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(54) Titre : COMPOSES ET PROCEDES DE THERAPIE ET DE DIAGNOSTIC DU CANCER DU POUMON

(54) Title: COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

(57) Abrégé/Abstract:

Compounds and methods for the treatment and diagnosis of lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or DNA molecules encoding such polypeptides, are also provided, together with DNA molecules for preparing the inventive polypeptides.

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(54) Title: COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

(57) Abstract: Compounds and methods for the treatment and diagnosis of lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or DNA molecules encoding such polypeptides, are also provided, together with DNA molecules for preparing the inventive polypeptides.



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COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

TECHNICAL FIELD

5 The present invention relates generally to therapy and diagnosis of cancer, such as lung cancer. The invention is more specifically related to polypeptides comprising at least a portion of a lung tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of lung cancer, and for the
10 diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

 Lung cancer is the primary cause of cancer death among both men and women in the U.S., with an estimated 172,000 new cases being reported in 1994. The five-year survival rate among all lung cancer patients, regardless of the stage of disease
15 at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among cases detected while the disease is still localized. However, only 16% of lung cancers are discovered before the disease has spread.

 Early detection is difficult since clinical symptoms are often not seen until the disease has reached an advanced stage. Currently, diagnosis is aided by the
20 use of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic examination of the bronchial passages. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In spite of considerable research into therapies for the disease, lung cancer remains difficult to treat.

25 Accordingly, there remains a need in the art for improved vaccines, treatment methods and diagnostic techniques for lung cancer.

SUMMARY OF THE INVENTION

 Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as lung cancer. In one aspect, the present

invention provides polypeptides comprising at least a portion of a lung tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; (b) variants of a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; and (c) complements of a sequence of (a) or (b). In specific embodiments, the polypeptides of the present invention comprise at least a portion of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 152, 155, 156, 165, 166, 169, 170, 172, 174, 176, 226-252, 338-344 and 346, and variants thereof.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a lung tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a lung tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical
5 compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an
10 antigen presenting cell that expresses a polypeptide as described above, and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

15 Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an
20 immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for
25 removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the
30 development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Determined T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells determined from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a lung tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be lung cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the

sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

5

SEQUENCE IDENTIFIERS

SEQ ID NO: 1 is the determined cDNA sequence for LST-S1-2

SEQ ID NO: 2 is the determined cDNA sequence for LST-S1-28

SEQ ID NO: 3 is the determined cDNA sequence for LST-S1-90

10

SEQ ID NO: 4 is the determined cDNA sequence for LST-S1-144

SEQ ID NO: 5 is the determined cDNA sequence for LST-S1-133

SEQ ID NO: 6 is the determined cDNA sequence for LST-S1-169

SEQ ID NO: 7 is the determined cDNA sequence for LST-S2-6

SEQ ID NO: 8 is the determined cDNA sequence for LST-S2-11

15

SEQ ID NO: 9 is the determined cDNA sequence for LST-S2-17

SEQ ID NO: 10 is the determined cDNA sequence for LST-S2-25

SEQ ID NO: 11 is the determined cDNA sequence for LST-S2-39

SEQ ID NO: 12 is a first determined cDNA sequence for LST-S2-43

SEQ ID NO: 13 is a second determined cDNA sequence for LST-S2-43

20

SEQ ID NO: 14 is the determined cDNA sequence for LST-S2-65

SEQ ID NO: 15 is the determined cDNA sequence for LST-S2-68

SEQ ID NO: 16 is the determined cDNA sequence for LST-S2-72

SEQ ID NO: 17 is the determined cDNA sequence for LST-S2-74

SEQ ID NO: 18 is the determined cDNA sequence for LST-S2-103

25

SEQ ID NO: 19 is the determined cDNA sequence for LST-S2-N1-1F

SEQ ID NO: 20 is the determined cDNA sequence for LST-S2-N1-2A

SEQ ID NO: 21 is the determined cDNA sequence for LST-S2-N1-4H

SEQ ID NO: 22 is the determined cDNA sequence for LST-S2-N1-5A

SEQ ID NO: 23 is the determined cDNA sequence for LST-S2-N1-6B

30

SEQ ID NO: 24 is the determined cDNA sequence for LST-S2-N1-7B

SEQ ID NO: 25 is the determined cDNA sequence for LST-S2-N1-7H

- SEQ ID NO: 26 is the determined cDNA sequence for LST-S2-N1-8A
SEQ ID NO: 27 is the determined cDNA sequence for LST-S2-N1-8D
SEQ ID NO: 28 is the determined cDNA sequence for LST-S2-N1-9A
SEQ ID NO: 29 is the determined cDNA sequence for LST-S2-N1-9E
5 SEQ ID NO: 30 is the determined cDNA sequence for LST-S2-N1-10A
SEQ ID NO: 31 is the determined cDNA sequence for LST-S2-N1-10G
SEQ ID NO: 32 is the determined cDNA sequence for LST-S2-N1-11A
SEQ ID NO: 33 is the determined cDNA sequence for LST-S2-N1-12C
SEQ ID NO: 34 is the determined cDNA sequence for LST-S2-N1-12E
10 SEQ ID NO: 35 is the determined cDNA sequence for LST-S2-B1-3D
SEQ ID NO: 36 is the determined cDNA sequence for LST-S2-B1-6C
SEQ ID NO: 37 is the determined cDNA sequence for LST-S2-B1-5D
SEQ ID NO: 38 is the determined cDNA sequence for LST-S2-B1-5F
SEQ ID NO: 39 is the determined cDNA sequence for LST-S2-B1-6G
15 SEQ ID NO: 40 is the determined cDNA sequence for LST-S2-B1-8A
SEQ ID NO: 41 is the determined cDNA sequence for LST-S2-B1-8D
SEQ ID NO: 42 is the determined cDNA sequence for LST-S2-B1-10A
SEQ ID NO: 43 is the determined cDNA sequence for LST-S2-B1-9B
SEQ ID NO: 44 is the determined cDNA sequence for LST-S2-B1-9F
20 SEQ ID NO: 45 is the determined cDNA sequence for LST-S2-B1-12D
SEQ ID NO: 46 is the determined cDNA sequence for LST-S2-I2-2B
SEQ ID NO: 47 is the determined cDNA sequence for LST-S2-I2-5F
SEQ ID NO: 48 is the determined cDNA sequence for LST-S2-I2-6B
SEQ ID NO: 49 is the determined cDNA sequence for LST-S2-I2-7F
25 SEQ ID NO: 50 is the determined cDNA sequence for LST-S2-I2-8G
SEQ ID NO: 51 is the determined cDNA sequence for LST-S2-I2-9E
SEQ ID NO: 52 is the determined cDNA sequence for LST-S2-I2-12B
SEQ ID NO: 53 is the determined cDNA sequence for LST-S2-H2-2C
SEQ ID NO: 54 is the determined cDNA sequence for LST-S2-H2-1G
30 SEQ ID NO: 55 is the determined cDNA sequence for LST-S2-H2-4G
SEQ ID NO: 56 is the determined cDNA sequence for LST-S2-H2-3H

