys Ile Pro Lys Glu Gln
                      485                      490                      495

Leu Ser Thr Ser Phe Gln Trp Val Thr Lys Trp Val Asp Tyr Ser Asn
                      500                      505                      510

Lys Tyr Gly Phe Gly Tyr Gln Leu Ser Asp His Thr Val Gly Val Leu
  515                      520                      525

Phe Asn Asn Gly Ala His Met Ser Leu Leu Pro Asp Lys Lys Thr Val
  530                      535                      540

His Tyr Tyr Ala Glu Leu Gly Gln Cys Ser Val Phe Pro Ala Thr Asp
  545                      550                      555                      560

Ala Pro Glu Gln Phe Ile Ser Gln Val Thr Val Leu Lys Tyr Phe Ser
                      565                      570                      575

His Tyr Met Glu Glu Asn Leu Met Asp Gly Gly Asp Leu Pro Ser Val
  580                      585                      590

Thr Asp Ile Arg Arg Pro Arg Leu Tyr Leu Leu Gln Trp Leu Lys Ser
  595                      600                      605

Asp Lys Ala Leu Met Met Leu Phe Asn Asp Gly Thr Phe Gln Val Asn
  610                      615                      620

Phe Tyr His Asp His Thr Lys Ile Ile Ile Cys Ser Gln Asn Glu Glu
  625                      630                      635                      640

Tyr Leu Leu Thr Tyr Ile Asn Glu Asp Arg Ile Ser Thr Thr Phe Arg
  645                      650                      655

Leu Thr Thr Leu Leu Met Ser Gly Cys Ser Ser Glu Leu Lys Asn Arg
  660                      665                      670

Met Glu Tyr Ala Leu Asn Met Leu Leu Gln Arg Cys Asn
  675                      680                      685

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<210> SEQ ID NO 70

<211> LENGTH: 767

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 70

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Met Ala Thr Tyr Leu Glu Phe Ile Gln Gln Asn Glu Glu Arg Asp Gly
  1                      5                      10                      15

Val Arg Phe Ser Trp Asn Val Trp Pro Ser Ser Arg Leu Glu Ala Thr
  20                      25                      30

Arg Met Val Val Pro Leu Ala Cys Leu Leu Thr Pro Leu Lys Glu Arg
  35                      40                      45

Pro Asp Leu Pro Pro Val Gln Tyr Glu Pro Val Leu Cys Ser Arg Pro
  50                      55                      60

Thr Cys Lys Ala Val Leu Asn Pro Leu Cys Gln Val Asp Tyr Arg Ala
  65                      70                      75                      80

Lys Leu Trp Ala Cys Asn Phe Cys Phe Gln Arg Asn Gln Phe Pro Pro
  85                      90                      95

Ala Tyr Gly Gly Ile Ser Glu Val Asn Gln Pro Ala Glu Leu Met Pro

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100							105					110				
Gln	Phe	Ser	Thr	Ile	Glu	Tyr	Val	Ile	Gln	Arg	Gly	Ala	Gln	Ser	Pro	
		115					120					125				
Leu	Ile	Phe	Leu	Tyr	Val	Val	Asp	Thr	Cys	Leu	Glu	Glu	Asp	Asp	Leu	
	130					135					140					
Gln	Ala	Leu	Lys	Glu	Ser	Leu	Gln	Met	Ser	Leu	Ser	Leu	Leu	Pro	Pro	
145					150					155					160	
Asp	Ala	Leu	Val	Gly	Leu	Ile	Thr	Phe	Gly	Arg	Met	Val	Gln	Val	His	
				165					170					175		
Glu	Leu	Ser	Cys	Glu	Gly	Ile	Ser	Lys	Ser	Tyr	Val	Phe	Arg	Gly	Thr	
			180					185						190		
Lys	Asp	Leu	Thr	Ala	Lys	Gln	Ile	Gln	Asp	Met	Leu	Gly	Leu	Thr	Lys	
	195						200					205				
Pro	Ala	Met	Pro	Met	Gln	Gln	Ala	Arg	Pro	Ala	Gln	Pro	Gln	Glu	His	
	210					215					220					
Pro	Phe	Ala	Ser	Ser	Arg	Phe	Leu	Gln	Pro	Val	His	Lys	Ile	Asp	Met	
225					230					235					240	
Asn	Leu	Thr	Asp	Leu	Leu	Gly	Glu	Leu	Gln	Arg	Asp	Pro	Trp	Pro	Val	
				245					250					255		
Thr	Gln	Gly	Lys	Arg	Pro	Leu	Arg	Ser	Thr	Gly	Val	Ala	Leu	Ser	Ile	
			260					265					270			
Ala	Val	Gly	Leu	Leu	Glu	Gly	Thr	Phe	Pro	Asn	Thr	Gly	Ala	Arg	Ile	
	275						280					285				
Met	Leu	Phe	Thr	Gly	Gly	Pro	Pro	Thr	Gln	Gly	Pro	Gly	Met	Val	Val	
	290					295					300					
Gly	Asp	Glu	Leu	Lys	Ile	Pro	Ile	Arg	Ser	Trp	His	Asp	Ile	Glu	Lys	
305				310						315					320	
Asp	Asn	Ala	Arg	Phe	Met	Lys	Lys	Ala	Thr	Lys	His	Tyr	Glu	Met	Leu	
				325					330					335		
Ala	Asn	Arg	Thr	Ala	Ala	Asn	Gly	His	Cys	Ile	Asp	Ile	Tyr	Ala	Cys	
			340				345						350			
Ala	Leu	Asp	Gln	Thr	Gly	Leu	Leu	Glu	Met	Lys	Cys	Cys	Ala	Asn	Leu	
	355						360					365				
Thr	Gly	Gly	Tyr	Met	Val	Met	Gly	Asp	Ser	Phe	Asn	Thr	Ser	Leu	Phe	
	370					375					380					
Lys	Gln	Thr	Phe	Gln	Arg	Ile	Phe	Thr	Lys	Asp	Phe	Asn	Gly	Asp	Phe	
385					390					395					400	
Arg	Met	Ala	Phe	Gly	Ala	Thr	Leu	Asp	Val	Lys	Thr	Ser	Arg	Glu	Leu	
				405					410					415		
Lys	Ile	Ala	Gly	Ala	Ile	Gly	Pro	Cys	Val	Ser	Leu	Asn	Val	Lys	Gly	
			420					425					430			
Pro	Cys	Val	Ser	Glu	Asn	Glu	Leu	Gly	Val	Gly	Gly	Thr	Ser	Gln	Trp	
	435						440					445				
Lys	Ile	Cys	Gly	Leu	Asp	Pro	Thr	Ser	Thr	Leu	Gly	Ile	Tyr	Phe	Glu	
	450					455					460					
Val	Val	Asn	Gln	His	Asn	Thr	Pro	Ile	Pro	Gln	Gly	Gly	Arg	Gly	Ala	
465					470					475					480	
Ile	Gln	Phe	Val	Thr	His	Tyr	Gln	His	Ser	Ser	Thr	Gln	Arg	Arg	Ile	
				485					490					495		
Arg	Val	Thr	Thr	Ile	Ala	Arg	Asn	Trp	Ala	Asp	Val	Gln	Ser	Gln	Leu	
			500					505						510		

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Arg His Ile Glu Ala Ala Phe Asp Gln Glu Ala Ala Ala Val Leu Met
    515                      520                      525

Ala Arg Leu Gly Val Phe Arg Ala Glu Ser Glu Glu Gly Pro Asp Val
    530                      535                      540

Leu Arg Trp Leu Asp Arg Gln Leu Ile Arg Leu Cys Gln Lys Phe Gly
    545                      550                      555                      560

Gln Tyr Asn Lys Glu Asp Pro Thr Ser Phe Arg Leu Ser Asp Ser Phe
    565                      570                      575

Ser Leu Tyr Pro Gln Phe Met Phe His Leu Arg Arg Ser Pro Phe Leu
    580                      585                      590

Gln Val Phe Asn Asn Ser Pro Asp Glu Ser Ser Tyr Tyr Arg His His
    595                      600                      605

Phe Ala Arg Gln Asp Leu Thr Gln Ser Leu Ile Met Ile Gln Pro Ile
    610                      615                      620

Leu Tyr Ser Tyr Ser Phe His Gly Pro Pro Glu Pro Val Leu Leu Asp
    625                      630                      635                      640

Ser Ser Ser Ile Leu Ala Asp Arg Ile Leu Leu Met Asp Thr Phe Phe
    645                      650                      655

Gln Ile Val Ile Tyr Leu Gly Glu Thr Ile Ala Gln Trp Arg Lys Ala
    660                      665                      670

Gly Tyr Gln Asp Met Pro Glu Tyr Glu Asn Phe Lys His Leu Leu Gln
    675                      680                      685

Ala Pro Leu Asp Asp Ala Gln Glu Ile Leu Gln Ala Arg Phe Pro Met
    690                      695                      700

Pro Arg Tyr Ile Asn Thr Glu His Gly Gly Ser Gln Ala Arg Phe Leu
    705                      710                      715                      720

Leu Ser Lys Val Asn Pro Ser Gln Thr His Asn Asn Leu Tyr Ala Trp
    725                      730                      735

Gly Gln Glu Thr Gly Ala Pro Ile Leu Thr Asp Asp Val Ser Leu Gln
    740                      745                      750

Val Phe Met Asp His Leu Lys Lys Leu Ala Val Ser Ser Ala Cys
    755                      760                      765