SEQ ID NO: 57 is the determined cDNA sequence for LST-S2-H2-5G

SEQ ID NO: 58 is the determined cDNA sequence for LST-S2-H2-9B

SEQ ID NO: 59 is the determined cDNA sequence for LST-S2-H2-10H

SEQ ID NO: 60 is the determined cDNA sequence for LST-S2-H2-12D

5 SEQ ID NO: 61 is the determined cDNA sequence for LST-S3-2

SEQ ID NO: 62 is the determined cDNA sequence for LST-S3-4

SEQ ID NO: 63 is the determined cDNA sequence for LST-S3-7

SEQ ID NO: 64 is the determined cDNA sequence for LST-S3-8

SEQ ID NO: 65 is the determined cDNA sequence for LST-S3-12

10 SEQ ID NO: 66 is the determined cDNA sequence for LST-S3-13

SEQ ID NO: 67 is the determined cDNA sequence for LST-S3-14

SEQ ID NO: 68 is the determined cDNA sequence for LST-S3-16

SEQ ID NO: 69 is the determined cDNA sequence for LST-S3-21

SEQ ID NO: 70 is the determined cDNA sequence for LST-S3-22

15 SEQ ID NO: 71 is the determined cDNA sequence for LST-S1-7

SEQ ID NO: 72 is the determined cDNA sequence for LST-S1-A-1E

SEQ ID NO: 73 is the determined cDNA sequence for LST-S1-A-1G

SEQ ID NO: 74 is the determined cDNA sequence for LST-S1-A-3E

SEQ ID NO: 75 is the determined cDNA sequence for LST-S1-A-4E

20 SEQ ID NO: 76 is the determined cDNA sequence for LST-S1-A-6D

SEQ ID NO: 77 is the determined cDNA sequence for LST-S1-A-8D

SEQ ID NO: 78 is the determined cDNA sequence for LST-S1-A-10A

SEQ ID NO: 79 is the determined cDNA sequence for LST-S1-A-10C

SEQ ID NO: 80 is the determined cDNA sequence for LST-S1-A-9D

25 SEQ ID NO: 81 is the determined cDNA sequence for LST-S1-A-10D

SEQ ID NO: 82 is the determined cDNA sequence for LST-S1-A-9H

SEQ ID NO: 83 is the determined cDNA sequence for LST-S1-A-11D

SEQ ID NO: 84 is the determined cDNA sequence for LST-S1-A-12D

SEQ ID NO: 85 is the determined cDNA sequence for LST-S1-A-11E

30 SEQ ID NO: 86 is the determined cDNA sequence for LST-S1-A-12E

SEQ ID NO: 87 is the determined cDNA sequence for L513S (T3).

SEQ ID NO: 88 is the determined cDNA sequence for L513S contig 1.

SEQ ID NO: 89 is a first determined cDNA sequence for L514S.

SEQ ID NO: 90 is a second determined cDNA sequence for L514S.

SEQ ID NO: 91 is a first determined cDNA sequence for L516S.

5 SEQ ID NO: 92 is a second determined cDNA sequence for L516S.

SEQ ID NO: 93 is the determined cDNA sequence for L517S.

SEQ ID NO: 94 is the extended cDNA sequence for LST-S1-169 (also known as L519S).

SEQ ID NO: 95 is a first determined cDNA sequence for L520S.

10 SEQ ID NO: 96 is a second determined cDNA sequence for L520S.

SEQ ID NO: 97 is a first determined cDNA sequence for L521S.

SEQ ID NO: 98 is a second determined cDNA sequence for L521S.

SEQ ID NO: 99 is the determined cDNA sequence for L522S.

SEQ ID NO: 100 is the determined cDNA sequence for L523S.

15 SEQ ID NO: 101 is the determined cDNA sequence for L524S.

SEQ ID NO: 102 is the determined cDNA sequence for L525S.

SEQ ID NO: 103 is the determined cDNA sequence for L526S.

SEQ ID NO: 104 is the determined cDNA sequence for L527S.

SEQ ID NO: 105 is the determined cDNA sequence for L528S.

20 SEQ ID NO: 106 is the determined cDNA sequence for L529S.

SEQ ID NO: 107 is a first determined cDNA sequence for L530S.

SEQ ID NO: 108 is a second determined cDNA sequence for L530S.

SEQ ID NO: 109 is the determined full-length cDNA sequence for L531S short form

SEQ ID NO: 110 is the predicted amino acid sequence encoded by SEQ ID NO: 109.

25 SEQ ID NO: 111 is the determined full-length cDNA sequence for L531S long form

SEQ ID NO: 112 is the predicted amino acid sequence encoded by SEQ ID NO: 111.

SEQ ID NO: 113 is the determined full-length cDNA sequence for L520S.

SEQ ID NO: 114 is the predicted amino acid sequence encoded by SEQ ID NO: 113.

SEQ ID NO: 115 is the determined cDNA sequence for contig 1.

30 SEQ ID NO: 116 is the determined cDNA sequence for contig 3.

SEQ ID NO: 117 is the determined cDNA sequence for contig 4.

SEQ ID NO: 118 is the determined cDNA sequence for contig 5.

SEQ ID NO: 119 is the determined cDNA sequence for contig 7.

SEQ ID NO: 120 is the determined cDNA sequence for contig 8.

SEQ ID NO: 121 is the determined cDNA sequence for contig 9.

5 SEQ ID NO: 122 is the determined cDNA sequence for contig 10.

SEQ ID NO: 123 is the determined cDNA sequence for contig 12.

SEQ ID NO: 124 is the determined cDNA sequence for contig 11.

SEQ ID NO: 125 is the determined cDNA sequence for contig 13.

SEQ ID NO: 126 is the determined cDNA sequence for contig 15.

10 SEQ ID NO: 127 is the determined cDNA sequence for contig 16.

SEQ ID NO: 128 is the determined cDNA sequence for contig 17.

SEQ ID NO: 129 is the determined cDNA sequence for contig 19.

SEQ ID NO: 130 is the determined cDNA sequence for contig 20.

SEQ ID NO: 131 is the determined cDNA sequence for contig 22.

15 SEQ ID NO: 132 is the determined cDNA sequence for contig 24.

SEQ ID NO: 133 is the determined cDNA sequence for contig 29.

SEQ ID NO: 134 is the determined cDNA sequence for contig 31.

SEQ ID NO: 135 is the determined cDNA sequence for contig 33.

SEQ ID NO: 136 is the determined cDNA sequence for contig 38.

20 SEQ ID NO: 137 is the determined cDNA sequence for contig 39.

SEQ ID NO: 138 is the determined cDNA sequence for contig 41.

SEQ ID NO: 139 is the determined cDNA sequence for contig 43.

SEQ ID NO: 140 is the determined cDNA sequence for contig 44.

SEQ ID NO: 141 is the determined cDNA sequence for contig 45.

25 SEQ ID NO: 142 is the determined cDNA sequence for contig 47.

SEQ ID NO: 143 is the determined cDNA sequence for contig 48.

SEQ ID NO: 144 is the determined cDNA sequence for contig 49.

SEQ ID NO: 145 is the determined cDNA sequence for contig 50.

SEQ ID NO: 146 is the determined cDNA sequence for contig 53.

30 SEQ ID NO: 147 is the determined cDNA sequence for contig 54.

SEQ ID NO: 148 is the determined cDNA sequence for contig 56.

SEQ ID NO: 149 is the determined cDNA sequence for contig 57.

SEQ ID NO: 150 is the determined cDNA sequence for contig 58.

SEQ ID NO: 151 is the full-length cDNA sequence for L530S.

SEQ ID NO: 152 is the amino acid sequence encoded by SEQ ID NO: 151

5 SEQ ID NO: 153 is the full-length cDNA sequence of a first variant of L514S

SEQ ID NO: 154 is the full-length cDNA sequence of a second variant of L514S

SEQ ID NO: 155 is the amino acid sequence encoded by SEQ ID NO: 153.

SEQ ID NO: 156 is the amino acid sequence encoded by SEQ ID NO: 154.

SEQ ID NO: 157 is the determined cDNA sequence for contig 59.

10 SEQ ID NO: 158 is the full-length cDNA sequence for L763P (also referred to as contig 22).

SEQ ID NO: 159 is the amino acid sequence encoded by SEQ ID NO: 158.

SEQ ID NO: 160 is the full-length cDNA sequence for L762P (also referred to as contig 17).

15 SEQ ID NO: 161 is the amino acid sequence encoded by SEQ ID NO: 160.

SEQ ID NO: 162 is the determined cDNA sequence for L515S.

SEQ ID NO: 163 is the full-length cDNA sequence of a first variant of L524S.

SEQ ID NO: 164 is the full-length cDNA sequence of a second variant of L524S.

SEQ ID NO: 165 is the amino acid sequence encoded by SEQ ID NO: 163.

20 SEQ ID NO: 166 is the amino acid sequence encoded by SEQ ID NO: 164.

SEQ ID NO: 167 is the full-length cDNA sequence of a first variant of L762P.

SEQ ID NO: 168 is the full-length cDNA sequence of a second variant of L762P.

SEQ ID NO: 169 is the amino acid sequence encoded by SEQ ID NO: 167.

SEQ ID NO: 170 is the amino acid sequence encoded by SEQ ID NO: 168.

25 SEQ ID NO: 171 is the full-length cDNA sequence for L773P (also referred to as contig 56).

SEQ ID NO: 172 is the amino acid sequence encoded by SEQ ID NO: 171.

SEQ ID NO: 173 is an extended cDNA sequence for L519S.

SEQ ID NO: 174 is the predicted amino acid sequence encoded by SEQ ID NO: 174.

30 SEQ ID NO: 175 is the full-length cDNA sequence for L523S.

SEQ ID NO: 176 is the predicted amino acid sequence encoded by SEQ ID NO: 175.

- SEQ ID NO: 177 is the determined cDNA sequence for LST-sub5-7A.
SEQ ID NO: 178 is the determined cDNA sequence for LST-sub5-8G.
SEQ ID NO: 179 is the determined cDNA sequence for LST-sub5-8H.
SEQ ID NO: 180 is the determined cDNA sequence for LST-sub5-10B.
5 SEQ ID NO: 181 is the determined cDNA sequence for LST-sub5-10H.
SEQ ID NO: 182 is the determined cDNA sequence for LST-sub5-12B.
SEQ ID NO: 183 is the determined cDNA sequence for LST-sub5-11C.
SEQ ID NO: 184 is the determined cDNA sequence for LST-sub6-1c.
SEQ ID NO: 185 is the determined cDNA sequence for LST-sub6-2f.
10 SEQ ID NO: 186 is the determined cDNA sequence for LST-sub6-2G.
SEQ ID NO: 187 is the determined cDNA sequence for LST-sub6-4d.
SEQ ID NO: 188 is the determined cDNA sequence for LST-sub6-4e.
SEQ ID NO: 189 is the determined cDNA sequence for LST-sub6-4f.
SEQ ID NO: 190 is the determined cDNA sequence for LST-sub6-3h.
15 SEQ ID NO: 191 is the determined cDNA sequence for LST-sub6-5d.
SEQ ID NO: 192 is the determined cDNA sequence for LST-sub6-5h.
SEQ ID NO: 193 is the determined cDNA sequence for LST-sub6-6h.
SEQ ID NO: 194 is the determined cDNA sequence for LST-sub6-7a.
SEQ ID NO: 195 is the determined cDNA sequence for LST-sub6-8a.
20 SEQ ID NO: 196 is the determined cDNA sequence for LST-sub6-7d.
SEQ ID NO: 197 is the determined cDNA sequence for LST-sub6-7e.
SEQ ID NO: 198 is the determined cDNA sequence for LST-sub6-8e.
SEQ ID NO: 199 is the determined cDNA sequence for LST-sub6-7g.
SEQ ID NO: 200 is the determined cDNA sequence for LST-sub6-9f.
25 SEQ ID NO: 201 is the determined cDNA sequence for LST-sub6-9h.
SEQ ID NO: 202 is the determined cDNA sequence for LST-sub6-11b.
SEQ ID NO: 203 is the determined cDNA sequence for LST-sub6-11c.
SEQ ID NO: 204 is the determined cDNA sequence for LST-sub6-12c.
SEQ ID NO: 205 is the determined cDNA sequence for LST-sub6-12e.
30 SEQ ID NO: 206 is the determined cDNA sequence for LST-sub6-12f.
SEQ ID NO: 207 is the determined cDNA sequence for LST-sub6-11g.