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<210> SEQ ID NO 71

<211> LENGTH: 188

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 71

```

Met Asn Gly Asp Asp Thr Phe Ala Lys Arg Pro Arg Asp Asp Ala Lys
 1                      5                      10                      15

Ala Ser Glu Lys Arg Ser Lys Ala Phe Asp Asp Ile Ala Thr Tyr Phe
    20                      25                      30

Ser Lys Lys Glu Trp Lys Lys Met Lys Tyr Ser Glu Lys Ile Ser Tyr
    35                      40                      45

Val Tyr Met Lys Arg Asn Tyr Lys Ala Met Thr Lys Leu Gly Phe Lys
    50                      55                      60

Val Thr Leu Pro Pro Phe Met Cys Asn Lys Gln Ala Thr Asp Phe Gln
    65                      70                      75                      80

Gly Asn Asp Phe Asp Asn Asp His Asn Arg Arg Ile Gln Val Glu His
    85                      90                      95

Pro Gln Met Thr Phe Gly Arg Leu His Arg Ile Ile Pro Lys Ile Met

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100	105	110
Pro Lys Lys Pro Ala Glu Asp Glu Asn Asp Ser Lys Gly Val Ser Glu		
115	120	125
Ala Ser Gly Pro Gln Asn Asp Gly Lys Gln Leu His Pro Pro Gly Lys		
130	135	140
Ala Asn Ile Ser Glu Lys Ile Asn Lys Arg Ser Gly Pro Lys Arg Gly		
145	150	155
Lys His Ala Trp Thr His Arg Leu Arg Glu Arg Lys Gln Leu Val Ile		
165	170	175
Tyr Glu Glu Ile Ser Asp Pro Glu Glu Asp Asp Glu		
180	185	

<210> SEQ ID NO 72
 <211> LENGTH: 1038
 <212> TYPE: PRT
 <213> ORGANISM: homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: MISC_FEATURE
 <222> LOCATION: (910)..(910)
 <223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 72

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

His	Tyr	His	Pro	Ser	Asn	Ala	Arg	Phe	Phe	Thr	Tyr	Gly	Asn	Phe	Pro
			260					265					270		
Leu	Glu	Gln	His	Leu	Lys	Gln	Ile	His	Glu	Glu	Ala	Leu	Ser	Lys	Phe
		275					280					285			
Gln	Lys	Ile	Glu	Pro	Ser	Thr	Val	Val	Pro	Ala	Gln	Thr	Pro	Trp	Asp
		290				295					300				
Lys	Pro	Arg	Glu	Phe	Gln	Ile	Thr	Cys	Gly	Pro	Asp	Ser	Phe	Ala	Thr
		305			310					315					320
Asp	Pro	Ser	Lys	Gln	Thr	Thr	Val	Ser	Val	Ser	Phe	Leu	Leu	Pro	Asp
				325					330					335	
Ile	Thr	Asp	Thr	Phe	Glu	Ala	Phe	Thr	Leu	Ser	Leu	Leu	Ser	Ser	Leu
			340					345					350		
Leu	Thr	Ser	Gly	Pro	Asn	Ser	Pro	Phe	Tyr	Lys	Ala	Leu	Ile	Glu	Ser
		355					360					365			
Gly	Leu	Gly	Thr	Glu	Phe	Ser	Pro	Asp	Val	Gly	Tyr	Asn	Gly	Tyr	Thr
		370				375					380				
Arg	Glu	Ala	Tyr	Phe	Ser	Val	Gly	Leu	Gln	Gly	Ile	Val	Glu	Lys	Asp
					390					395					400
Ile	Glu	Thr	Val	Arg	Ser	Leu	Ile	Asp	Arg	Thr	Ile	Asp	Glu	Val	Val
				405					410					415	
Glu	Thr	Arg	Ile	Glu	Asp	Asp	Arg	Ile	Glu	Ala	Leu	Leu	His	Lys	Ile
			420					425					430		
Glu	Ile	Gln	Met	Lys	His	Gln	Ser	Thr	Ser	Phe	Gly	Leu	Met	Leu	Thr
		435					440					445			
Ser	Tyr	Ile	Ala	Ser	Cys	Trp	Asn	His	Asp	Gly	Asp	Pro	Val	Glu	Leu
		450				455					460				
Leu	Lys	Leu	Gly	Asn	Gln	Leu	Ala	Lys	Phe	Arg	Gln	Cys	Leu	Gln	Glu
				470						475					480
Asn	Pro	Lys	Phe	Leu	Gln	Glu	Lys	Val	Lys	Gln	Tyr	Phe	Lys	Asn	Asn
				485					490					495	
Gln	His	Lys	Leu	Thr	Leu	Ser	Met	Arg	Pro	Asp	Asp	Lys	Tyr	His	Glu
			500					505					510		
Lys	Gln	Ala	Gln	Val	Glu	Ala	Thr	Lys	Leu	Lys	Gln	Lys	Val	Glu	Ala
		515					520				525				
Leu	Ser	Pro	Gly	Asp	Arg	Gln	Gln	Ile	Tyr	Glu	Lys	Gly	Leu	Glu	Leu
		530				535					540				
Arg	Ser	Gln	Gln	Ser	Lys	Pro	Gln	Asp	Ala	Ser	Cys	Leu	Pro	Ala	Leu
					550					555					560
Lys	Val	Ser	Asp	Ile	Glu	Pro	Thr	Ile	Pro	Val	Thr	Glu	Leu	Asp	Val
				565					570					575	
Val	Leu	Thr	Ala	Gly	Asp	Ile	Pro	Val	Gln	Tyr	Cys	Ala	Gln	Pro	Thr
			580					585					590		
Asn	Gly	Met	Val	Tyr	Phe	Arg	Ala	Phe	Ser	Ser	Leu	Asn	Thr	Leu	Pro
			595				600					605			
Glu	Glu	Leu	Arg	Pro	Tyr	Val</									

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Ser	His	Met	Asp	Thr	Tyr	Glu	Gln	Val	Gly	Val	Leu	Phe	Ser	Ser	Leu	660	665	670	
Cys	Leu	Asp	Arg	Asn	Leu	Pro	Asp	Met	Met	Gln	Leu	Trp	Ser	Glu	Ile	675	680	685	
Phe	Asn	Asn	Pro	Cys	Phe	Glu	Glu	Glu	Glu	His	Phe	Lys	Val	Leu	Val	690	695	700	
Lys	Met	Thr	Ala	Gln	Glu	Leu	Ala	Asn	Gly	Ile	Pro	Asp	Ser	Gly	His	705	710	715	720
Leu	Tyr	Ala	Ser	Ile	Arg	Ala	Gly	Arg	Thr	Leu	Thr	Pro	Ala	Gly	Asp	725	730	735	
Leu	Gln	Glu	Thr	Phe	Ser	Gly	Met	Asp	Gln	Val	Arg	Leu	Met	Lys	Arg	740	745	750	
Ile	Ala	Glu	Met	Thr	Asp	Ile	Lys	Pro	Ile	Leu	Arg	Lys	Leu	Pro	Arg	755	760	765	
Ile	Lys	Lys	His	Leu	Leu	Asn	Gly	Asp	Asn	Met	Arg	Cys	Ser	Val	Asn	770	775	780	
Ala	Thr	Pro	Gln	Gln	Met	Pro	Gln	Thr	Glu	Lys	Ala	Val	Glu	Asp	Phe	785	790	795	800
Leu	Arg	Ser	Ile	Gly	Arg	Ser	Lys	Lys	Glu	Arg	Arg	Pro	Val	Arg	Pro	805	810	815	
His	Thr	Val	Glu	Lys	Pro	Val	Pro	Ser	Ser	Ser	Gly	Gly	Asp	Ala	His	820	825	830	
Val	Pro	His	Gly	Ser	Gln	Val	Ile	Arg	Lys	Leu	Val	Met	Glu	Pro	Thr	835	840	845	
Phe	Lys	Pro	Trp	Gln	Met	Lys	Thr	His	Phe	Leu	Met	Pro	Phe	Pro	Val	850	855	860	
Asn	Tyr	Val	Gly	Glu	Cys	Ile	Arg	Thr	Val	Pro	Tyr	Thr	Asp	Pro	Asp	865	870	875	880
His	Ala	Ser	Leu	Lys	Ile	Leu	Ala	Arg	Leu	Met	Thr	Ala	Lys	Phe	Leu	885	890	895	
His	Thr	Glu	Ile	Arg	Glu	Lys	Gly	Gly	Ala	Tyr	Gly	Gly	Xaa	Ala	Lys	900	905	910	
Leu	Ser	His	Asn	Gly	Ile	Phe	Thr	Leu	Tyr	Ser	Tyr	Arg	Asp	Pro	Asn	915	920	925	
Thr	Ile	Glu	Thr	Leu	Gln	Ser	Phe	Gly	Lys	Ala	Val	Asp	Trp	Ala	Lys	930	935	940	
Ser	Gly	Lys	Phe	Thr	Gln	Gln	Asp	Ile	Asp	Glu	Ala	Lys	Leu	Ser	Val	945	950	955	960
Phe	Ser	Thr	Val	Asp	Ala	Pro	Val	Ala	Pro	Ser	Asp	Lys	Gly	Met	Asp	965	970	975	
His	Phe	Leu	Tyr	Gly	Leu	Ser	Asp	Glu	Met	Lys	Gln	Ala	His	Arg	Glu	980	985	990	
Gln	Leu	Phe	Ala	Val	Ser	His	Asp	Lys	Leu	Leu	Ala	Val	Ser	Asp	Arg	995	1000	1005	
Tyr	Leu	Gly	Thr	Gly	Lys	Ser	Thr	His	Gly	Leu	Ala	Ile	Leu	Gly		1010	1015	1020	
Pro	Glu	Asn	Pro	Lys	Ile	Ala	Lys	Asp	Pro	Ser	Trp	Ile	Ile	Arg		1025	1030	1035	

<210> SEQ ID NO 73

<211> LENGTH: 341

<212> TYPE: PRT

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<213> ORGANISM: homo sapiens

<400> SEQUENCE: 73

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

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<210> SEQ ID NO 74

<211> LENGTH: 377

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

-continued

<400> SEQUENCE: 74

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Met Val Leu Glu Ser Thr Met Val Cys Val Asp Asn Ser Glu Tyr Met
1      5      10      15

Arg Asn Gly Asp Phe Leu Pro Thr Arg Leu Gln Ala Gln Gln Asp Ala
20      25      30

Val Asn Ile Val Cys His Ser Lys Thr Arg Ser Asn Pro Glu Asn Asn
35      40      45

Val Gly Leu Ile Thr Leu Ala Asn Asp Cys Glu Val Leu Thr Thr Leu
50      55      60

Thr Pro Asp Thr Gly Arg Ile Leu Ser Lys Leu His Thr Val Gln Pro
65      70      75      80

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

Leu Lys His Arg Gln Gly Lys Asn His Lys Met Arg Ile Ile Ala Phe
100     105     110

Val Gly Ser Pro Val Glu Asp Asn Glu Lys Asp Leu Val Lys Leu Ala
115     120     125

Lys Arg Leu Lys Lys Glu Lys Val Asn Val Asp Ile Ile Asn Phe Gly
130     135     140

Glu Glu Glu Val Asn Thr Glu Lys Leu Thr Ala Phe Val Asn Thr Leu
145     150     155     160

Asn Gly Lys Asp Gly Thr Gly Ser His Leu Val Thr Val Pro Pro Gly
165     170     175

Pro Ser Leu Ala Asp Ala Leu Ile Ser Ser Pro Ile Leu Ala Gly Glu
180     185     190

Gly Gly Ala Met Leu Gly Leu Gly Ala Ser Asp Phe Glu Phe Gly Val
195     200     205

Asp Pro Ser Ala Asp Pro Glu Leu Ala Leu Ala Leu Arg Val Ser Met
210     215     220

Glu Glu Gln Arg Gln Arg Gln Glu Glu Glu Ala Arg Arg Ala Ala Ala
225     230     235     240

Ala Ser Ala Ala Glu Ala Gly Ile Ala Thr Thr Gly Thr Glu Asp Ser
245     250     255

Asp Asp Ala Leu Leu Lys Met Thr Ile Ser Gln Gln Glu Phe Gly Arg
260     265     270

Thr Gly Leu Pro Asp Leu Ser Ser Met Thr Glu Glu Glu Gln Ile Ala
275     280     285

Tyr Ala Met Gln Met Ser Leu Gln Gly Ala Glu Phe Gly Gln Ala Glu
290     295     300

Ser Ala Asp Ile Asp Ala Ser Ser Ala Met Asp Thr Ser Glu Pro Ala
305     310     315     320

Lys Glu Glu Asp Asp Tyr Asp Val Met Gln Asp Pro Glu Phe Leu Gln
325     330     335

Ser Val Leu Glu Asn Leu Pro Gly Val Asp Pro Asn Asn Glu Ala Ile
340     345     350

Arg Asn Ala Met Gly Ser Leu Ala Ser Gln Ala Thr Lys Asp Gly Lys
355     360     365

Lys Asp Lys Lys Glu Glu Asp Lys Lys
370     375

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<210> SEQ ID NO 75

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<211> LENGTH: 399
<212> TYPE: PRT
<213> ORGANISM: homo sapiens

<400> SEQUENCE: 75

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

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370	375	380
Leu Ser Leu Leu Val	Gln Asn Leu Ala Pro	Ala Glu Thr His Thr
385	390	395
<210> SEQ ID NO 76 <211> LENGTH: 296 <212> TYPE: PRT <213> ORGANISM: homo sapiens <400> SEQUENCE: 76		
Met Lys Asn Glu Ile Ala Ala Val Val Phe Phe Phe Thr Arg Leu Val		
1	5	10
Arg Lys His Asp Lys Leu Lys Lys Glu Ala Val Glu Arg Phe Ala Glu		
	20	25
Lys Leu Thr Leu Ile Leu Gln Glu Lys Tyr Lys Asn His Trp Tyr Pro		
	35	40
Glu Lys Pro Ser Lys Gly Gln Ala Tyr Arg Cys Ile Arg Val Asn Lys		
	50	55
Phe Gln Arg Val Asp Pro Asp Val Leu Lys Ala Cys Glu Asn Ser Cys		
65	70	75
Ile Leu Tyr Ser Asp Leu Gly Leu Pro Lys Glu Leu Thr Leu Trp Val		
	85	90
Asp Pro Cys Glu Val Cys Cys Arg Arg Asp Gly Val Ser Pro Cys Trp		
	100	105
Pro Asp Cys Ser Gln Thr Pro Asp Leu Val Ile Arg Pro Pro Trp Pro		
	115	120
Pro Lys Ala Leu Asp Tyr Arg Arg Glu Pro Leu Arg Pro Ala Ser Ser		
	130	135
Phe Leu Ile Met Tyr Gly Glu Lys Asn Asn Ala Phe Ile Val Ala Ser		
145	150	155
Phe Glu Asn Lys Asp Glu Asn Lys Asp Glu Ile Ser Arg Lys Val Thr		
	165	170
Arg Ala Leu Asp Lys Val Thr Ser Asp Tyr His Ser Gly Ser Ser Ser		
	180	185
Ser Asp Glu Glu Thr Ser Lys Glu Met Glu Val Lys Pro Ser Ser Val		
	195	200
Thr Ala Ala Ala Ser Pro Val Tyr Gln Ile Ser Glu Leu Ile Phe Pro		
	210	215
Pro Leu Pro Met Trp His Pro Leu Pro Arg Lys Lys Pro Gly Met Tyr		
225	230	235
Arg Gly Asn Gly His Gln Asn His Tyr Pro Pro Pro Val Pro Phe Gly		
	245	250
Tyr Pro Asn Gln Gly Arg Lys Asn Lys Pro Tyr Arg Pro Ile Pro Val		
	260	265
Thr Trp Val Pro Pro Pro Gly Met His Cys Asp Arg Asn His Trp Ile		
	275	280
Asn Pro His Met Leu Ala Pro His		
	290	295

<210> SEQ ID NO 77
 <211> LENGTH: 188
 <212> TYPE: PRT
 <213> ORGANISM: homo sapiens

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<400> SEQUENCE: 77

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

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<210> SEQ ID NO 78

<211> LENGTH: 602

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 78

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

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Phe	Val	Val	Gly	Cys	Glu	Arg	Gly	Lys	Ile	Leu	Phe	Val	Ser	Lys	Ser	165	170	175
Val	Ser	Lys	Ile	Leu	Asn	Tyr	Asp	Gln	Ala	Ser	Leu	Thr	Gly	Gln	Ser	180	185	190
Leu	Phe	Asp	Phe	Leu	His	Pro	Lys	Asp	Val	Ala	Lys	Val	Lys	Glu	Gln	195	200	205
Leu	Ser	Ser	Phe	Asp	Ile	Ser	Pro	Arg	Glu	Lys	Leu	Ile	Asp	Ala	Lys	210	215	220
Thr	Gly	Leu	Gln	Val	His	Ser	Asn	Leu	His	Ala	Gly	Arg	Thr	Arg	Val	225	230	235
Tyr	Ser	Gly	Ser	Arg	Arg	Ser	Phe	Phe	Cys	Arg	Ile	Lys	Ser	Cys	Lys	245	250	255
Ile	Ser	Val	Lys	Glu	Glu	His	Gly	Cys	Leu	Pro	Asn	Ser	Lys	Lys	Lys	260	265	270
Glu	His	Arg	Lys	Phe	Tyr	Thr	Ile	His	Cys	Thr	Gly	Tyr	Leu	Arg	Ser	275	280	285
Trp	Pro	Pro	Asn	Ile	Val	Gly	Met	Glu	Glu	Glu	Arg	Asn	Ser	Lys	Lys	290	295	300
Asp	Asn	Ser	Asn	Phe	Thr	Cys	Leu	Val	Ala	Ile	Gly	Arg	Leu	Gln	Pro	305	310	315
Tyr	Ile	Val	Pro	Gln	Asn	Ser	Gly	Glu	Ile	Asn	Val	Lys	Pro	Thr	Glu	325	330	335
Phe	Ile	Thr	Arg	Phe	Ala	Val	Asn	Gly	Lys	Phe	Val	Tyr	Val	Asp	Gln	340	345	350
Arg	Ala	Thr	Ala	Ile	Leu	Gly	Tyr	Leu	Pro	Gln	Glu	Leu	Leu	Gly	Thr	355	360	365
Ser	Cys	Tyr	Glu	Tyr	Phe	His	Gln	Asp	Asp	His	Asn	Asn	Leu	Thr	Asp	370	375	380
Lys	His	Lys	Ala	Val	Leu	Gln	Ser	Lys	Glu	Lys	Ile	Leu	Thr	Asp	Ser	385	390	395
Tyr	Lys	Phe	Arg	Ala	Lys	Asp	Gly	Ser	Phe	Val	Thr	Leu	Lys	Ser	Gln	405	410	415
Trp	Phe	Ser	Phe	Thr	Asn	Pro	Trp	Thr	Lys	Glu	Leu	Glu	Tyr	Ile	Val	420	425	430
Ser	Val	Asn	Thr	Leu	Val	Leu	Gly	His	Ser	Glu	Pro	Gly	Glu	Ala	Ser	435	440	445
Phe	Leu	Pro	Cys	Ser	Ser	Gln	Ser	Ser	Glu	Glu	Ser	Ser	Arg	Gln	Ser	450	455	460
Cys	Met	Ser	Val	Pro	Gly	Met	Ser	Thr	Gly	Thr	Val	Leu	Gly	Ala	Gly	465	470	475
Ser	Ile	Gly	Thr	Asp	Ile	Ala	Asn	Glu	Ile	Leu	Asp	Leu	Gln	Arg	Leu	485	490	495
Gln	Ser	Ser	Ser	Tyr	Leu	Asp	Asp	Ser	Ser	Pro	Thr	Gly	Leu	Met	Lys	500	505	510
Asp	Thr	His	Thr	Val	Asn	Cys	Arg	Ser	Met	Ser	Asn	Lys	Glu	Leu	Phe	515	520	525
Pro	Pro	Ser	Pro	Ser	Glu	Met	Gly	Glu	Leu	Glu	Ala	Thr	Arg	Gln	Asn	530	535	540