SEQ ID NO: 208 is the determined cDNA sequence for LST-sub6-12g.

SEQ ID NO: 209 is the determined cDNA sequence for LST-sub6-12h.

SEQ ID NO: 210 is the determined cDNA sequence for LST-sub6-II-1a.

SEQ ID NO: 211 is the determined cDNA sequence for LST-sub6-II-2b.

5 SEQ ID NO: 212 is the determined cDNA sequence for LST-sub6-II-2g.

SEQ ID NO: 213 is the determined cDNA sequence for LST-sub6-II-1h.

SEQ ID NO: 214 is the determined cDNA sequence for LST-sub6-II-4a.

SEQ ID NO: 215 is the determined cDNA sequence for LST-sub6-II-4b.

SEQ ID NO: 216 is the determined cDNA sequence for LST-sub6-II-3e.

10 SEQ ID NO: 217 is the determined cDNA sequence for LST-sub6-II-4f.

SEQ ID NO: 218 is the determined cDNA sequence for LST-sub6-II-4g.

SEQ ID NO: 219 is the determined cDNA sequence for LST-sub6-II-4h.

SEQ ID NO: 220 is the determined cDNA sequence for LST-sub6-II-5c.

SEQ ID NO: 221 is the determined cDNA sequence for LST-sub6-II-5e.

15 SEQ ID NO: 222 is the determined cDNA sequence for LST-sub6-II-6f.

SEQ ID NO: 223 is the determined cDNA sequence for LST-sub6-II-5g.

SEQ ID NO: 224 is the determined cDNA sequence for LST-sub6-II-6g.

SEQ ID NO: 225 is the amino acid sequence for L528S.

SEQ ID NO: 226-251 are synthetic peptides derived from L762P.

20 SEQ ID NO: 252 is the expressed amino acid sequence of L514S.

SEQ ID NO: 253 is the DNA sequence corresponding to SEQ ID NO: 252.

SEQ ID NO: 254 is the DNA sequence of a L762P expression construct.

SEQ ID NO: 255 is the determined cDNA sequence for clone 23785.

SEQ ID NO: 256 is the determined cDNA sequence for clone 23786.

25 SEQ ID NO: 257 is the determined cDNA sequence for clone 23788.

SEQ ID NO: 258 is the determined cDNA sequence for clone 23790.

SEQ ID NO: 259 is the determined cDNA sequence for clone 23793.

SEQ ID NO: 260 is the determined cDNA sequence for clone 23794.

SEQ ID NO: 261 is the determined cDNA sequence for clone 23795.

30 SEQ ID NO: 262 is the determined cDNA sequence for clone 23796.

SEQ ID NO: 263 is the determined cDNA sequence for clone 23797.

SEQ ID NO: 264 is the determined cDNA sequence for clone 23798.

SEQ ID NO: 265 is the determined cDNA sequence for clone 23799.

SEQ ID NO: 266 is the determined cDNA sequence for clone 23800.

SEQ ID NO: 267 is the determined cDNA sequence for clone 23802.

5 SEQ ID NO: 268 is the determined cDNA sequence for clone 23803.

SEQ ID NO: 269 is the determined cDNA sequence for clone 23804.

SEQ ID NO: 270 is the determined cDNA sequence for clone 23805.

SEQ ID NO: 271 is the determined cDNA sequence for clone 23806.

SEQ ID NO: 272 is the determined cDNA sequence for clone 23807.

10 SEQ ID NO: 273 is the determined cDNA sequence for clone 23808.

SEQ ID NO: 274 is the determined cDNA sequence for clone 23809.

SEQ ID NO: 275 is the determined cDNA sequence for clone 23810.

SEQ ID NO: 276 is the determined cDNA sequence for clone 23811.

SEQ ID NO: 277 is the determined cDNA sequence for clone 23812.

15 SEQ ID NO: 278 is the determined cDNA sequence for clone 23813.

SEQ ID NO: 279 is the determined cDNA sequence for clone 23815.

SEQ ID NO: 280 is the determined cDNA sequence for clone 25298.

SEQ ID NO: 281 is the determined cDNA sequence for clone 25299.

SEQ ID NO: 282 is the determined cDNA sequence for clone 25300.

20 SEQ ID NO: 283 is the determined cDNA sequence for clone 25301

SEQ ID NO: 284 is the determined cDNA sequence for clone 25304

SEQ ID NO: 285 is the determined cDNA sequence for clone 25309.

SEQ ID NO: 286 is the determined cDNA sequence for clone 25312.

SEQ ID NO: 287 is the determined cDNA sequence for clone 25317.

25 SEQ ID NO: 288 is the determined cDNA sequence for clone 25321.

SEQ ID NO: 289 is the determined cDNA sequence for clone 25323.

SEQ ID NO: 290 is the determined cDNA sequence for clone 25327.

SEQ ID NO: 291 is the determined cDNA sequence for clone 25328.

SEQ ID NO: 292 is the determined cDNA sequence for clone 25332.

30 SEQ ID NO: 293 is the determined cDNA sequence for clone 25333.

SEQ ID NO: 294 is the determined cDNA sequence for clone 25336.

- SEQ ID NO: 295 is the determined cDNA sequence for clone 25340.
SEQ ID NO: 296 is the determined cDNA sequence for clone 25342.
SEQ ID NO: 297 is the determined cDNA sequence for clone 25356.
SEQ ID NO: 298 is the determined cDNA sequence for clone 25357.
5 SEQ ID NO: 299 is the determined cDNA sequence for clone 25361.
SEQ ID NO: 300 is the determined cDNA sequence for clone 25363.
SEQ ID NO: 301 is the determined cDNA sequence for clone 25397.
SEQ ID NO: 302 is the determined cDNA sequence for clone 25402.
SEQ ID NO: 303 is the determined cDNA sequence for clone 25403.
10 SEQ ID NO: 304 is the determined cDNA sequence for clone 25405.
SEQ ID NO: 305 is the determined cDNA sequence for clone 25407.
SEQ ID NO: 306 is the determined cDNA sequence for clone 25409.
SEQ ID NO: 307 is the determined cDNA sequence for clone 25396.
SEQ ID NO: 308 is the determined cDNA sequence for clone 25414.
15 SEQ ID NO: 309 is the determined cDNA sequence for clone 25410.
SEQ ID NO: 310 is the determined cDNA sequence for clone 25406.
SEQ ID NO: 311 is the determined cDNA sequence for clone 25306.
SEQ ID NO: 312 is the determined cDNA sequence for clone 25362.
SEQ ID NO: 313 is the determined cDNA sequence for clone 25360.
20 SEQ ID NO: 314 is the determined cDNA sequence for clone 25398.
SEQ ID NO: 315 is the determined cDNA sequence for clone 25355.
SEQ ID NO: 316 is the determined cDNA sequence for clone 25351.
SEQ ID NO: 317 is the determined cDNA sequence for clone 25331.
SEQ ID NO: 318 is the determined cDNA sequence for clone 25338.
25 SEQ ID NO: 319 is the determined cDNA sequence for clone 25335.
SEQ ID NO: 320 is the determined cDNA sequence for clone 25329.
SEQ ID NO: 321 is the determined cDNA sequence for clone 25324.
SEQ ID NO: 322 is the determined cDNA sequence for clone 25322.
SEQ ID NO: 323 is the determined cDNA sequence for clone 25319.
30 SEQ ID NO: 324 is the determined cDNA sequence for clone 25316.
SEQ ID NO: 325 is the determined cDNA sequence for clone 25311.

SEQ ID NO: 326 is the determined cDNA sequence for clone 25310.

SEQ ID NO: 327 is the determined cDNA sequence for clone 25302.

SEQ ID NO: 328 is the determined cDNA sequence for clone 25315.

SEQ ID NO: 329 is the determined cDNA sequence for clone 25308.

5 SEQ ID NO: 330 is the determined cDNA sequence for clone 25303.

SEQ ID NO: 331-337 are the cDNA sequences of isoforms of the p53 tumor suppressor homologue, p63 (also referred to as L530S).

SEQ ID NO: 338-344 are the amino acid sequences encoded by SEQ ID NO: 331-337, respectively.

10 SEQ ID NO: 345 is a second cDNA sequence for the antigen L763P.

SEQ ID NO: 346 is the amino acid sequence encoded by the sequence of SEQ ID NO: 345.

SEQ ID NO: 347 is a determined full-length cDNA sequence for L523S.

SEQ ID NO: 348 is the predicted amino acid sequence encoded by SEQ ID NO: 347.

15 SEQ ID NO: 349 is the cDNA sequence encoding the N-terminal portion of L773P.

SEQ ID NO: 350 is the amino acid sequence of the N-terminal portion of L773P.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to
20 compositions and methods for the therapy and diagnosis of cancer, such as lung cancer. The compositions described herein may include lung tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic
25 portion) of a lung tumor protein or a variant thereof. A "lung tumor protein" is a protein that is expressed in lung tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain lung tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western
30 blot) with antisera of a patient afflicted with lung cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of

such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery human lung tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

LUNG TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a lung tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a lung tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a lung tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a lung tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the

encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native lung tumor protein or a portion thereof. The term “variants” also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be “identical” if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20

positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native lung tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that

is at least two fold greater in a lung tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and
5 Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as lung tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

10 An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a lung tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be
15 preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ³²P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured
20 bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using
25 a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be
30 generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed
5 using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

10 One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be
15 retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO
20 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids.*
25 *Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be
30 performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs

may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding portions of lung tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a lung tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (*e.g.*, by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a lung tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In* Huber and Carr, *Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription

initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled
5 with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*.
10 Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

15 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation
20 vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to
25 permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not
30 limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus).). The polynucleotides may also be administered as naked

plasmid vectors. Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

15 LUNG TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a lung tumor protein or a variant thereof, as described herein. As noted above, a "lung tumor protein" is a protein that is expressed by lung tumor cells. Proteins that are lung tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with lung cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a lung tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may

contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-
5 247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins).
10 Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native lung tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is
15 similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the
20 sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native lung tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native lung tumor protein in one or more substitutions, deletions, additions
25 and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above
30 polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include

those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

5 Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the

polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above
5 may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host
10 cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or
15 more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example,
20 such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems
25 Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known
30 tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans,

or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second

polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible

for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see
5 *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides
10 as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is
15 considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and
20 antigen-binding fragments thereof, that specifically bind to a lung tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a lung tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a lung tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association
25 between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding
30 constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as lung cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a lung tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically.

Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest
5 may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as
10 described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid
15 cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

20 Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by
25 conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be
30 prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane,

Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or
5 more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria
10 toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a
15 substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an
20 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents,
25 which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups,
30 sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody
5 used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a lung tumor protein. Such cells may generally be prepared *in vitro* or
10 *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO
15 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a lung tumor polypeptide, polynucleotide encoding a lung tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a
20 time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a lung tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a lung tumor polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the
25 polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et
30 al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell

proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a lung tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a lung tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Lung tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a lung tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a lung tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a lung tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a lung tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant

may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is
5 generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present,
10 either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of
15 delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for
20 expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus),
25 which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805;
30 Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl.*

Acad. Sci. USA 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 5 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier 10 will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. 15 For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres 20 are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide) 25 and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a 30 substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A,

Bordetella pertussis or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA);
5 aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

10 Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6 and IL-10) tend to favor the
15 induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using
20 standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

 Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt.
25 MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT) (*see* US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences
30 are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc.,

Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with
5 cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France),
10 SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Ribi ImmunoChem Research Inc., Hamilton, MT) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

15 Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound
20 following administration). Such formulations may generally be prepared using well known technology (*see, e.g.* Coombes et al., *Vaccine* 14:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained
25 within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-
30 release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally,

an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood,

bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes
5 harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

10 Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which
15 correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

20 APCs may generally be transfected with a polynucleotide encoding a lung tumor protein (or portion or other variant thereof) such that the lung tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein.
25 Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell*
30 *Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the lung tumor polypeptide, DNA

(naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

15 CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as lung cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive

long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free

survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a lung tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using
5 samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more lung tumor proteins and/or polynucleotides encoding such proteins in a
10 biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as lung cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the
15 biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a lung tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in
20 the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c)
25 comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding
30 agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent

that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length lung tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the

binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at
5 A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody.
10 Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

15 More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to
20 bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.,* incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of
25 that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

30 Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second

antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide.

5 An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are
10 generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of
15 the reaction products.

To determine the presence or absence of a cancer, such as lung cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average
20 mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical*
25 *Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that
30 encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered

positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

5 In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution
10 containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent.
15 Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the
20 biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about
25 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to
30 those of ordinary skill in the art that the above protocols may be readily modified to use lung tumor polypeptides to detect antibodies that bind to such polypeptides in a

biological sample. The detection of such lung tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a lung tumor protein in a biological sample. Within
5 certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a lung tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells.
10 For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (*e.g.*, 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of lung tumor polypeptide to serve as a control. For CD4⁺ T cells,
15 activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

20 As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a lung tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a lung tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for
25 (*i.e.*, hybridizes to) a polynucleotide encoding the lung tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a lung tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

30 To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%,

preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a lung tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed
5 herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a
10 sequence recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

15 One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification
20 may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered
25 positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be
30 performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the

level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor.