Gln	Ser	Thr	Val	Ala	Val	His	Ser	His	Glu	Pro	Leu	Leu	Ser	Asp	Gly	545	550	555
Ala	Gln	Leu	Asp	Phe	Asp	Ala	Leu	Cys	Asp	Asn	Asp	Asp	Thr	Ala	Met			

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565	570	575
Ala Ala Phe Met Asn Tyr Leu Glu	Ala Glu Gly Gly Leu Gly Asp Pro	
580	585	590
Gly Asp Phe Ser Asp Ile Gln Trp Thr Leu		
595	600	

<210> SEQ ID NO 79
 <211> LENGTH: 745
 <212> TYPE: PRT
 <213> ORGANISM: homo sapiens
 <400> SEQUENCE: 79

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

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Val	Met	Ala	Thr	Tyr	Leu	Leu	Leu	Gly	Tyr	Lys	Ser	Ser	Glu	Leu	Glu	325	330	335
Gly	Asp	Thr	Ile	Thr	Leu	Lys	Pro	Arg	Pro	Ser	Ala	Asp	Leu	Thr	Asn	340	345	350
Ser	Ser	Ala	Gln	Phe	Pro	Ser	His	Lys	Val	Gln	Arg	Ser	Val	Ser	Ala	355	360	365
Asn	Pro	Lys	Gln	Arg	Arg	Phe	Ser	Asp	Gln	Ala	Gly	Pro	Ala	Ile	Pro	370	375	380
Thr	Ser	Asn	Ser	Tyr	Ser	Lys	Lys	Thr	Gln	Ser	Asn	Asn	Ala	Glu	Asn	385	390	395
Lys	Arg	Pro	Glu	Glu	Asp	Arg	Glu	Ser	Gly	Arg	Lys	Ala	Ser	Ser	Thr	405	410	415
Ala	Lys	Val	Pro	Ala	Ser	Pro	Leu	Pro	Gly	Leu	Glu	Arg	Lys	Lys	Thr	420	425	430
Thr	Pro	Thr	Pro	Ser	Thr	Asn	Ser	Val	Leu	Ser	Thr	Ser	Thr	Asn	Arg	435	440	445
Ser	Arg	Asn	Ser	Pro	Leu	Leu	Glu	Arg	Ala	Ser	Leu	Gly	Gln	Ala	Ser	450	455	460
Ile	Gln	Asn	Gly	Lys	Asp	Ser	Leu	Thr	Met	Pro	Gly	Ser	Arg	Ala	Ser	465	470	475
Thr	Ala	Ser	Ala	Ser	Ala	Ala	Val	Ser	Ala	Ala	Arg	Pro	Arg	Gln	His	485	490	495
Gln	Lys	Ser	Met	Ser	Ala	Ser	Val	His	Pro	Asn	Lys	Ala	Ser	Gly	Leu	500	505	510
Pro	Pro	Thr	Glu	Ser	Asn	Cys	Glu	Val	Pro	Arg	Pro	Ser	Thr	Ala	Pro	515	520	525
Gln	Arg	Val	Pro	Val	Ala	Ser	Pro	Ser	Ala	His	Asn	Ile	Ser	Ser	Ser	530	535	540
Gly	Gly	Ala	Pro	Asp	Arg	Thr	Asn	Phe	Pro	Arg	Gly	Val	Ser	Ser	Arg	545	550	555
Ser	Thr	Phe	His	Ala	Gly	Gln	Leu	Arg	Gln	Val	Arg	Asp	Gln	Gln	Asn	565	570	575
Leu	Pro	Tyr	Gly	Val	Thr	Pro	Ala	Ser	Pro	Ser	Gly	His	Ser	Gln	Gly	580	585	590
Arg	Arg	Gly	Ala	Ser	Gly	Ser	Ile	Phe	Ser	Lys	Phe	Thr	Ser	Lys	Phe	595	600	605
Val	Arg	Arg	Asn	Leu	Asn	Glu	Pro	Glu	Ser	Lys	Asp	Arg	Val	Glu	Thr	610	615	620
Leu	Arg	Pro	His	Val	Val	Gly	Ser	Gly	Gly	Asn	Asp	Lys	Glu	Lys	Glu	625	630	635
Glu	Phe	Arg	Glu	Ala	Lys	Pro	Arg	Ser	Leu	Arg	Phe	Thr	Trp	Ser	Met	645	650	655
Lys	Thr	Thr	Ser	Ser	Met	Glu	Pro	Asn	Glu	Met	Met	Arg	Glu	Ile	Arg	660	665	670
Lys	Val	Leu	Asp	Ala	Asn	Ser	Cys	Gln	Ser	Glu	Leu	His	Glu	Lys	Tyr	675	680	685
Met	Leu	Leu	Cys	Met	His	Gly	Thr	Pro	Gly	His	Glu	Asp	Phe	Val	Gln	690	695	700
Trp	Glu	Met	Glu	Val	Cys	Lys	Leu	Pro	Arg	Leu	Ser	Leu	Asn	Gly	Val	705	710	715
Arg	Phe	Lys	Arg	Ile	Ser	Gly	Thr	Ser	Met	Ala	Phe	Lys	Asn	Ile	Ala			

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725										730										735									
Ser	Lys	Ile	Ala	Asn	Glu	Leu	Lys	Leu																					
			740					745																					
<210> SEQ ID NO 80 <211> LENGTH: 319 <212> TYPE: PRT <213> ORGANISM: homo sapiens <400> SEQUENCE: 80																													
Met	Ser	Val	Gly	Phe	Ile	Gly	Ala	Gly	Gln	Leu	Ala	Phe	Ala	Leu	Ala														
1			5					10						15															
Lys	Gly	Phe	Thr	Ala	Ala	Gly	Val	Leu	Ala	Ala	His	Lys	Ile	Met	Ala														
			20					25					30																
Ser	Ser	Pro	Asp	Met	Asp	Leu	Ala	Thr	Val	Ser	Ala	Leu	Arg	Lys	Met														
		35				40						45																	
Gly	Val	Lys	Leu	Thr	Pro	His	Asn	Lys	Glu	Thr	Val	Gln	His	Ser	Asp														
		50				55					60																		
Val	Leu	Phe	Leu	Ala	Val	Lys	Pro	His	Ile	Ile	Pro	Phe	Ile	Leu	Asp														
65					70				75					80															
Glu	Ile	Gly	Ala	Asp	Ile	Glu	Asp	Arg	His	Ile	Val	Val	Ser	Cys	Ala														
			85					90						95															
Ala	Gly	Val	Thr	Ile	Ser	Ser	Ile	Glu	Lys	Lys	Leu	Ser	Ala	Phe	Arg														
			100					105						110															
Pro	Ala	Pro	Arg	Val	Ile	Arg	Cys	Met	Thr	Asn	Thr	Pro	Val	Val	Val														
		115					120					125																	
Arg	Glu	Gly	Ala	Thr	Val	Tyr	Ala	Thr	Gly	Thr	His	Ala	Gln	Val	Glu														
		130				135					140																		
Asp	Gly	Arg	Leu	Met	Glu	Gln	Leu	Leu	Ser	Thr	Val	Gly	Phe	Cys	Thr														
145					150				155					160															
Glu	Val	Glu	Glu	Asp	Leu	Ile	Asp	Ala	Val	Thr	Gly	Leu	Ser	Gly	Ser														
			165					170						175															
Gly	Pro	Ala	Tyr	Ala	Phe	Thr	Ala	Leu	Asp	Ala	Leu	Ala	Asp	Gly	Gly														
			180					185						190															
Val	Lys	Met	Gly	Leu	Pro	Arg	Arg	Leu	Ala	Val	Arg	Leu	Gly	Ala	Gln														
		195				200					205																		
Ala	Leu	Leu	Gly	Ala	Ala	Lys	Met	Leu	Leu	His	Ser	Glu	Gln	His	Pro														
		210				215					220																		
Gly	Gln	Leu	Lys	Asp	Asn	Val	Ser	Ser	Pro	Gly	Gly	Ala	Thr	Ile	His														
225					230				235					240															
Ala	Leu	His	Val	Leu	Glu	Ser	Gly	Gly	Phe	Arg	Ser	Leu	Leu	Ile	Asn														
		245						250						255															
Ala	Val	Glu	Ala	Ser	Cys	Ile	Arg	Thr	Arg	Glu	Leu	Gln	Ser	Met	Ala														
		260						265						270															
Asp	Gln	Glu	Gln	Val	Ser	Pro	Ala	Ala	Ile	Lys	Lys	Thr	Ile	Leu	Asp														
		275				280						285																	
Lys	Val	Lys	Leu	Asp	Ser	Pro	Ala	Gly	Thr	Ala	Leu	Ser	Pro	Ser	Gly														
		290				295					300																		
His	Thr	Lys	Leu	Leu	Pro	Arg	Ser	Leu	Ala	Pro	Ala	Gly	Lys	Asp															
305					310				315																				

<210> SEQ ID NO 81
 <211> LENGTH: 148

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<212> TYPE: PRT
<213> ORGANISM: homo sapiens

<400> SEQUENCE: 81

Met Ala Glu Ser Asp Trp Asp Thr Val Thr Val Leu Arg Lys Lys Gly
1      5      10      15

Pro Thr Ala Ala Gln Ala Lys Ser Lys Gln Ala Ile Leu Ala Ala Gln
20     25     30

Arg Arg Gly Glu Asp Val Glu Thr Ser Lys Lys Trp Ala Ala Gly Gln
35     40     45

Asn Lys Gln His Ser Ile Thr Lys Asn Thr Ala Lys Leu Asp Arg Glu
50     55     60

Thr Glu Glu Leu His His Asp Arg Val Thr Leu Glu Val Gly Lys Val
65     70     75     80

Ile Gln Gln Gly Arg Gln Ser Lys Gly Leu Thr Gln Lys Asp Leu Ala
85     90     95

Thr Lys Ile Asn Glu Lys Pro Gln Val Ile Ala Asp Tyr Glu Ser Gly
100    105    110

Arg Ala Ile Pro Asn Asn Gln Val Leu Gly Lys Ile Glu Arg Ala Ile
115    120    125

Gly Leu Lys Leu Arg Gly Lys Asp Ile Gly Lys Pro Ile Glu Lys Gly
130    135    140

Pro Arg Ala Lys
145

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<210> SEQ ID NO 82
<211> LENGTH: 375
<212> TYPE: PRT
<213> ORGANISM: homo sapiens

<400> SEQUENCE: 82

Met Asp Asp Asp Ile Ala Ala Leu Val Val Asp Asn Gly Ser Gly Met
1      5      10      15

Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val Phe Pro
20     25     30

Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly Met Gly
35     40     45

Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg Gly Ile
50     55     60

Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Val Thr Asn Trp Asp
65     70     75     80

Asp Met Glu Lys Ile Trp His His Thr Phe Tyr Asn Glu Leu Arg Val
85     90     95

Ala Pro Glu Glu His Pro Val Leu Leu Thr Glu Ala Pro Leu Asn Pro
100    105    110

Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr Phe Asn
115    120    125

Thr Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu Tyr Ala
130    135    140

Ser Gly Arg Thr Thr Gly Ile Val Met Asp Ser Gly Asp Gly Val Thr
145    150    155    160

His Thr Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala Ile Leu
165    170    175

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

<210> SEQ ID NO 83

<211> LENGTH: 268

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 83

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

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His Asp Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly
 165 170 175

Asp Glu Glu Val Asn Gln Glu Phe Ile Asn Met Asn Glu Ser Asp Ala
 180 185 190

His Ala Phe Asp Glu Glu Trp Gln Ser Glu Val Leu Lys Tyr Lys Pro
 195 200 205

Gly Arg His Asn Leu Gly Asn Thr Arg Met Arg Ser Val Gly His Glu
 210 215 220

Asn Pro Gly Ser Arg Glu Leu Lys Arg Arg Glu Lys Pro Gln Gln Ser
 225 230 235 240

Pro Ala Ile Glu His Gly Arg Arg Ser Asn Val Leu Gly Asp Lys Leu
 245 250 255

His Ile Lys Gly Ser Ser Val Lys Ser Asn Lys Lys
 260 265

<210> SEQ ID NO 84
 <211> LENGTH: 837
 <212> TYPE: PRT
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 84

Met Ala Glu Pro Ser Gln Ala Pro Thr Pro Ala Pro Ala Ala Gln Pro
 1 5 10 15

Arg Pro Leu Gln Ser Pro Ala Pro Ala Pro Thr Pro Thr Pro Ala Pro
 20 25 30

Ser Pro Ala Ser Ala Pro Ile Pro Thr Pro Thr Pro Ala Pro Ala Pro
 35 40 45

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

Val Gly Ser Gly Gly Ala Gly Ser Gly Gly Asp Pro Ala Arg Pro Gly
 65 70 75 80

Leu Ser Gln Gln Gln Arg Ala Ser Gln Arg Lys Ala Gln Val Arg Gly
 85 90 95

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

Lys Ala Asn Gly Thr Cys Lys Cys Asn Gly Trp Lys Asn Pro Lys Pro
 115 120 125

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

Glu Leu Cys Arg Ser Cys Glu His Pro Leu Ala Asp His Val Ser His
 145 150 155 160

Leu Glu Asn Val Ser Glu Asp Glu Ile Asn Arg Leu Leu Gly Met Val
 165 170 175

Val Asp Val Glu Asn Leu Phe Met Ser Val His Lys Glu Glu Asp Thr
 180 185 190

Asp Thr Lys Gln Val Tyr Phe Tyr Leu Phe Lys Leu Leu Arg Lys Cys
 195 200 205

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

Pro Phe Glu Lys Pro Asn Ile Glu Gln Gly Val Leu Asn Phe Val Gln
 225 230 235 240

Tyr Lys Phe Ser His Leu Ala Pro Arg Glu Arg Gln Thr Met Phe Glu

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245								250					255				
Leu	Ser	Lys	Met	Phe	Leu	Leu	Cys	Leu	Asn	Tyr	Trp	Glu	Leu	Glu	Thr		
			260							265				270			
Pro	Ala	Gln	Phe	Arg	Gln	Arg	Ser	Gln	Ala	Glu	Asp	Val	Ala	Thr	Tyr		
			275				280							285			
Lys	Val	Asn	Tyr	Thr	Arg	Trp	Leu	Cys	Tyr	Cys	His	Val	Pro	Gln	Ser		
			290				295				300						
Cys	Asp	Ser	Leu	Pro	Arg	Tyr	Glu	Thr	Thr	His	Val	Phe	Gly	Arg	Ser		
			305				310				315			320			
Leu	Leu	Arg	Ser	Ile	Phe	Thr	Val	Thr	Arg	Arg	Gln	Leu	Leu	Glu	Lys		
				325							330				335		
Phe	Arg	Val	Glu	Lys	Asp	Lys	Leu	Val	Pro	Glu	Lys	Arg	Thr	Leu	Ile		
			340							345				350			
Leu	Thr	His	Phe	Pro	Lys	Phe	Leu	Ser	Met	Leu	Glu	Glu	Glu	Ile	Tyr		
			355				360						365				
Gly	Ala	Asn	Ser	Pro	Ile	Trp	Glu	Ser	Gly	Phe	Thr	Met	Pro	Pro	Ser		
			370				375						380				
Glu	Gly	Thr	Gln	Leu	Val	Pro	Arg	Pro	Ala	Ser	Val	Ser	Ala	Ala	Val		
			385				390						395				
Val	Pro	Ser	Thr	Pro	Ile	Phe	Ser	Pro	Ser	Met	Gly	Gly	Gly	Ser	Asn		
				405						410							
Ser	Ser	Leu	Ser	Leu	Asp	Ser	Ala	Gly	Ala	Glu	Pro	Met	Pro	Gly	Glu		
				420						425			430				
Lys	Arg	Thr	Leu	Pro	Glu	Asn	Leu	Thr	Leu	Glu	Asp	Ala	Lys	Arg	Leu		
			435				440						445				
Arg	Val	Met	Gly	Asp	Ile	Pro	Met	Glu	Leu	Val	Asn	Glu	Val	Met	Leu		
			450				455						460				
Thr	Ile	Thr	Asp	Pro	Ala	Ala	Met	Leu	Gly	Pro	Glu	Thr	Ser	Leu	Leu		
			465				470						475				
Ser	Ala	Asn	Ala	Ala	Arg	Asp	Glu	Thr	Ala	Arg	Leu	Glu	Glu	Arg	Arg		
				485						490							
Gly	Ile	Ile	Glu	Phe	His	Val	Ile	Gly	Asn	Ser	Leu	Thr	Pro	Lys	Ala		
			500				505						510				
Asn	Arg	Arg	Val	Leu	Leu	Trp	Leu	Val	Gly	Leu	Gln	Asn	Val	Phe	Ser		
			515				520						525				
His	Gln	Leu	Pro	Arg	Met	Pro	Lys	Glu	Tyr	Ile	Ala	Arg	Leu	Val	Phe		
			530				535						540				
Asp	Pro	Lys	His	Lys	Thr	Leu	Ala	Leu	Ile	Lys	Asp	Gly	Arg	Val	Ile		
			545				550						555				
Gly	Gly	Ile	Cys	Phe	Arg	Met	Phe	Pro	Thr	Gln	Gly	Phe	Thr	Glu	Ile		
				565						570							
Val	Phe	Cys	Ala	Val	Thr	Ser	Asn	Glu	Gln	Val	Lys	Gly	Tyr	Gly	Thr		
			580				585						590				
His	Leu	Met	Asn	His	Leu	Lys	Glu	Tyr	His	Ile	Lys	His	Asn	Ile	Leu		
			595				600						605				
Tyr	Phe	Leu	Thr	Tyr	Ala	Asp	Glu	Tyr	Ala	Ile	Gly	Tyr	Phe	Lys	Lys		
			610				615						620				
Gln	Gly	Phe	Ser	Lys	Asp	Ile	Lys	Val	Pro	Lys	Ser	Arg	Tyr	Leu	Gly		
			625				630						635				
Tyr	Ile	Lys	Asp	Tyr	Glu	Gly	Ala	Thr	Leu	Met	Glu	Cys	Glu	Leu	Asn		
				645						650							

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Pro Arg Ile Pro Tyr Thr Glu Leu Ser His Ile Ile Lys Lys Gln Lys
 660 665 670
 Glu Ile Ile Lys Lys Leu Ile Glu Arg Lys Gln Ala Gln Ile Arg Lys
 675 680 685
 Val Tyr Pro Gly Leu Ser Cys Phe Lys Glu Gly Val Arg Gln Ile Pro
 690 695 700
 Val Glu Ser Val Pro Gly Ile Arg Glu Thr Gly Trp Lys Pro Leu Gly
 705 710 715 720
 Lys Glu Lys Gly Lys Glu Leu Lys Asp Pro Asp Gln Leu Tyr Thr Thr
 725 730 735
 Leu Lys Asn Leu Leu Ala Gln Ile Lys Ser His Pro Ser Ala Trp Pro
 740 745 750
 Phe Met Glu Pro Val Lys Lys Ser Glu Ala Pro Asp Tyr Tyr Glu Val
 755 760 765
 Ile Arg Phe Pro Ile Asp Leu Lys Thr Met Thr Glu Arg Leu Arg Ser