5 One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple lung tumor protein
10 markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins
15 provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components
20 necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a lung tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements,
25 such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a lung tumor protein in a biological sample. Such kits generally comprise at
30 least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a lung tumor protein. Such an oligonucleotide may be used,

for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a lung tumor protein.

The following Examples are offered by way of illustration and not by
5 way of limitation.

EXAMPLE 1

ISOLATION AND CHARACTERIZATION OF cDNA SEQUENCES
ENCODING LUNG TUMOR POLYPEPTIDES

5

This example illustrates the isolation of cDNA molecules encoding lung tumor-specific polypeptides from lung tumor cDNA libraries.

A. ISOLATION OF cDNA SEQUENCES FROM A LUNG SQUAMOUS CELL
10 CARCINOMA LIBRARY

A human lung squamous cell carcinoma cDNA expression library was constructed from poly A⁺ RNA from a pool of two patient tissues using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD) following the manufacturer's protocol. Specifically, lung carcinoma
15 tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using an oligo dT cellulose column as described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989. First-strand cDNA was
20 synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with BstXI/EcoRI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with cDNA size fractionation columns (BRL Life Technologies), the cDNA was ligated into the BstXI/NotI site of pcDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life
25 Technologies) by electroporation.

Using the same procedure, a normal human lung cDNA expression library was prepared from a pool of four tissue specimens. The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The lung
30 squamous cell carcinoma library contained 2.7×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 2100 base pairs. The normal

lung cDNA library contained 1.4×10^6 independent colonies, with 90% of clones having inserts and the average insert size being 1800 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA

5 cDNA library subtraction was performed using the above lung squamous cell carcinoma and normal lung cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a lung squamous cell carcinoma-specific subtracted cDNA library was generated as follows. Normal tissue cDNA library (80 μ g) was digested with BamHI and XhoI, followed by a filling-in
10 reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 133 μ l of H₂O, heat-denatured and mixed with 133 μ l (133 μ g) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (67 μ l) was added
15 and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 μ l H₂O to form the driver DNA.

To form the tracer DNA, 10 μ g lung squamous cell carcinoma cDNA library was digested with NotI and SpeI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech, Palo Alto, CA). Typically, 5 μ g of
20 cDNA was recovered after the sizing column. Following ethanol precipitation, the tracer DNA was dissolved in 5 μ l H₂O. Tracer DNA was mixed with 15 μ l driver DNA and 20 μ l of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and
25 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 μ l H₂O, mixed with 8 μ l driver DNA and 20 μ l of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After
30 removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into NotI/SpeI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA) and

transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a lung squamous cell carcinoma specific subtracted cDNA library (herein after referred to as "lung subtraction I").

5 A second lung squamous cell carcinoma specific subtracted cDNA library (referred to as "lung subtraction II") was generated in a similar way to the lung subtraction library I, except that eight frequently recovered genes from lung subtraction I were included in the driver DNA, and 24,000 independent clones were recovered.

To analyze the subtracted cDNA libraries, plasmid DNA was prepared from 320 independent clones, randomly picked from the subtracted lung squamous cell carcinoma specific libraries. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). The cDNA sequences for sixty isolated clones are provided in SEQ ID NO: 1-60. These sequences were compared to known sequences in the gene bank using the EMBL and GenBank
10 databases (release 96). No significant homologies were found to the sequences provided in SEQ ID NO: 2, 3, 19, 38 and 46. The sequences of SEQ ID NO: 1, 6-8, 10-13, 15, 17, 18, 20-27, 29, 30, 32, 34-37, 39-45, 47-49, 51, 52, 54, 55 and 57-59 were found to show some homology to previously identified expressed sequence tags (ESTs). The sequences of SEQ ID NO: 9, 28, 31 and 33 were found to show some homology to
15 previously identified non-human gene sequences and the sequences of SEQ ID NO: 4, 5, 14, 50, 53, 56 and 60 were found to show some homology to gene sequences previously identified in humans.

The subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and the above normal lung tissue cDNA library and a cDNA library from normal liver and heart (constructed from a pool of one sample of each tissue as described above), plus twenty other cDNA clones that were frequently recovered in lung subtractions I and II, as the driver DNA (lung subtraction III). The normal liver and heart cDNA library contained 1.76×10^6 independent colonies, with 100% of clones having inserts and the average insert size
25 being 1600 base pairs. Ten additional clones were isolated (SEQ ID NO: 61-70). Comparison of these cDNA sequences with those in the gene bank as described above,

revealed no significant homologies to the sequences provided in SEQ ID NO: 62 and 67. The sequences of SEQ ID NO: 61, 63-66, 68 and 69 were found to show some homology to previously isolated ESTs and the sequence provided in SEQ ID NO: 70 was found to show some homology to a previously identified rat gene.

5 In further studies, the subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and a cDNA library from a pool of normal lung, kidney, colon, pancreas, brain, resting PBMC, heart, skin and esophagus as the driver DNA, with esophagus cDNAs making up one third of the driver material. Since esophagus is enriched in normal
10 epithelial cells, including differentiated squamous cells, this procedure is likely to enrich genes that are tumor specific rather than tissues specific. The cDNA sequences of 48 clones determined in this subtraction are provided in SEQ ID NO: 177-224. The sequences of SEQ ID NO: 177, 178, 180, 181, 183, 187, 192, 195-197, 208, 211, 212, 215, 216, 218 and 219 showed some homology to previously identified genes. The
15 sequences of SEQ ID NO: 179, 182, 184-186, 188-191, 193, 194, 198-207, 209 210, 213, 214, 217, 220 and 224 showed some homology to previously determined ESTs. The sequence of SEQ ID NO: 221-223 showed no homology to any previously determined sequence.

20 B. ISOLATION OF cDNA SEQUENCES FROM A LUNG ADENOCARCINOMA LIBRARY

A human lung adenocarcinoma cDNA expression library was constructed as described above. The library contained 3.2×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 1500 base pairs.
25 Library subtraction was performed as described above using the normal lung and normal liver and heart cDNA expression libraries described above as the driver DNA. Twenty-six hundred independent clones were recovered.