 770 775 780
 Arg Tyr Tyr Val Thr Arg Lys Leu Phe Val Ala Asp Leu Gln Arg Val
 785 790 795 800
 Ile Ala Asn Cys Arg Glu Tyr Asn Pro Pro Asp Ser Glu Tyr Cys Arg
 805 810 815
 Cys Ala Ser Ala Leu Glu Lys Phe Phe Tyr Phe Lys Leu Lys Glu Gly
 820 825 830
 Gly Leu Ile Asp Lys
 835

<210> SEQ ID NO 85
 <211> LENGTH: 483
 <212> TYPE: PRT
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 85

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

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165				170				175							
Thr	Pro	Glu	Thr	Leu	Leu	Glu	Glu	Ile	Glu	Ala	Lys	Asn	Arg	Glu	Leu
			180						185				190		
Ile	Ala	Lys	Lys	Thr	Thr	Pro	Leu	Leu	Ser	Phe	Leu	Lys	Asn	Lys	Gln
		195					200						205		
Arg	Met	Arg	Glu	Glu	Lys	Arg	Glu	Glu	Arg	Arg	Arg	Arg	Glu	Ile	Glu
	210					215							220		
Arg	Lys	Arg	Gln	Arg	Glu	Glu	Glu	Arg	Arg	Lys	Trp	Lys	Glu	Glu	Glu
	225					230				235					240
Lys	Arg	Lys	Arg	Lys	Asp	Ile	Glu	Lys	Leu	Lys	Lys	Ile	Asp	Arg	Ile
			245						250				255		
Pro	Glu	Arg	Asp	Lys	Leu	Lys	Asp	Glu	Pro	Lys	Ile	Lys	Val	His	Arg
			260						265				270		
Phe	Leu	Leu	Gln	Ala	Val	Asn	Gln	Lys	Asn	Leu	Leu	Lys	Lys	Pro	Glu
			275				280						285		
Lys	Gly	Asp	Glu	Lys	Glu	Leu	Asp	Lys	Arg	Glu	Lys	Ala	Lys	Lys	Leu
	290					295							300		
Asp	Lys	Glu	Asn	Leu	Ser	Asp	Glu	Arg	Ala	Ser	Gly	Gln	Ser	Cys	Thr
	305					310				315					320
Leu	Pro	Lys	Arg	Ser	Asp	Ser	Glu	Leu	Lys	Asp	Glu	Lys	Pro	Lys	Arg
			325						330					335	
Pro	Glu	Asp	Glu	Ser	Gly	Arg	Asp	Tyr	Arg	Glu	Arg	Glu	Arg	Glu	Tyr
			340						345				350		
Glu	Arg	Asp	Gln	Glu	Arg	Ile	Leu	Arg	Glu	Arg	Glu	Arg	Leu	Lys	Arg
		355					360						365		
Gln	Glu	Glu	Glu	Arg	Arg	Arg	Gln	Lys	Glu	Arg	Tyr	Glu	Lys	Glu	Lys
		370				375							380		
Thr	Phe	Lys	Arg	Lys	Glu	Glu	Glu	Met	Lys	Lys	Glu	Lys	Asp	Thr	Leu
					390					395					400
Arg	Asp	Lys	Gly	Lys	Lys	Ala	Glu	Ser	Thr	Glu	Ser	Ile	Gly	Ser	Ser
			405						410					415	
Glu	Lys	Thr	Glu	Lys	Lys	Glu	Glu	Val	Val	Lys	Arg	Asp	Arg	Ile	Arg
		420							425				430		
Asn	Lys	Asp	Arg	Pro	Ala	Met	Gln	Leu	Tyr	Gln	Pro	Gly	Ala	Arg	Ser
		435				440							445		
Arg	Asn	Arg	Leu	Cys	Pro	Pro	Asp	Asp	Ser	Thr	Lys	Ser	Gly	Asp	Ser
		450				455					460				
Ala	Ala	Glu	Arg	Lys	Gln	Glu	Ser	Gly	Ile	Ser	His	Arg	Lys	Glu	Gly
		465			470				475					480	
Gly	Glu	Glu													

<210> SEQ ID NO 86

<211> LENGTH: 426

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 86

Met	Ala	Asn	Asp	Ser	Gly	Gly	Pro	Gly	Gly	Pro	Ser	Pro	Ser	Glu	Arg
1				5					10					15	
Asp	Arg	Gln	Tyr	Cys	Glu	Leu	Cys	Gly	Lys	Met	Glu	Asn	Leu	Leu	Arg
		20						25					30		
Cys	Ser	Arg	Cys	Arg	Ser	Ser	Phe	Tyr	Cys	Cys	Lys	Glu	His	Gln	Arg

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

<210> SEQ ID NO 87

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<211> LENGTH: 1320

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 87

Met Ser Gly Gly Ala Ser Ala Thr Gly Pro Arg Arg Gly Pro Pro Gly
1 5 10 15

Leu Glu Asp Thr Thr Ser Lys Lys Lys Gln Lys Asp Arg Ala Asn Gln
20 25 30

Glu Ser Lys Asp Gly Asp Pro Arg Lys Glu Thr Gly Ser Arg Tyr Val
35 40 45

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

Ala Ser His Ala Ala Gly Ile Thr Gly Ser Arg His Arg Thr Arg Leu
65 70 75 80

Phe Phe Pro Ser Ser Ser Gly Ser Ala Ser Thr Pro Gln Glu Glu Gln
85 90 95

Thr Lys Glu Gly Ala Cys Glu Asp Pro His Asp Leu Leu Ala Thr Pro
100 105 110

Thr Pro Glu Leu Leu Leu Asp Trp Arg Gln Ser Ala Glu Glu Val Ile
115 120 125

Val Lys Leu Arg Val Gly Val Gly Pro Leu Gln Leu Glu Asp Val Asp
130 135 140

Ala Ala Phe Thr Asp Thr Asp Cys Val Val Arg Phe Ala Gly Gly Gln
145 150 155 160

Gln Trp Gly Gly Val Phe Tyr Ala Glu Ile Lys Ser Ser Cys Ala Lys
165 170 175

Val Gln Thr Arg Lys Gly Ser Leu Leu His Leu Thr Leu Pro Lys Lys
180 185 190

Val Pro Met Leu Thr Trp Pro Ser Leu Leu Val Glu Ala Asp Glu Gln
195 200 205

Leu Cys Ile Pro Pro Leu Asn Ser Gln Thr Cys Leu Leu Gly Ser Glu
210 215 220

Glu Asn Leu Ala Pro Leu Ala Gly Glu Lys Ala Val Pro Pro Gly Asn
225 230 235 240

Asp Pro Val Ser Pro Ala Met Val Arg Ser Arg Asn Pro Gly Lys Asp
245 250 255

Asp Cys Ala Lys Glu Glu Met Ala Val Ala Ala Asp Ala Ala Thr Leu
260 265 270

Val Asp Glu Pro Glu Ser Met Val Asn Leu Ala Phe Val Lys Asn Asp
275 280 285

Ser Tyr Glu Lys Gly Pro Asp Ser Val Val Val His Val Tyr Val Lys
290 295 300

Glu Ile Cys Arg Asp Thr Ser Arg Val Leu Phe Arg Glu Gln Asp Phe
305 310 315 320

Thr Leu Ile Phe Gln Thr Arg Asp Gly Asn Phe Leu Arg Leu His Pro
325 330 335

Gly Cys Gly Pro His Thr Thr Phe Arg Trp Gln Val Lys Leu Arg Asn
340 345 350

Leu Ile Glu Pro Glu Gln Cys Thr Phe Cys Phe Thr Ala Ser Arg Ile
355 360 365

Asp Ile Cys Leu Arg Lys Arg Gln Ser Gln Arg Trp Gly Gly Leu Glu

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370					375					380					
Ala	Pro	Ala	Ala	Arg	Gly	Ala	Val	Gly	Gly	Ala	Lys	Val	Ala	Val	Pro
385					390					395					400
Thr	Gly	Pro	Thr	Pro	Leu	Asp	Ser	Thr	Pro	Pro	Gly	Gly	Ala	Pro	His
				405					410					415	
Pro	Leu	Thr	Gly	Gln	Glu	Glu	Ala	Arg	Ala	Val	Glu	Lys	Asp	Lys	Ser
			420					425					430		
Lys	Ala	Arg	Ser	Glu	Asp	Thr	Gly	Leu	Asp	Ser	Val	Ala	Thr	Arg	Thr
		435					440					445			
Pro	Met	Glu	His	Val	Thr	Pro	Lys	Pro	Glu	Thr	His	Leu	Ala	Ser	Pro
	450					455					460				
Lys	Pro	Thr	Cys	Met	Val	Pro	Pro	Met	Pro	His	Ser	Pro	Val	Ser	Gly
465					470					475					480
Asp	Ser	Val	Glu	Glu	Glu	Glu	Glu	Glu	Glu	Lys	Lys	Val	Cys	Leu	Pro
			485						490					495	
Gly	Phe	Thr	Gly	Leu	Val	Asn	Leu	Gly	Asn	Thr	Cys	Phe	Met	Asn	Ser
			500					505					510		
Val	Ile	Gln	Ser	Leu	Ser	Asn	Thr	Arg	Glu	Leu	Arg	Asp	Phe	Phe	His
		515					520					525			
Asp	Arg	Ser	Phe	Glu	Ala	Glu	Ile	Asn	Tyr	Asn	Asn	Pro	Leu	Gly	Thr
	530					535					540				
Gly	Gly	Arg	Leu	Ala	Ile	Gly	Phe	Ala	Val	Leu	Leu	Arg	Ala	Leu	Trp
545				550						555					560
Lys	Gly	Thr	His	His	Ala	Phe	Gln	Pro	Ser	Lys	Leu	Lys	Ala	Ile	Val
			565						570					575	
Ala	Ser	Lys	Ala	Ser	Gln	Phe	Thr	Gly	Tyr	Ala	Gln	His	Asp	Ala	Gln
			580					585					590		
Glu	Phe	Met	Ala	Phe	Leu	Leu	Asp	Gly	Leu	His	Glu	Asp	Leu	Asn	Arg
	595						600					605			
Ile	Gln	Asn	Lys	Pro	Tyr	Thr	Glu	Thr	Val	Asp	Ser	Asp	Gly	Arg	Pro
	610					615					620				
Asp	Glu	Val	Val	Ala	Glu	Glu	Ala	Trp	Gln	Arg	His	Lys	Met	Arg	Asn
625				630						635					640
Asp	Ser	Phe	Ile	Val	Asp	Leu	Phe	Gln	Gly	Gln	Tyr	Lys	Ser	Lys	Leu
			645						650					655	
Val	Cys	Pro	Val	Cys	Ala	Lys	Val	Ser	Ile	Thr	Phe	Asp	Pro	Phe	Leu
			660					665					670		
Tyr	Leu	Pro	Val	Pro	Leu	Pro	Gln	Lys	Gln	Lys	Val	Leu	Pro	Val	Phe
	675						680					685			
Tyr	Phe	Ala	Arg	Glu	Pro	His	Ser	Lys	Pro	Ile	Lys	Phe	Leu	Val	Ser
	690					695					700				
Val	Ser	Lys	Glu	Asn	Ser	Thr	Ala	Ser	Glu	Val	Leu	Asp	Ser	Leu	Ser
705				710						715					720
Gln	Ser	Val	His	Val	Lys	Pro	Glu	Asn	Leu	Arg	Leu	Ala	Glu	Val	Ile
			725						730					735	
Lys	Asn	Arg	Phe	His	Arg	Val	Phe	Leu	Pro	Ser	His	Ser	Leu	Asp	Thr
			740					745					750		
Val	Ser	Pro	Ser	Asp	Thr	Leu	Leu	Cys	Phe	Glu	Leu	Leu	Ser	Ser	Glu
		755					760					765			
Leu	Ala	Lys	Glu	Arg	Val	Val	Val	Leu	Glu	Val	Gln	Gln	Arg	Pro	Gln
	770					775					780				

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Val	Pro	Ser	Val	Pro	Ile	Ser	Lys	Cys	Ala	Ala	Cys	Gln	Arg	Lys	Gln	
785					790					795					800	
Gln	Ser	Glu	Asp	Glu	Lys	Leu	Lys	Arg	Cys	Thr	Arg	Cys	Tyr	Arg	Val	
				805					810					815		
Gly	Tyr	Cys	Asn	Gln	Leu	Cys	Gln	Lys	Thr	His	Trp	Pro	Asp	His	Lys	
			820					825					830			
Gly	Leu	Cys	Arg	Pro	Glu	Asn	Ile	Gly	Tyr	Pro	Phe	Leu	Val	Ser	Val	
	835						840					845				
Pro	Ala	Ser	Arg	Leu	Thr	Tyr	Ala	Arg	Leu	Ala	Gln	Leu	Leu	Glu	Gly	
	850					855					860					
Tyr	Ala	Arg	Tyr	Ser	Val	Ser	Val	Phe	Gln	Pro	Pro	Phe	Gln	Pro	Gly	
865				870					875					880		
Arg	Met	Ala	Leu	Glu	Ser	Gln	Ser	Pro	Gly	Cys	Thr	Thr	Leu	Leu	Ser	
			885						890					895		
Thr	Gly	Ser	Leu	Glu	Ala	Gly	Asp	Ser	Glu	Arg	Asp	Pro	Ile	Gln	Pro	
		900						905					910			
Pro	Glu	Leu	Gln	Leu	Val	Thr	Pro	Met	Ala	Glu	Gly	Asp	Thr	Gly	Leu	
	915						920					925				
Pro	Arg	Val	Trp	Ala	Ala	Pro	Asp	Arg	Gly	Pro	Val	Pro	Ser	Thr	Ser	
	930					935					940					
Gly	Ile	Ser	Ser	Glu	Met	Leu	Ala	Ser	Gly	Pro	Ile	Glu	Val	Gly	Ser	
945				950					955					960		
Leu	Pro	Ala	Gly	Glu	Arg	Val	Ser	Arg	Pro	Glu	Ala	Ala	Val	Pro	Gly	
			965						970					975		
Tyr	Gln	His	Pro	Ser	Glu	Ala	Met	Asn	Ala	His	Thr	Pro	Gln	Phe	Phe	
			980					985					990			
Ile	Tyr	Lys	Ile	Asp	Ser	Ser	Asn	Arg	Glu	Gln	Arg	Leu	Glu	Asp	Lys	
		995					1000					1005				
Gly	Asp	Thr	Pro	Leu	Glu	Leu	Gly	Asp	Asp	Cys	Ser	Leu	Ala	Leu		
	1010					1015					1020					
Val	Trp	Arg	Asn	Asn	Glu	Arg	Leu	Gln	Glu	Phe	Val	Leu	Val	Ala		
	1025					1030						1035				
Ser	Lys	Glu	Leu	Glu	Cys	Ala	Glu	Asp	Pro	Gly	Ser	Ala	Gly	Glu		
	1040					1045						1050				
Ala	Ala	Arg	Ala	Gly	His	Phe	Thr	Leu	Asp	Gln	Cys	Leu	Asn	Leu		
	1055					1060						1065				
Phe	Thr	Arg	Pro	Glu	Val	Leu	Ala	Pro	Glu	Glu	Ala	Trp	Tyr	Cys		
	1070					1075					1080					
Pro	Gln	Cys	Lys	Gln	His	Arg	Glu	Ala	Ser	Lys	Gln	Leu	Leu	Leu		
	1085					1090					1095					
Trp	Arg	Leu	Pro	Asn	Val	Leu	Ile	Val	Gln	Leu	Lys	Arg	Phe	Ser		
	1100					1105						1110				
Phe	Arg	Ser	Phe	Ile	Trp	Arg	Asp	Lys	Ile	Asn	Asp	Leu	Val	Glu		
	1115					1120					1125					
Phe	Pro	Val	Arg	Asn	Leu	Asp	Leu	Ser	Lys	Phe	Cys	Ile	Gly	Gln		
	1130					1135						1140				
Lys	Glu	Glu	Gln	Leu	Pro	Ser	Tyr	Asp	Leu	Tyr	Ala	Val	Ile	Asn		
	1145					1150						1155				
His	Tyr	Gly	Gly	Met	Ile	Gly	Gly	His	Tyr	Thr	Ala	Cys	Ala	Arg		
	1160					1165						1170				

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Leu	Pro	Asn	Asp	Arg	Ser	Ser	Gln	Arg	Ser	Asp	Val	Gly	Trp	Arg
1175						1180					1185			
Leu	Phe	Asp	Asp	Ser	Thr	Val	Thr	Thr	Val	Asp	Glu	Ser	Gln	Val
1190						1195					1200			
Val	Thr	Arg	Tyr	Ala	Tyr	Val	Leu	Phe	Tyr	Arg	Arg	Arg	Asn	Ser
1205						1210					1215			
Pro	Val	Glu	Arg	Pro	Pro	Arg	Ala	Gly	His	Ser	Glu	His	His	Pro
1220						1225					1230			
Asp	Leu	Gly	Pro	Ala	Ala	Glu	Ala	Ala	Ala	Ser	Gln	Ala	Ser	Arg
1235						1240					1245			
Ile	Trp	Gln	Glu	Leu	Glu	Ala	Glu	Glu	Glu	Pro	Val	Pro	Glu	Gly
1250						1255					1260			
Ser	Gly	Pro	Leu	Gly	Pro	Trp	Gly	Pro	Gln	Asp	Trp	Val	Gly	Pro
1265						1270					1275			
Leu	Pro	Arg	Gly	Pro	Thr	Thr	Pro	Asp	Glu	Gly	Cys	Leu	Arg	Tyr
1280						1285					1290			
Phe	Val	Leu	Gly	Thr	Val	Ala	Ala	Leu	Val	Ala	Leu	Val	Leu	Asn
1295						1300					1305			
Val	Phe	Tyr	Pro	Leu	Val	Ser	Gln	Ser	Arg	Trp	Arg			
1310						1315					1320			

<210> SEQ ID NO 88

<211> LENGTH: 325

<212> TYPE: PRT

<213> ORGANISM: homo sapiens

<400> SEQUENCE: 88

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

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His Phe Gly Gly Lys Leu His Leu Gly Phe Ile Gln Ile Arg Glu Lys
 210 215 220
 Leu Asp Gln Leu Arg Lys Thr Val Ala Glu Lys Gln Glu Lys Arg Asn
 225 230 235 240
 Gln Asp Arg Leu Arg Arg Arg Glu Glu Arg Glu Arg Glu Glu Arg Leu
 245 250 255
 Ser Arg Arg Ser Gly Ser Arg Thr Arg Asp Arg Arg Arg Ser Arg Ser
 260 265 270
 Arg Asp Arg Arg Arg Arg Arg Ser Arg Ser Thr Ser Arg Glu Arg Arg
 275 280 285
 Lys Leu Ser Arg Ser Arg Ser Arg Asp Arg His Arg Arg His Arg Ser
 290 295 300
 Arg Ser Arg Ser His Ser Arg Gly His Arg Arg Ala Ser Arg Asp Arg
 305 310 315 320
 Ser Ala Lys Tyr Lys
 325

<210> SEQ ID NO 89
 <211> LENGTH: 181
 <212> TYPE: PRT
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 89

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

<210> SEQ ID NO 90
 <211> LENGTH: 217
 <212> TYPE: PRT
 <213> ORGANISM: homo sapiens

<400> SEQUENCE: 90

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

Val Leu His Gly Asn Gln Arg Lys Arg Arg Lys Phe Leu Glu Thr Val
 20 25 30

Glu Leu Gln Ile Ser Leu Lys Asn Tyr Asp Pro Gln Lys Asp Lys Arg
 35 40 45

Phe Ser Gly Thr Val Arg Leu Lys Ser Thr Pro Arg Pro Lys Phe Ser
 50 55 60

Val Cys Val Leu Gly Asp Gln Gln His Cys Asp Glu Ala Lys Ala Val
 65 70 75 80

Asp Ile Pro His Met Asp Ile Glu Ala Leu Lys Lys Leu Asn Lys Asn
 85 90 95

Lys Lys Leu Val Lys Lys Leu Ala Lys Lys Tyr Asp Ala Phe Leu Ala
 100 105 110

Ser Glu Ser Leu Ile Lys Gln Ile Pro Arg Ile Leu Gly Pro Gly Leu
 115 120 125

Asn Lys Ala Gly Lys Phe Pro Ser Leu Leu Thr His Asn Glu Asn Met
 130 135 140

Val Ala Lys Val Asp Glu Val Lys Ser Thr Ile Lys Phe Gln Met Lys
 145 150 155 160

Lys Val Leu Cys Leu Ala Val Ala Val Gly His Val Lys Met Thr Asp
 165 170 175

Asp Glu Leu Val Tyr Asn Ile His Leu Ala Val Asn Phe Leu Val Ser
 180 185 190

Leu Leu Lys Lys Asn Trp Gln Asn Val Arg Ala Leu Tyr Ile Lys Ser
 195 200 205

Thr Met Gly Lys Pro Gln Arg Leu Tyr
 210 215

<210> SEQ ID NO 91