Initial cDNA sequence analysis from 100 independent clones revealed many ribosomal protein genes. The cDNA sequences for fifteen clones isolated in this
30 subtraction are provided in SEQ ID NO: 71-86. Comparison of these sequences with those in the gene bank as described above revealed no significant homologies to the

59

sequence provided in SEQ ID NO: 84. The sequences of SEQ ID NO: 71, 73, 74, 77, 78 and 80-82 were found to show some homology to previously isolated ESTs, and the sequences of SEQ ID NO: 72, 75, 76, 79, 83 and 85 were found to show some homology to previously identified human genes.

5 In further studies, a cDNA library (referred to as mets3616A) was constructed from a metastatic lung adenocarcinoma. The determined cDNA sequences of 25 clones sequenced at random from this library are provided in SEQ ID NO: 255-279. The mets3616A cDNA library was subtracted against a cDNA library prepared from a pool of normal lung, liver, pancreas, skin, kidney, brain and resting PBMC. To
10 increase the specificity of the subtraction, the driver was spiked with genes that were determined to be most abundant in the mets3616A cDNA library, such as EF1-alpha, integrin-beta and anticoagulant protein PP4, as well as with cDNAs that were previously found to be differentially expressed in subtracted lung adenocarcinoma cDNA libraries. The determined cDNA sequences of 51 clones isolated from the
15 subtracted library (referred to as mets3616A-S1) are provided in SEQ ID NO: 280-330.

Comparison of the sequences of SEQ ID NO: 255-330 with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 255-258, 260, 262-264, 270, 272, 275, 276, 279, 281, 287, 291, 296, 300 and 310. The sequences of SEQ ID NO: 259, 261, 265-269, 271, 273, 274, 277, 278, 282-285, 288-
20 290, 292, 294, 297-299, 301, 303-309, 313, 314, 316, 320-324 and 326-330 showed some homology to previously identified gene sequences, while the sequences of SEQ ID NO: 280, 286, 293, 302, 310, 312, 315, 317-319 and 325 showed some homology to previously isolated expressed sequence tags (ESTs).

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EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for seven
30 representative lung tumor polypeptides described in Example 1 were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 2 μ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β -actin was used as an internal control for each of the tissues examined. 1 μ l of 1:30 dilution of cDNA was employed to enable the linear range amplification of the β -actin template and was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in five different types of tumor tissue (lung squamous cell carcinoma from 3 patients, lung adenocarcinoma, colon tumor from 2 patients, breast tumor and prostate tumor), and thirteen different normal tissues (lung from 4 donors, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, stomach, myocardium, retina and testes). Using a 10-fold amount of cDNA, the antigen LST-S1-90 (SEQ ID NO: 3) was found to be expressed at high levels in lung squamous cell carcinoma and in breast tumor, and at low to undetectable levels in the other tissues examined.

The antigen LST-S2-68 (SEQ ID NO: 15) appears to be specific to lung and breast tumor, however, expression was also detected in normal kidney. Antigens LST-S1-169 (SEQ ID NO: 6) and LST-S1-133 (SEQ ID NO: 5) appear to be very abundant in lung tissues (both normal and tumor), with the expression of these two genes being decreased in most of the normal tissues tested. Both LST-S1-169 and LST-S1-133 were also expressed in breast and colon tumors. Antigens LST-S1-6 (SEQ ID NO: 7) and LST-S2-I2-5F (SEQ ID NO: 47) did not show tumor or tissue specific expression, with the expression of LST-S1-28 being rare and only detectable in a few tissues. The antigen LST-S3-7 (SEQ ID NO: 63) showed lung and breast tumor specific expression, with its message only being detected in normal testes when the PCR was performed for 30 cycles. Lower level expression was detected in some

normal tissues when the cycle number was increased to 35. Antigen LST-S3-13 (SEQ ID NO: 66) was found to be expressed in 3 out of 4 lung tumors, one breast tumor and both colon tumor samples. Its expression in normal tissues was lower compared to tumors, and was only detected in 1 out of 4 normal lung tissues and in normal tissues from kidney, ovary and retina. Expression of antigens LST-S3-4 (SEQ ID NO: 62) and LST-S3-14 (SEQ ID NO: 67) was rare and did not show any tissue or tumor specificity. Consistent with Northern blot analyses, the RT-PCT results on antigen LAT-S1-A-10A (SEQ ID NO: 78) suggested that its expression is high in lung, colon, stomach and small intestine tissues, including lung and colon tumors, whereas its expression was low or undetectable in other tissues.

A total of 2002 cDNA fragments isolated in lung subtractions I, II and III, described above, were colony PCR amplified and their mRNA expression levels in lung tumor, normal lung, and various other normal and tumor tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Seventeen non-redundant cDNA clones showed over-expression in lung squamous tumors, with expression in normal tissues tested (lung, skin, lymph node, colon, liver, pancreas, breast, heart, bone marrow, large intestine, kidney, stomach, brain, small intestine, bladder and salivary gland) being either undetectable, or 10-fold less compared to lung squamous tumors. The determined partial cDNA sequences for the clone L513S are provided in SEQ ID NO: 87 and 88; those for L514S are provided in SEQ ID NO: 89 and 90; those for L516S in SEQ ID NO: 91 and 92; that for L517S in SEQ ID NO: 93; that for L519S in SEQ ID NO: 94; those for L520S in SEQ ID NO: 95 and 96; those for L521S in SEQ ID NO: 97 and 98; that for L522S in SEQ ID NO: 99; that for L523S in SEQ ID NO: 100; that for L524S in SEQ ID NO: 101; that for L525S in SEQ ID NO: 102; that for L526S in SEQ ID NO: 103; that for L527S in SEQ ID NO: 104; that for L528S in SEQ ID NO: 105; that for L529S in SEQ ID NO: 106;

and those for L530S in SEQ ID NO: 107 and 108. Additionally, the full-length cDNA sequence for L530S is provided in SEQ ID NO: 151, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 152. L530S shows homology to a splice variant of a p53 tumor suppressor homologue, p63. The cDNA sequences of 7
5 known isoforms of p63 are provided in SEQ ID NO: 331-337, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 338-344, respectively.

Due to polymorphisms, the clone L531S appears to have two forms. A first determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 109, with the corresponding predicted amino acid sequence being provided in SEQ ID NO:
10 110. A second determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 111, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 112. The sequence of SEQ ID NO: 111 is identical to that of SEQ ID NO: 109, except that it contains a 27 bp insertion. Similarly, L514S also has two alternatively spliced forms; the first variant cDNA is listed as SEQ ID NO: 153, with
15 the corresponding amino acid sequence being provided in SEQ ID NO: 155. The second variant form of L514S full-length cDNA is provided in SEQ ID NO: 154, with its corresponding amino acid sequence being provided in SEQ ID NO: 156.