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 91

tggcgcagaa aggaaaagga aaat

24

<210> SEQ ID NO 92
 <211> LENGTH: 23
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 92

agaggtagct ggcaggatgt tag

23

<210> SEQ ID NO 93
 <211> LENGTH: 20
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 93

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cttggtgcga tcagccttat 20

<210> SEQ ID NO 94
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 94

ttgatgcatg aaaacagaac tc 22

<210> SEQ ID NO 95
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 95

agaattggca gaggtcgtc atca 24

<210> SEQ ID NO 96
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 96

ttccaatttt gccttctcta actg 24

<210> SEQ ID NO 97
<211> LENGTH: 884
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (727)..(727)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (729)..(729)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (868)..(868)
<223> OTHER INFORMATION: n is a, c, g, or t

<400> SEQUENCE: 97

cacgaggcaa ggggtgcacc cccgcaggat ttccaaagaa ggccagtaga actgctagaa 60

tagcctccga tgaggaaatt caaggcacia aggatgctgt tattcaagac ctggaacgaa 120

aacttcgctt caaggaggac ctctgaaca atggccagcc gaggttaaca tacgaagaaa 180

gaatggctcg tcgactgcta ggtgctgaca gtgcaactgt ctttaatat caggagccag 240

aagaggaaac agctaatacag gaatacaaaag tctccagctg tgaacagaga ctcatcagtg 300

aaatagagta caggctagaa aggtctcctg tggatgaatc aggtgatgaa gttcagtatg 360

gagatgtgcc tgtggaaaat ggaatggcac cattctttga gatgaagctg aaacattaca 420

agatctttga gggaaatgcca gtaactttca catgtagagt ggctggaaat ccaaagccaa 480

agatctattg gtttaaagat gggaagcaga tctctccaaa gagtgatcac tacaccatc 540

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aaagagatct cgatgggacc tgctccctcc ataccacagc ctccacccta gatgatgatg    600
ggaattatac aattatggct gcaaacccctc agggccgcat cagttgtact ggacggctaa    660
tggtacaggc tgtcaaccaa agaggtegaa gtccccggtc tccctcaggc catcctcatg    720
tcagaangnc tcgttctaga tcaagggaca gtggagacga aaatgaccca attcaggagc    780
gattcttcag acctcacttc ttgcaggctc ctggagatct gactgggtcaa gaaggaaact    840
ctgcagatgg actgcaaaagt cagtgggnta ccaccccgaga tcta                    884

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<210> SEQ ID NO 98
<211> LENGTH: 886
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (695)..(695)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (731)..(731)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (740)..(740)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (798)..(798)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (807)..(807)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (809)..(809)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (844)..(844)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (852)..(852)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (857)..(857)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (876)..(876)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (878)..(878)
<223> OTHER INFORMATION: n is a, c, g, or t

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<400> SEQUENCE: 98

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cgaggggaaa ttacaatatg tgaccaaacc aaagcagatt tggactcgtc tctagatata    60
aaaaaaaaatc ctgttccatg tcagaaatat agtttacgga attcaagtaa tgttatgtta    120
gatgataaac aatgtaaaaa aaaacaaata caactgttaa ctaaaaaaag tgagtcgagc    180
atattacttt ctaaacaaac ttcagatttt ctgcaagtct gtaatgatac ttagagaaaa    240
tctgaactaa ctgttccctg tgatatagta atcgaccacc atgtttcata tgctgttttt    300
agtgctaatt caaaactact tctgaagaac tcagataaaa atgtccatag tatgtctatg    360

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ttggtgaaac ctaactcaag ccttggggga aaaactatgt gtaaaaatat gagtgatatg	420
caaaacagtc aatttaataa ctgtttggga tacttagaaa aactaatgt gaacatttcc	480
catcttcac ttaacaatga gaatagtcac gtttcacaag ccaaatgtg gaaaactgct	540
gttcacatga aaacttgcac agaacagag tttccaata aaaagaatca gattgatgag	600
aatcaggtaa ctgaagccac aaaaaatgac ctcttccttt ttgtgagcat taatgaaaga	660
cagcatacat tgtttaataa atacagagga aaacnggaat cattaaatga cattgtttcc	720
aggaaaaatg ntcagtgaan gacagctgga ggaatcacat tcatttcaca tagagcctct	780
ggagatttag taacagancg ggaaggnona cctttgatct ttcacttcag ataaaaaact	840
gagnaaactc cngtatnatg atttttcaga cccggnctg ggcaag	886

<210> SEQ ID NO 99

<211> LENGTH: 851

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 99

cacgaggggc gagaggccgg catcactgga gtggtggcgc agctgtttcc tccggatatc	60
catcaaatat tgagaagaaa gaatatcagg agcaaagtgt tctaagtgc tgctcagaac	120
gtaaagatgc gaaccccaaa tcagtggttt gttcattctt catgcaagag caatgcacta	180
aaggagagaa gcaagctgtg gtgatcagtg actttgggtga aagctaagaa ggttcaaaca	240
aatttgcaaa tgatatacaa cttctaagca ttccatattg gaagaagaga tttctacaca	300
tgaaaaaat gcctttgttt agtaaatcac acaaaaatcc agcagaaatt gtgaaaatcc	360
tgaaagacaa ttgggccatt ttggaaaagc aagacaaaaa gacagacaag gcttcagaag	420
aagtgtctaa atcactgcaa gcaatgaaag aaattctgtg tggtaacaac gagaaagaac	480
ccccaacaga agcagtggct cagctagcac aagaactcta cagcagtggc ctgctagtga	540
cactgatagc tgacctgcag ctgatagact ttgagggaaa aaaagatgtg acccagatat	600
ttaacaacat cttgagaaga cagataggca ctcgagtcct tactgtggag tatattagtg	660
ctcatcctca tatectgttt atgctcctca aaggatatga agccccacag attgccttac	720
gttgtgggga ttatgctgag agaattgatt cgacatgaac cccttgccaa aatcatcctc	780
ttttctaate aattcagaga tttctttagg tacgtggagt tgtccacatt tgatattgct	840
tcaaatgcct t	851

<210> SEQ ID NO 100

<211> LENGTH: 639

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 100

cgaggggatg acagtgtttt cattgcagtt aaagaaattg gtcgtgatct gtacaggggc	60
ttgcctacag aggaaaggat ccagaaacta gagttcatgt tggataagct acagaatgaa	120
attgatcagg agttggaaca caataattcc cttgttagag aagaaaaaga gacaactgat	180
acaaggaaaa aatcactttc ttctgctgcc ttagctaaat caggtgaaag gctacaagct	240
ctaacacttc ttatgattca ctacagagca ggcatggaag atatagaaac tttagaaagt	300
ctgtctttag accagcactc caaaaaata agcaagtaca cagatgatac agaagaagac	360

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cttgataatg aaataagcca actaatagac tctcagccat tcagcagcat atcagatgac 420
ttatttggcc catccgagtc tgtgtagcag acaggtctat ttaaactttc aaatgaacag 480
ggtaaagttg catctaaagt accacagata caacatgtt taaatcctcg tatgcactct 540
ggcctgcttc tccagttact tgcttgtgta agaacaaaaa tgagaaaggt tgttttccag 600
taaaaacatg accagcttac taaaaaaaaa aaaaaaaaaa 639

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<210> SEQ ID NO 101
<211> LENGTH: 907
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (797)..(797)
<223> OTHER INFORMATION: n is a, c, g, or t

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<400> SEQUENCE: 101
cgaggggtcat gtgccaaact gctcagcaag gaagaggaag caggtgttaa ggaattagca 60
aagcaggtga agagtttggc agtggttaaat tacaacctcc tcaagtatat ttgcagattc 120
ttggatgaag tacagtccta ctctgggagtt aacaaaatga gtgtgcagaa cttggcaacg 180
gtcttttggtc ctaatatcct gcgccccaaa gtggaagatc ctttgactat catggagggc 240
actgtgtgtg tccagcagtt gatgtcagtg atgattagca aacatgattg cctctttccc 300
aaagatgcag aactacaaag caagcccccga gatggagtga gcaacaacaa tgaatttcag 360
aagaaagcca ccatggggca gttacagaac aaggagaaca ataacaccaa ggacagccct 420
agtaggcagt gctcctggga caagtctgag tcaccccaga gaagcagcat gaacaatgga 480
tccccacag ctctatcagg cagcaaaaacc aacagcccaa agaacagtgt tcacaagcta 540
gatgtgtcta gaagccccc tctcatggtc aaaaagaacc cagcctttaa taagggtagt 600
gggatatgta ccaatgggtc cttcagcagc agtaatgcag aaggtcttga gaaaacccaa 660
accaccccc aatgggagcct acaggccaga aggagctctt cactgaaggt atctggtacc 720
aaaatgggca cgcacagtgt acagaatgga acggtgcgca tgggcatttt gaacagcgac 780
acactcgga accacnaat gttcgaacat gagctggctg ccaatggcta tgtgacctga 840
gggatacaag cagaagacag ctggagagta ggcacacaca gatgtccctt tgatatgtca 900
tcacagt 907

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<210> SEQ ID NO 102
<211> LENGTH: 931
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (881)..(881)
<223> OTHER INFORMATION: n is a, c, g, or t

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<400> SEQUENCE: 102
cgagggcaca acaaggcggc gccgccgag atccccgaca cccggcggga gctggcggag 60
ctcgtgaagc ggaagcagga gctggcggaa acattggcaa atttgagcg acagatctat 120
gcttttgagg gaagctacct ggaagacact cagatgtatg gcaatattat tctgggctgg 180
gatcggtatc tgaccaacca aaaaaactcc aatagcaaaa atgatcgaag gaaccggaag 240
tttaaggaag ctgagcggct cttcagtaaa tcctcgggta cctcagcagc tgcagtaagt 300

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gcattggcag gagttcagga ccagctcatt gaaaagaggg agccaggaag tgggacggaa    360
agtgcactt ctccagactt ccacaatcag gaaaatgagc ccagccagga ggaccttgag    420
gatctggatg gatctgtgca gggagtgaaa cctcagaagg ctgcttcttc tacttcctca    480
gggagtcacc acagcagcca taaaaagcga aagaataaaa accggcacag gattgatctg    540
aagttaaaca aaaaaccacg agctgactat tagaagacac attagtgcag aagcttcacg    600
gctgtagagc cctgcttccc ttctctgacc tcacaagat aaacatcctt cacctgagtt    660
cgtggccatc cactctgct ctcccagacc cagtgcctgt gactttgagt agtttgttct    720
aatgtgggtg acaacaagt catttctgta agacattggg tcttacttta tgtcattttt    780
agtaacagaa ctgcaggaag atcaagacat gttgtaatcc cggcaagttg ctactgtgcg    840
ttctcccttc ttatgatgatt gtctccccaa actggctggc ncagcttctc tgtgatacct    900
tcagaatggt ctctggtttg tttatgctga a                                931

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<210> SEQ ID NO 103
<211> LENGTH: 737
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (636)..(636)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (646)..(646)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (689)..(689)
<223> OTHER INFORMATION: n is a, c, g, or t

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<400> SEQUENCE: 103

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ggaagaacag catgctaaca catctgccc aaatgatgtg gagctacttc atcacaaaga    60
tgcacatgta gatttccctga aaagtgggtg ttgcgcatcta ggtggcggca gtcgagaagg    120
ctcgtttaaa gaaacaataa cattaaagtg gtgtacacca aggacaaata acattgaatt    180
acactattgt actggagctt atcggatttc acctgtagat gtaaatagta gaccttcctc    240
ctgccttact aattttcttc taaatggtcg ttctgtttta ttggaacaac cagcaaagtc    300
agggttctaaa gtcattagtc atatgcttag tagccatgga ggagagattt ttttgacgt    360
ccttagcagt tctcgatcca ttctagaaga tccaccttca attagtgaag gatgtggagg    420
aagagttaca gactaccggg attacagatt ttggtgaatt tatgagggaa aacagattaa    480
ctccttttct agaccocaga tataaaatcg atggaagtct tgaggctcct ttgggaacga    540
gcaaaagatc agttagaaaa acataccgt tactggccta tgatcatttc acaaaccacc    600
atttttaaca tgcaagcggg agttccatta gccagngtta ttgtgnaaaa aatctctgac    660
agaagagaat gtgttaaact gtcaaaaanc atatacaact tagttgatat ggaagaaaaa    720
atgatcctct acctatt                                737

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<210> SEQ ID NO 104
<211> LENGTH: 770
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature

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<222> LOCATION: (141)..(141)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (640)..(641)
<223> OTHER INFORMATION: n is a, c, g, or t

<400> SEQUENCE: 104

cgaggactac ttgtacctac aagacctgct actcgccaag ggctgattgg gagaataatg 60
gaatctgaaa atatggattc tgaaaatatg aagacagaaa atatggaatc tcaaaatgta 120
gactttgaga gtgtttcttc ngttacagct ctggaagccc tctctaagct acttaatcct 180
gaagaagagg atgattctga ctatggacag acaaatgggt tatctactat tggagccatg 240
ggctctggga atattggacc accccaaata gaagagctca aagtcatccc tgaaccagc 300
gaggaaaata atgaggacat ctggaattca gaagagattc cagaaggagc agaatatgat 360
gatatgtggg atgttagaga aatccagag tatgagatta tattcagaca gcagggtggga 420
actgaagata tatttttagg gttgtcaaaa aaggactcct caacaggttg tgcagtgaa 480
ctagtggcta aaattaattt gccaaataca aacccttctg atattcaaat tgatatccag 540
ggaaacaatc ctgaccttc gtactcctca gaagaagctg ttgataactc ttctgagct 600
gggtggaatgt accagtgcc aagcattcta tatccagan nactgaaact ctgaaatca 660
ctatgactat gaaaagagag ttagatattg ctaatttctt ctgaaactgc atgaaaaaga 720
taaaaagtag taaaatggca ttggtacaa ttaaaaaact ttgaaaaaag 770

<210> SEQ ID NO 105
<211> LENGTH: 920
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (687)..(687)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (750)..(750)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (807)..(807)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (810)..(810)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (826)..(827)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (849)..(849)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (870)..(870)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (874)..(874)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (882)..(882)
<223> OTHER INFORMATION: n is a, c, g, or t

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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (889)..(889)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (909)..(909)
<223> OTHER INFORMATION: n is a, c, g, or t

<400> SEQUENCE: 105

gaggctttac gcgcgtgcc ttcacccact ggttcttctc cttcgtggaa gacccgctga      60
tcgacttcga ggtgcgctcc cagtttgaag ggcgcccat gccccagctc acctccatca      120
tcgtcaacca gctcaagaag atcatcaagc gcaagcacac cctaccgaat tacaagatca      180
ggtttaagcc gttttttcca taccagacct tgcaaggatt tgaagaagat gaagagcata      240
tccatataca acaatgggca cttactgaag gccgtcttaa agttacgttg ttagaatgta      300
gcagggttact catttttggg tccatgaca gagaggcaaa tgttcattgc acacttgagt      360
taagcagtag tgtttgggaa gaaaaacaga ggagttctat taagacgggt gaattaataa      420
aaggaaatth acaaatgtgt ggacttacac ttcgtcttgt ccagtcaact gatgggtatg      480
ctgggcacgt catcattgaa actgtggctc caaactcgcc tgctgcaatt gcagatcttc      540
agcggggaga tcgacttata gccattggga ggtgtgaaaa tcacatcaac actgcaagtg      600
ttgaagctta tcaagcaggc tggtgaccga gtcctgggtg actatgaaag gcctgttggc      660
cagagtaatc aagggtcagt gctgcangat aactttggcc agttggaaga aaactttttg      720
tcaagctcat gccaatcggg ttatgaagan gaaactgccg ggttgacagt aaatactgaa      780
aagtaaagag ctgggattct gaatttngan aacttgcaa gtgganmtcc agagcccaaa      840
atgagttcna agatgaggca caatcattan gtcntagtcc cnaacgggnt ccaacaacac      900
ttttctatna aacccttggg                                     920

<210> SEQ ID NO 106
<211> LENGTH: 938
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (678)..(678)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (728)..(728)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (860)..(860)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (865)..(865)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (867)..(867)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (874)..(874)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (876)..(876)
<223> OTHER INFORMATION: n is a, c, g, or t
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (882)..(882)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (908)..(908)
<223> OTHER INFORMATION: n is a, c, g, or t

<400> SEQUENCE: 106

ctgcagaggc gccatcagga aaccaacctg tctaagctcc gaagcgggcc cgtgtccct      60
tgggcctcta agacgaacaa actcaatcag gctaagtctg aggggctaaa gaagtctgag      120
gaggatgaca tgattttggt ttcttgccag tgtgctggaa aggatgtgaa agccttggtt      180
gacacaggct gccatatataa tctcatctct ttggcctgtg tggacagatt gggactcaag      240
gagcatgtca aatcccacaa gcatgaagga gaaaagcttt ctctaccgcc gcatctcaaa      300
gtagtgggcc agattgagca cctagtgtgc acactgggct cctccgccct ggactgccc      360
gcagctgtgg ttgatgacaa tgagaaaaac ttgtcccttg gtctacagac tctccgatct      420
ctgaagtgtc tcataaactt ggataagcac cggctgtatc tggggaagac agacaaggaa      480
gaaatccctt ttgtggagac agtctctttg aatgaagaca acacttcaga agcataacta      540
cagcctgcag catgtctgtc cgtgtgcatg catacacacc gggttgacag attgagaaaa      600
ctgggtttga accaaatgcc gtagtgactt gctgtggacc aagtccttcc atctaataga      660
agctccaggg gctccttncc attcagacct ctctagacta tagtctatgc ttagagatct      720
tgtctggnta tggccattgt tttttactac ttgtatcact taacttatag accttttttg      780
acactgccag tctcactggg ggctatttct ctgctccttc cagaatttgc ttttattagt      840
caagtatagg gctgccaggn tctgngnccc atananatat gngcttcttt cctaagctaa      900
tggaataanaa caggacctga cttttaaaaa aaaaaaaaaa                        938

<210> SEQ ID NO 107
<211> LENGTH: 949
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (705)..(705)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (765)..(765)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (818)..(818)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (831)..(831)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (844)..(844)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (865)..(865)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (875)..(875)
<223> OTHER INFORMATION: n is a, c, g, or t
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (893)..(893)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (906)..(906)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (908)..(908)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (910)..(910)
<223> OTHER INFORMATION: n is a, c, g, or t
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (918)..(918)
<223> OTHER INFORMATION: n is a, c, g, or t

<400> SEQUENCE: 107

cacgaggggtg gtgtctgtca gacacacaca ggccgccagt gacttcacac acacctcatg      60
tgagaacccat gccctttttta gtgtgtccta ttccatacct gtacacactt cctcggttttg      120
taatgagatt tacttacacc caaacagatc ctgaaagaaa gcttcaagtt ttctcagatg      180
atggatatgt ttctactgta ttcaataact gacggatgta aggtgcacgt ttctgatgt      240
gacgcactgt attccagctg gtgatcaagt ctgggaacag ccgtaacagg tcaaccttgt      300
ggagccatcg cgaggttagag ggtgaaagat gccagaaaaa aaagtcttgt gtgtgagtgt      360
gttttttgag ttgtcatcaa tottaatgtc ttttcataat acctttataa tacattaagc      420
ctcttgtcta catatttgga gagaatatga ctttactagc agagaaatac aatatatctt      480
gtctactgga ctgtaaaaaa tatgtatgaa ataaaattag ttccatttgg tcttctagta      540
tattaaagtg ctatctgacg ttgttatcct gtttttgcaa aaaaaaaaaa aaaaaagtta      600
actacagacc attgtttcta ataagcagag agatctatct tagtagtaaa ctgaaggttt      660
agttgtgagc ttcagatttt gtgaactcca gatgttgtgc ggggnttttt tttttttttt      720
aagaccacca ctaaaaaatg ccaggaatat gtacctggga actgnagggg agctttcagt      780
attggaaaaa gattgttcta tacggacott ttgtgtntt atccgggatg naaaaaagcct      840
tcnnaaacct atgggaaaaa aaagngagca ctgantctcc cctgttcctt cngggaccct      900
tttgnnangn aaactgggct gtttttaaaa tgggactaaa aaaaaaaaaa      949

<210> SEQ ID NO 108
<211> LENGTH: 784
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 108

agaaggcttt ggcttctgat agtcatggac tcactaggct gctgaggaag atcaataata      60
cctactggaa tcagtcatga gaagtcaagc atggaaattg tgaatttgtg gtgtggccag      120
accagtacct ccaagtgttc agaagatgtg tgaccagaca aaacacagta aatgctgccc      180
agcaaaaggc aatcaatgct gccaccaca gcagaaccag tgctgccagt caaaaggcaa      240
tcaatgctgc ccacaaaaac agaaccagtg ctgccagcca aaaggcagtc aatgctgccc      300
acaaaaacac aatcactgct gccagccaaa acccccatgc tgcattcagg ccagggtgctg      360
tggtttggag accaagcctg aagtctcacc ccttaacatg gagtctgagc ccaactcacc      420
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gcaaactcag gacaagggct gtcaaaccga gcagcagccc catagccac aaaatgagtc 480
caggccaagc aaatgagagc agaagaagtc aaacaaagaa gaagtcctctg gggccatgcc 540
tttctactttg taggggtgggg gattactgag agtcaggcta gacctgtgtt tagagaagca 600
gttttcacag tgactacatc ttccacccaa tgagaggctc ctatttccca tcatagctcc 660
ctaccctagg gaggcctcca tctggaaatg ggaggatgaa gaggetagaa tcatctttcc 720
tagtgatcct gacatttaga cagcacagaa ataaagagca ataaaaagaa aaaaaaaaaa 780
aaaa 784

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<210> SEQ ID NO 109
<211> LENGTH: 294
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (242)..(243)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (289)..(289)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<400> SEQUENCE: 109

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

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Arg Xaa Xaa Arg Ser Arg Ser Arg Asp Ser Gly Asp Glu Asn Asp Pro
245 250 255

Ile Gln Glu Arg Phe Phe Arg Pro His Phe Leu Gln Ala Pro Gly Asp
260 265 270

Leu Thr Gly Gln Glu Gly Asn Ser Ala Asp Gly Leu Gln Ser Gln Trp
275 280 285

Xaa Thr Thr Pro Asp Leu
290

<210> SEQ ID NO 110
 <211> LENGTH: 226
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 110

Arg Gly Glu Ile Thr Asn Ser Asp Gln Thr Lys Ala Asp Leu Asp Ser
1 5 10 15

Ser Leu Asp Ile Lys Lys Asn Pro Val Pro Cys Gln Lys Tyr Ser Leu
20 25 30

Arg Asn Ser Ser Asn Val Met Leu Asp Asp Lys Gln Cys Lys Ile Lys
35 40 45

Gln Ile Gln Leu Leu Thr Lys Lys Ser Glu Cys Ser Ile Leu Leu Ser
50 55 60

Lys Gln Thr Ser Asp Phe Leu Gln Val Cys Asn Asp Thr Leu Glu Lys
65 70 75 80

Ser Glu Leu Thr Val Pro Cys Asp Ile Val Ile Asp His His Val Ser
85 90 95

Tyr Ala Ala Phe Ser Ala Asn Ser Lys Leu Leu Leu Lys Asn Ser Asp
100 105 110

Lys Asn Val His Ser Met Ser Met Leu Val Lys Pro Asn Ser Ser Pro
115 120 125

Gly Gly Lys Thr Met Cys Lys Asn Met Ser Asp Met Gln Asn Ser Gln
130 135 140

Phe Asn Asn Cys Leu Gly Tyr Leu Glu Asn Thr Asn Val Asn Ile Ser
145 150 155 160

His Leu His Leu Asn Asn Glu Asn Ser His Ala Ser Gln Ala Lys Asp
165 170 175

Val Lys Thr Ala Val His Met Lys Thr Cys Thr Glu Thr Glu Phe Ser
180 185 190

Asn Lys Lys Asn Gln Ile Asp Glu Asn Gln Val Thr Glu Ala Thr Lys
195 200 205

Asn Asp Leu Phe Leu Phe Val Ser Ile Asn Glu Arg Gln His Thr Leu
210 215 220

Phe Lys
225

<210> SEQ ID NO 111
 <211> LENGTH: 74
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 111

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

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Ser Gly Tyr Pro Ser Asn Ile Glu Lys Lys Glu Tyr Gln Glu Gln Ser
    20                      25                      30

Val Leu Ser Cys Cys Ser Glu Arg Lys Asp Ala Asn Pro Lys Ser Val
    35                      40                      45

Val Cys Ser Phe Phe Met Gln Glu Gln Cys Thr Lys Gly Glu Lys Gln
    50                      55                      60

Ala Val Val Ile Ser Asp Phe Gly Glu Ser
    65                      70

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<210> SEQ ID NO 112
<211> LENGTH: 148
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 112

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Arg Gly Asp Asp Ser Val Phe Ile Ala Val Lys Glu Ile Gly Arg Asp
  1                      5                      10                      15

Leu Tyr Arg Gly Leu Pro Thr Glu Glu Arg Ile Gln Lys Leu Glu Phe
    20                      25                      30

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

Asn Ser Leu Val Arg Glu Glu Lys Glu Thr Thr Asp Thr Arg Lys Lys
    50                      55                      60

Ser Leu Leu Ser Ala Ala Leu Ala Lys Ser Gly Glu Arg Leu Gln Ala
    65                      70                      75                      80

Leu Thr Leu Leu Met Ile His Tyr Arg Ala Gly Ile Glu Asp Ile Glu
    85                      90                      95

Thr Leu Glu Ser Leu Ser Leu Asp Gln His Ser Lys Lys Ile Ser Lys
    100                     105                     110

Tyr Thr Asp Asp Thr Glu Glu Asp Leu Asp Asn Glu Ile Ser Gln Leu
    115                     120                     125

Ile Asp Ser Gln Pro Phe Ser Ser Ile Ser Asp Asp Leu Phe Gly Pro
    130                     135                     140

Ser Glu Ser Val
145

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<210> SEQ ID NO 113
<211> LENGTH: 279
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (266)..(266)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid

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<400> SEQUENCE: 113

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Arg Gly Ser Cys Ala Lys Leu Leu Ser Lys Glu Glu Glu Ala Gly Val
  1                      5                      10                      15

Lys Glu Leu Ala Lys Gln Val Lys Ser Leu Pro Val Val Asn Tyr Asn
    20                      25                      30

Leu Leu Lys Tyr Ile Cys Arg Phe Leu Asp Glu Val Gln Ser Tyr Ser
    35                      40                      45

Gly Val Asn Lys Met Ser Val Gln Asn Leu Ala Thr Val Phe Gly Pro
    50                      55                      60

Asn Ile Leu Arg Pro Lys Val Glu Asp Pro Leu Thr Ile Met Glu Gly
    65                      70                      75                      80

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Thr Val Val Val Gln Gln Leu Met Ser Val Met Ile Ser Lys His Asp
 85 90 95
 Cys Leu Phe Pro Lys Asp Ala Glu Leu Gln Ser Lys Pro Gln Asp Gly
 100 105 110
 Val Ser Asn Asn Asn Glu Ile Gln Lys Lys Ala Thr Met Gly Gln Leu
 115 120 125
 Gln Asn Lys Glu Asn Asn Asn Thr Lys Asp Ser Pro Ser Arg Gln Cys
 130 135 140
 Ser Trp Asp Lys Ser Glu Ser Pro Gln Arg Ser Ser Met Asn Asn Gly
 145 150 155 160
 Ser Pro Thr Ala Leu Ser Gly Ser Lys Thr Asn Ser Pro Lys Asn Ser
 165 170 175
 Val His Lys Leu Asp Val Ser Arg Ser Pro Pro Leu Met Val Lys Lys
 180 185 190
 Asn Pro Ala Phe Asn Lys Gly Ser Gly Ile Val Thr Asn Gly Ser Phe
 195 200 205
 Ser Ser Ser Asn Ala Glu Gly Leu Glu Lys Thr Gln Thr Thr Pro Asn
 210 215 220
 Gly Ser Leu Gln Ala Arg Arg Ser Ser Ser Leu Lys Val Ser Gly Thr
 225 230 235 240
 Lys Met Gly Thr His Ser Val Gln Asn Gly Thr Val Arg Met Gly Ile
 245 250 255
 Leu Asn Ser Asp Thr Leu Gly Asn Pro Xaa Met Phe Glu His Glu Leu
 260 265 270
 Ala Ala Asn Gly Tyr Val Thr
 275

<210> SEQ ID NO 114
 <211> LENGTH: 190
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 114

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

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145	150	155	160
Gly Ser His His Ser Ser His Lys Lys Arg Lys Asn Lys Asn Arg His	165	170	175
Arg Ile Asp Leu Lys Leu Asn Lys Lys Pro Arg Ala Asp Tyr	180	185	190

<210> SEQ ID NO 115
 <211> LENGTH: 151
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 115

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

<210> SEQ ID NO 116
 <211> LENGTH: 184
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 116

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

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115	120	125
Pro Glu Tyr Glu Ile Ile Phe Arg Gln Gln Val Gly Thr Glu Asp Ile		
130	135	140
Phe Leu Gly Leu Ser Lys Lys Asp Ser Ser Thr Gly Cys Cys Ser Glu		
145	150	155
Leu Val Ala Lys Ile Lys Leu Pro Asn Thr Asn Pro Ser Asp Ile Gln		
165	170	175
Ile Asp Ile Gln Gly Asn Asn Pro		
180		

<210> SEQ ID NO 117

<211> LENGTH: 207

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 117

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

<210> SEQ ID NO 118

<211> LENGTH: 178

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 118

Leu Gln Arg Arg Leu Met Glu Thr Asn Leu Ser Lys Leu Arg Ser Gly		
1	5	10
Pro Arg Val Pro Trp Ala Ser Lys Thr Asn Lys Leu Asn Gln Ala Lys		
20	25	30
Ser Glu Gly Leu Lys Lys Ser Glu Glu Asp Asp Met Ile Leu Val Ser		

-continued

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

Glu Ala

<210> SEQ ID NO 119
 <211> LENGTH: 69
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 119

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

<210> SEQ ID NO 120
 <211> LENGTH: 116
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 120

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

-continued

Lys Gly Cys Gln Thr Gln Gln Gln Pro His Ser Pro Gln Asn Glu Ser
 100 105 110

Arg Pro Ser Lys
 115

<210> SEQ ID NO 121
 <211> LENGTH: 372
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 121

atgcgggtca gcaaacccctt tgggatgctc atgctctcca tttggatcct gctgttcgtg 60
 tgctactacc tgctactacta cctgtgctcc gggtcctcat attttgtgct tgcaaatgga 120
 catatcctgc ccaacagtga aaatgctcat ggccaatctc tggaagaaga ttccgcattg 180
 gaagctttgc tgaatttttt ctttccaaca acttgcaatc tgagggaaaa tcaggtggca 240
 aagccttgta atgagctgca agatcttagt gagagtgaat gtttgagaca caaatgctgt 300
 ttttcatcat cggggaccac gagcttcaaa tgttttgctc catttagaga tgtgcctaaa 360
 cagatgatgc aa 372

<210> SEQ ID NO 122
 <211> LENGTH: 124
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 122

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

<210> SEQ ID NO 123
 <211> LENGTH: 129
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 123

acttgcaatc tgagggaaaa tcaggtggca aagccttgta atgagctgca agatcttagt 60
 gagagtgaat gtttgagaca caaatgctgt ttttcatcat cggggaccac gagcttcaaa 120
 tgttttgct 129

-continued

<210> SEQ ID NO 124

<211> LENGTH: 43

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 124

Thr Cys Asn Leu Arg Glu Asn Gln Val Ala Lys Pro Cys Asn Glu Leu
1 5 10 15

Gln Asp Leu Ser Glu Ser Glu Cys Leu Arg His Lys Cys Cys Phe Ser
20 25 30

Ser Ser Gly Thr Thr Ser Phe Lys Cys Phe Ala
35 40

<210> SEQ ID NO 125

<211> LENGTH: 30

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 125

aagaaacaaa gaaggaagcg aaagaggaag 30

<210> SEQ ID NO 126

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 126

Lys Lys Gln Arg Arg Lys Arg Lys Arg Lys
1 5 10

<210> SEQ ID NO 127

<211> LENGTH: 75

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 127

atgcgggtca gcaaaccctt tgggatgctc atgctctcca tttggatcct gctgttcgtg 60

tgctactacc tgtcc 75

<210> SEQ ID NO 128

<211> LENGTH: 25

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 128

Met Arg Val Ser Lys Pro Phe Gly Met Leu Met Leu Ser Ile Trp Ile
1 5 10 15

Leu Leu Phe Val Cys Tyr Tyr Leu Ser
20 25

<210> SEQ ID NO 129

<211> LENGTH: 69

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 129

atgtttgggc ttggtgcgat cagccttata ctggtatgta tgcccattta ttgccgctct 60

cttttctgg 69

-continued

<210> SEQ ID NO 130
 <211> LENGTH: 23
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 130

Met Phe Gly Leu Gly Ala Ile Ser Leu Ile Leu Val Cys Leu Pro Ile
 1 5 10 15
 Tyr Cys Arg Ser Leu Phe Trp
 20

<210> SEQ ID NO 131
 <211> LENGTH: 582
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 131

atgcgggtca gcaaacccctt tgggatgctc atgctctcca tttggatcct gctgttcgtg 60
 tgctactacc tgcctacta cctgtgctcc gggtcctcat atttgtgct tgcaaatgga 120
 catacctgc ccaacagtga aaatgctcat ggccaatctc tggaagaaga ttccgcattg 180
 gaagctttgc tgaattttt ctttccaaca acttgcaatc tgagggaaaa tcaggtggca 240
 aagccttgta atgagctgca agatcttagt gagagtgaat gtttgagaca caaatgctgt 300
 ttttcatcat cggggaccac gagcttcaaa tgttttgctc catttagaga tgtgcctaaa 360
 cagatgatgc aaatgtttgg gcttgggtgcg atcagcctta tcctgggatg tctgcccatt 420
 tattgccgct ctctttttctg gaggagcgaa ccggccgatg atttacaag gcaggacaac 480
 agagttgtaa cgggtttgaa gaaacaaaga aggaagcgaa agaggaagtc tgaaatgtta 540
 cagaaagcag caagaggacg tgaggaacat ggtgacgagc tc 582

<210> SEQ ID NO 132
 <211> LENGTH: 193
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 132

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

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Leu	Phe	Trp	Arg	Ser	Glu	Pro	Ala	Asp	Asp	Leu	Gln	Arg	Gln	Asp	Asn
145					150					155					160
Arg	Val	Val	Thr	Gly	Leu	Lys	Lys	Gln	Arg	Arg	Lys	Arg	Lys	Arg	Lys
				165					170					175	
Ser	Glu	Met	Leu	Gln	Lys	Ala	Ala	Arg	Gly	Arg	Glu	Glu	His	Gly	Asp
			180					185					190		

Glu

<210> SEQ ID NO 133
 <211> LENGTH: 717
 <212> TYPE: DNA
 <213> ORGANISM: Mus musculus

<400> SEQUENCE: 133

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atgccttcgg atcgaaggcc aagtcagaga aggaatagat ctaagagccg tgattatcgt      60
gggtgcacggt caaaggtaac aagagctgat acgaggaaca gagacgatac tcttgccctc      120
agtatgtatc aggggcctcc gagtgccgac caggggaaca acatggcgga tgcccctcgg      180
tttggcttct ggacttcagt aagccaatgt ctgcaatact tgtgggccag gaggcacttg      240
ggcctgcttc tacttttatt ctggacgctg gtgacccgtg tccgtcctgt gaacactgcg      300
aaattgcccc ttcttgctga agctgcagaa cttgaacccc ctttgggaaa tatgttggac      360
tttttctttc caacagcctg catcataagg gacaaccagg tgggtggtggc atgtaataac      420
cagccgtatc ttagcgagag tgaatgttta aaatccaagt gctgttcttc aacatctggg      480
actataatca aatgctatgc cccagtaagg gacaagccta cacagggtct acgggtgttt      540
ggccttgctg cgatcagcat tctagtcctg ggatttctgc ctatgtgctg ctgctccatg      600
tgctggagga ggaagaggat gaacaggatg ttgaagggtt tgaagaaaca gaaatcaaaa      660
gggaagaagc ctaaggaag gaaggcgtca gaagagagag ctttactgtc ccattga      717

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<210> SEQ ID NO 134
 <211> LENGTH: 238
 <212> TYPE: PRT
 <213> ORGANISM: Mus musculus

<400> SEQUENCE: 134

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

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130	135	140	
Ser Glu Ser Glu Cys Leu Lys Ser Lys Cys Cys Ser Ser Thr Ser Gly			
145	150	155	160
Thr Ile Ile Lys Cys Tyr Ala Pro Val Arg Asp Lys Pro Thr Gln Val			
	165	170	175
Leu Arg Val Phe Gly Leu Ala Ala Ile Ser Ile Leu Val Leu Gly Phe			
	180	185	190
Leu Pro Met Cys Cys Cys Ser Met Cys Trp Arg Arg Lys Arg Met Asn			
	195	200	205
Arg Met Leu Lys Val Leu Lys Lys Gln Lys Ser Lys Gly Lys Lys Pro			
	210	215	220
Lys Gly Arg Lys Ala Ser Glu Glu Arg Ala Leu Leu Ser His			
225	230	235	
<210> SEQ ID NO 135			
<211> LENGTH: 22			
<212> TYPE: DNA			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic Oligonucleotide			
<400> SEQUENCE: 135			
cccggagcac gtcgaggtct ac			22
<210> SEQ ID NO 136			
<211> LENGTH: 19			
<212> TYPE: DNA			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic Oligonucleotide			
<400> SEQUENCE: 136			
ggtgaggggc ccaggaagc			19
<210> SEQ ID NO 137			
<211> LENGTH: 21			
<212> TYPE: DNA			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic Oligonucleotide			
<400> SEQUENCE: 137			
cacaatgtat cctgttgaaa g			21
<210> SEQ ID NO 138			
<211> LENGTH: 20			
<212> TYPE: DNA			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic Oligonucleotide			
<400> SEQUENCE: 138			
gagatgatac attcttccag			20
<210> SEQ ID NO 139			
<211> LENGTH: 21			
<212> TYPE: DNA			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic Oligonucleotide			

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<400> SEQUENCE: 139

cttcgcgcaa ctctcctac c

21

<210> SEQ ID NO 140

<211> LENGTH: 20

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 140

gatgcccgtg tcttgctctt

20

<210> SEQ ID NO 141

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 141

cactaggctg ctgaggaaga t

21

<210> SEQ ID NO 142

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 142

gttttggtgg gcagcattga g

21

<210> SEQ ID NO 143

<211> LENGTH: 18

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 143

ggaccacccc aaatagaa

18

<210> SEQ ID NO 144

<211> LENGTH: 17

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 144

ccaccagctc aggaaga

17

<210> SEQ ID NO 145

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 145

tctgatggag cggtagggatg c

21

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<210> SEQ ID NO 146
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 146
gtgtgcctcg gcttctttct tc 22

<210> SEQ ID NO 147
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 147
tggtagcgtc agccttatcc 20

<210> SEQ ID NO 148
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 148
cggttcgctc ctccagaa 18

<210> SEQ ID NO 149
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 149
tgtctgcccc tttattgccc ctctct 26

<210> SEQ ID NO 150
<211> LENGTH: 795
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 150
catatgtctt cacataggag gaaagcgaag gggaggaata ggagaagtca ccgtgccatg 60
cgtgtggctc acttagagct ggcaacttat gagttggcgg caactgagtc gaatcccgag 120
agcagccatc ctggatacga ggccgccatg gctgacaggc ctcagccagg atggcgggaa 180
tctctaaaga tgcgggtcag caaacccctt gggtatgctc tgcctccat ttggatcctg 240
ctgttcgtgt gctactacct gtctactac ctgtgctccg ggtcctcata ttttgtgctt 300
gcaaatggac atatcctgcc caacagtga aatgctcatg gccaatctct ggaagaagat 360
tccgcattgg aagcttttgt gaattttttc tttccaacaa cttgcaatct gagggaaaaa 420
caggtagcaa agccttgtaa tgagctgcaa gatcttagtg agagtgaatg tttgagacac 480
aaatgctgtt tttcatcatc ggggaccacg agcttcaaat gttttgctcc atttagagat 540

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gtgcctaaac agatgatgca aatgtttggg cttggtgcga tcagccttat cctggtatgt    600
ctgcccattt attgccgctc tcttttctgg aggagcgaac cggccgatga ttacaaagg    660
caggacaaca gagttgtaac gggtttgaag aaacaaagaa ggaagcgaaa gaggaagtct    720
gaaatgttac agaaagcagc aagaggacgt gaggaacatg gtgacgagct cgagcaccac    780
caccaccacc actga                                                    795

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<210> SEQ ID NO 151
<211> LENGTH: 263
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

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<400> SEQUENCE: 151

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

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<210> SEQ ID NO 152
<211> LENGTH: 609
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 152

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catatgcggg tcagcaaac ctttgggatg ctcatgctct ccatttggat cctgctgttc      60
gtgtgctact acctgtccta ctacctgtgc tccgggtcct catattttgt gcttgcaaat      120
ggacatatcc tgcccaacag tgaaaatgct catggccaat ctctggaaga agattccgca      180
ttggaagcctt tgcgtaatTT tttctttcca acaacttgca atctgaggga aaatcagggtg      240
gcaaagcctt gtaatgagct gcaagatcct agtgagagtg aatgtttgag acacaaatgc      300
tgTTTTTcat catcggggac cacgagcttc aaatgttttg ctccatttag agatgtgcct      360
aaacagatga tgcaaatggt tgggcttggt gcgatcagcc ttatcctggt atgtctgccc      420
atttattgcc gctctctttt ctggaggagc gaaccggccg atgatttaca aaggcaggac      480
aacagagttg taacgggttt gaagaaacaa agaaggaagc gaaagaggaa gtctgaaatg      540
ttacagaaag cagcaagagg acgtgaggaa catggtgacg agctcgagca ccaccaccac      600
caccactga                                         609

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<210> SEQ ID NO 153

<211> LENGTH: 201

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 153

```

Met Arg Val Ser Lys Pro Phe Gly Met Leu Met Leu Ser Ile Trp Ile
1           5           10           15

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

Ser Tyr Phe Val Leu Ala Asn Gly His Ile Leu Pro Asn Ser Glu Asn
35           40           45

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

Asn Phe Phe Phe Pro Thr Thr Cys Asn Leu Arg Glu Asn Gln Val Ala
65           70           75           80

Lys Pro Cys Asn Glu Leu Gln Asp Leu Ser Glu Ser Glu Cys Leu Arg
85           90           95

His Lys Cys Cys Phe Ser Ser Ser Gly Thr Thr Ser Phe Lys Cys Phe
100          105          110

Ala Pro Phe Arg Asp Val Pro Lys Gln Met Met Gln Met Phe Gly Leu
115          120          125

Gly Ala Ile Ser Leu Ile Leu Val Cys Leu Pro Ile Tyr Cys Arg Ser
130          135          140

Leu Phe Trp Arg Ser Glu Pro Ala Asp Asp Leu Gln Arg Gln Asp Asn
145          150          155          160

Arg Val Val Thr Gly Leu Lys Lys Gln Arg Arg Lys Arg Lys Arg Lys
165          170          175

Ser Glu Met Leu Gln Lys Ala Ala Arg Gly Arg Glu Glu His Gly Asp
180          185          190

Glu Leu Glu His His His His His His
195          200

```

-continued

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<210> SEQ ID NO 154
<211> LENGTH: 405
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 154

catatgctggg tcagcaaacc ctttgggatg ctcctgctct ccatttggat cctgctgttc      60
gtgtgctact acctgtccta ctacctgtgc tccgggtcct catattttgt gcttgcaaat      120
ggacatatcc tgcccaacag tgaaaatgct catggccaat ctctggaaga agattccgca      180
ttggaagcctt tgcgtgaattt tttctttcca acaacttgca atctgaggga aaatcagggtg      240
gcaaagcctt gtaatgagct gcaagatcct agtgagagtg aatgtttgag acacaaatgc      300
tgtttttcat catcggggac cactgagcttc aaatgttttg ctccatttag agatgtgcct      360
aaacagatga tgcaaatgct cgagcaccac caccaccacc actga                          405

```

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<210> SEQ ID NO 155
<211> LENGTH: 133
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 155

Met Arg Val Ser Lys Pro Phe Gly Met Leu Met Leu Ser Ile Trp Ile
1          5          10          15

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

Ser Tyr Phe Val Leu Ala Asn Gly His Ile Leu Pro Asn Ser Glu Asn
35          40          45

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

Asn Phe Phe Phe Pro Thr Thr Cys Asn Leu Arg Glu Asn Gln Val Ala
65          70          75          80

Lys Pro Cys Asn Glu Leu Gln Asp Leu Ser Glu Ser Glu Cys Leu Arg
85          90          95

His Lys Cys Cys Phe Ser Ser Ser Gly Thr Thr Ser Phe Lys Cys Phe
100         105         110

Ala Pro Phe Arg Asp Val Pro Lys Gln Met Met Gln Met Leu Glu His
115         120         125

His His His His His
130

```

```

<210> SEQ ID NO 156
<211> LENGTH: 38
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 156

cacacacaca tatgttttca cataggagga aagcgaag      38

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<210> SEQ ID NO 157
<211> LENGTH: 35

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-continued

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 157

cacacactcg agctcgtcac catgttcctc acgtc 35

<210> SEQ ID NO 158
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 158

cacacacaca tatgcggggc agcaaacctc ttggga 36

<210> SEQ ID NO 159
<211> LENGTH: 35
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 159

cacacactcg agctcgtcac catgttcctc acgtc 35

<210> SEQ ID NO 160
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 160

cacacacaca tatgcggggc agcaaacctc ttggga 36

<210> SEQ ID NO 161
<211> LENGTH: 34
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 161

cacacactcg agcatttgca tcattctgtt aggc 34

<210> SEQ ID NO 162
<211> LENGTH: 936
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 162

gaattccttc tgggccacgg actgccggac cgttgggctg tgaggcagcg tctcagcgag 60

gcggcacccg gagccatgtc ttcacatagg aggaaagcga agggaggagg taggagaagt 120

caccgtgcc a tgcgtgtggc tcacttagag ctggcaactt atgagttggc ggcaactgag 180

tcgaatccc agagcagcca tcttgatag gaggcggcca tggctgacag gcctcagcca 240

ggatggcggg aatctctaaa gatcggggc agcaaacctc ttgggatgct catgctctcc 300

-continued

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atttggatcc tgctgttcgt gtgctactac ctgtcctact acctgtgtctc cgggtcctca   360
tattttgtgc ttgcaaatgg acatatcctg cccaacagtg aaaatgctca tggccaatct   420
ctggaagaag attccgcatt ggaagctttg ctgaattttt tctttccaac aacttgcaat   480
ctgagggaaa atcaggtggc aaagccttgt aatgagctgc aagatcttag tgagagtga   540
tgtttgagac acaaatgctg tttttcatca tcggggacca cgagcttcaa atgttttgct   600
ccatttagag atgtgcctaa acagatgatg caaatgtttg ggcttggtgc gatcagcctt   660
atcctggtat gtctgcccac ttattgccgc tctcttttct ggaggagcga accggccgat   720
gatttacaaa ggcaggacaa cagagttgta acgggtttga agaaacaaag aaggaagcga   780
aagaggaagt ctgaaatggt acagaaagca gcaagaggac gtgaggaaca tggtgacgag   840
ctcagagtcta gagggccctt cgaaggtaag cctatcccta accctctcct cgtctcgcgt   900
tctacgcgta cgggtcatca tcaccatcac cattga                               936

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<210> SEQ ID NO 163

<211> LENGTH: 311

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polypeptide

<400> SEQUENCE: 163

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

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225	230	235	240
Asp Leu Gln Arg Gln Asp Asn Arg Val Val Thr Gly Leu Lys Lys Gln			
245	250	255	
Arg Arg Lys Arg Lys Arg Lys Ser Glu Met Leu Gln Lys Ala Ala Arg			
260	265	270	
Gly Arg Glu Glu His Gly Asp Glu Leu Glu Ser Arg Gly Pro Phe Glu			
275	280	285	
Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr Arg Thr			
290	295	300	
Gly His His His His His His			
305	310		

<210> SEQ ID NO 164
 <211> LENGTH: 67
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 164

gggaattcat gtcttcacat aggaggaaag cgcacacact cgagctcgtc accatgttcc	60
tcacgtc	67

<210> SEQ ID NO 165
 <211> LENGTH: 73
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 165

cacacacaca tatgtcttca cataggagga aagcgaagca cacactcgag ctcgtcacca	60
tggtctctcac gtc	73

<210> SEQ ID NO 166
 <211> LENGTH: 74
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 166

cacacacaca tatgcgggtc agcaaacocct ttgggacaca cacacatatg tcttcacata	60
ggaggaaagc gaag	74

<210> SEQ ID NO 167
 <211> LENGTH: 39
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic Oligonucleotide

<400> SEQUENCE: 167

tactcccctg cctcaacaa gctcaggcgg ctcataggg	39
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What is claimed is:

1-179. (canceled)

180. An isolated binding polypeptide that selectively binds to a polypeptide consisting of a sequence as set forth as SEQ ID NO: 55 or a fragment thereof that is at least 8 amino acids in length.

181. The isolated binding polypeptide of claim **180**, wherein the fragment is at least 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, 75 or 100 amino acids in length.

182-189. (canceled)

190. The isolated binding polypeptide of claim **180**, wherein the isolated binding polypeptide is an antibody or an antigen-binding fragment thereof.

191. A method for diagnosing cancer in a subject comprising:

obtaining a biological sample from a subject, and determining the expression of a sarcoma-associated antigen in the biological sample by contacting the sample with an isolated binding polypeptide of claim **180**, wherein the expression of the sarcoma-associated antigen in the sample is diagnostic for cancer in the subject.

192-195. (canceled)

196. The method of claim **191**, wherein the isolated binding polypeptide is an antibody or antigen-binding fragment thereof.

197. The isolated binding polypeptide of claim **190**, wherein the antibody is a monoclonal, chimeric, human, humanized or single chain antibody; or wherein the antigen-binding fragment is a F(ab')₂, Fab, Fd, or Fv fragment.

198-200. (canceled)

201. The isolated binding polypeptide of claim **190**, wherein the antibody or antigen-binding fragment is labeled with a detectable label.

202. The isolated binding polypeptide of claim **201**, wherein the detectable label is a fluorescent or radioactive label.

203. The method of claim **191**, wherein the sample is selected from the group consisting of tissue, cells, and blood.

204. The method of claim **191**, wherein the cancer is a sarcoma.

205. A method for determining onset, progression, or regression, of cancer in a subject comprising:

obtaining from a subject a first biological sample, determining the expression of a sarcoma-associated antigen in the first sample by contacting the first sample with an isolated binding polypeptide of claim **180**, obtaining from the subject a second biological sample, determining the expression of the sarcoma-associated antigen in the second sample by contacting the second sample with the isolated binding polypeptide of claim **180**, and

comparing the expression in the first sample to the expression in the second sample as a determination of the onset, progression, or regression of the cancer.

206-209. (canceled)

210. The method of claim **205**, wherein the isolated binding polypeptide is an antibody or antigen-binding fragment thereof.

211-214. (canceled)

215. The method of claim **205**, wherein the sample is selected from the group consisting of tissue, cells, and blood.

216. The method of claim **205**, wherein the cancer is a sarcoma.

217. A kit for the diagnosis of cancer in a subject, comprising:

one or more isolated binding polypeptides of claim **180** and instructions for the use of the one or more isolated binding polypeptides in the diagnosis of cancer.

218. The kit of claim **217**, wherein the one or more isolated binding polypeptides are antibodies or antigen-binding fragments thereof.

219. The kit of claim **217**, wherein the one or more isolated binding polypeptides are bound to a substrate.

220. The kit of claim **217**, further comprising one or more agents that bind specifically to a cancer-associated antigen other than a polypeptide consisting of a sequence as set forth as SEQ ID NO: 55 or a fragment thereof that is at least 8 amino acids in length.

221. The kit of claim **217**, wherein the cancer is a sarcoma.

222-249. (canceled)

250. A composition, comprising:

an isolated binding polypeptide of claim **180**.

251-253. (canceled)

254. The composition of claim **250**, wherein the isolated binding polypeptide is an antibody or antigen-binding fragment thereof.

255. The composition of claim **254**, wherein the antibody is a monoclonal, chimeric, human, humanized or single chain antibody; or wherein the antigen-binding fragment is a F(ab')₂, Fab, Fd, or Fv fragment.

256-258. (canceled)

259. The composition of claim **254**, wherein the antibody or antigen-binding fragment is conjugated to a cytotoxic or chemotherapeutic agent.

260. The composition of claim **250**, further comprising a cytotoxic or chemotherapeutic agent.

261. The composition of claim **250**, further comprising a pharmaceutically acceptable carrier.

262-275. (canceled)

* * * * *

专利名称(译)	人肉瘤相关抗原		
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申请号	US12/683374	申请日	2010-01-06
[标]申请(专利权)人(译)	路德维格癌症研究所		
申请(专利权)人(译)	路德维希癌症研究所有限公司.		
当前申请(专利权)人(译)	路德维希癌症研究所		
[标]发明人	SCANLAN MATTHEW J SCANLAN CYNTHIA H LEE SANG YULL OLD LLOYD J		
发明人	SCANLAN, MATTHEW J. SCANLAN, CYNTHIA H. LEE, SANG-YULL OLD, LLOYD J.		
IPC分类号	A61K39/395 C07K16/00 G01N33/53 A61P35/00		
CPC分类号	A61K38/00 Y10T436/143333 G01N33/57488 C07K14/4748		
优先权	PCT/US2003/030870 2003-09-30 WO		
其他公开文献	US8252903		
外部链接	Espacenet USPTO		

摘要(译)

本发明涉及肉瘤相关抗原和编码它们的核酸分子。本发明进一步涉及与肉瘤相关的核酸分子，多肽及其片段在用于诊断和治疗诸如癌症的疾病的方法和组合物中的用途。更具体地，本发明涉及新型癌症/睾丸（CT）抗原NY-SAR-35的发现。