Full length cloning for L524S (SEQ ID NO: 101) yielded two variants (SEQ ID NO: 163 and 164) with the corresponding predicted amino acid sequences of
20 SEQ ID NO: 165 and 166, respectively. Both variants have been shown to encode parathyroid hormone-related peptide.

Attempts to isolate the full-length cDNA for L519S, resulted in the isolation of the extended cDNA sequence provided in SEQ ID NO: 173, which contains a potential open reading frame. The predicted amino acid sequence encoded by the
25 sequence of SEQ ID NO: 173 is provided in SEQ ID NO: 174. Additionally, the full-length cDNA sequence for the clone of SEQ ID NO: 100 (known as L523S), a known gene, is provided in SEQ ID NO: 175, with the corresponding predicted amino acid sequence provided in SEQ ID NO: 176. In further studies, a full-length cDNA sequence for L523S was isolated from a L523S-positive tumor cDNA library by PCR
30 amplification using gene specific primers designed from the sequence of SEQ ID NO: 175. The determined cDNA sequence is provided in SEQ ID NO: **. The amino acid

sequence encoded by this sequence is provided in SEQ ID NO: **. This protein sequence differs from the previously published protein sequence at two amino acid positions, namely at positions 158 and 410.

Comparison of the sequences of L514S and L531S (SEQ ID NO: 87 and 88, 89 and 90, and 109, respectively) with those in the gene bank, as described above, revealed no significant homologies to known sequences. The sequences of L513S, L516S, L517S, L519S, L520S and L530S (SEQ ID NO: 87 and 88, 91 and 92, 93, 94, 95 and 96, 107 and 108, respectively) were found to show some homology to previously identified ESTs. The sequences of L521S, L522S, L523S, L524S, L525S, L526S, L527S, L528S and L529S (SEQ ID NO: 97 and 98, 99, 99, 101, 102, 103, 104, 105, and 106, respectively) were found to represent known genes. The determined full-length cDNA sequences for L520S is provided in SEQ ID NO: 113, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 114. Subsequent microarray analysis has shown L520S to be overexpressed in breast tumors in addition to lung squamous tumors.

Further analysis has demonstrated that L529S (SEQ ID NO: 106 and 115), L525S (SEQ ID NO: 102 and 120) and L527S (SEQ ID NO: 104) are cytoskeletal components and potentially squamous cell specific proteins. L529S is connexin 26, a gap junction protein. It is highly expressed in lung squamous tumor 9688T, and moderately over-expressed in two others. However, lower level expression of connexin 26 is also detectable in normal skin, colon, liver and stomach. The over-expression of connexin 26 in some breast tumors has been reported and a mutated form of L529S may result in over-expression in lung tumors. L525S is plakophilin 1, a desmosomal protein found in plaque-bearing adhering junctions of the skin. Expression levels for L525S mRNA is highly elevated in three out of four lung squamous tumors tested, and in normal skin. L527S has been identified as keratin 6 isoform, type II 58 Kd keratin, and cytokeratin 13 and shows over-expression in squamous tumors and low expression in normal skin, breast and colon tissues. Notably, keratin and keratin-related genes have been extensively documented as potential markers for lung cancer including CYFRA2.1 (Pastor, A., et al, *Eur. Respir. J.*, 10:603-609, 1997). L513S (SEQ ID NO: 87 and 88)

shows moderate over-expression in several tumor tissues tested, and encodes a protein that was first isolated as a pemphigus vulgaris antigen.

L520S (SEQ ID NO: 95 and 96) and L521S (SEQ ID NO: 97 and 98) are highly expressed in lung squamous tumors, and L520S is up-regulated in normal salivary gland and L521S is over-expressed in normal skin. Both belong to a family of small proline rich proteins and represent markers for fully differentiated squamous cells. L521S has been described as a specific marker for lung squamous tumor (Hu, R., et al, *Lung Cancer*, 20:25-30, 1998). L515S (SEQ ID NO: 162) encodes IGF- β 2 and L516S is an aldose reductase homologue and both are moderately expressed in lung squamous tumors and in normal colon. Notably, L516S (SEQ ID NO: 91 and 92) is up-regulated in metastatic tumors but not primary lung adenocarcinoma, an indication of its potential role in metatasis and a potential prognostic marker. L522S (SEQ ID NO: 99) is moderately over-expressed in lung squamous tumors with minimum expression in normal tissues. L522S has been shown to belong to a class IV alcohol dehydrogenase, ADH7, and its expression profile suggests it is a squamous cell specific antigen. L523S (SEQ ID NO: 100) is moderately over-expressed in lung squamous tumor, human pancreatic cancer cell lines and pancreatic cancer tissues, suggesting this gene may be a shared antigen between pancreatic and lung squamous cell cancer.

L524S (SEQ ID NO: 101) is over-expressed in the majority of squamous tumors tested and is homologous with parathyroid hormone-related peptide (PTHrP), which is best known to cause humoral hypercalcaemia associated with malignant tumors such as leukemia, prostate and breast cancer. It is also believed that PTHrP is most commonly associated with squamous carcinoma of lung and rarely with lung adenocarcinoma (Davidson, L.A., et al, *J. Pathol.*, 178: 398-401, 1996). L528S (SEQ ID NO: 105) is highly over-expressed in two lung squamous tumors with moderate expression in two other squamous tumors, one lung adenocarcinoma and some normal tissues, including skin, lymph nodes, heart, stomach and lung. It encodes the NMB gene that is similar to the precursor of melanocyte specific gene Pmel17, wfhich is reported to be preferentially expressed in low-metastatic potential melanoma cell lines. This suggests that L528S may be a shared antigen in both melanoma and lung squamous cell carcinoma. L526S (SEQ ID NO: 103) is overexpressed in all lung

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squamous cell tumor tissues tested and has been shown to share homology with a gene (ATM) in which a mutation causes ataxia telangiectasia, a genetic disorder in humans causing a predisposition to cancer, among other symptoms. ATM encodes a protein that activates p53 mediated cell-cycle checkpoint through direct binding and phosphorylation of the p53 molecule. Approximately 40% of lung cancer is associated with p53 mutations, and it is speculated that over-expression of ATM is a result of compensation for loss of p53 function, but it is unknown whether over-expression is the cause of result of lung squamous cell carcinoma. Additionally, expression of L526S (ATM) is also detected in a metastatic but not lung adenocarcinoma, suggesting a role in metastasis.

Expression of L523S (SEQ ID NO: 175), was also examined by real time RT-PCR as described above. In a first study using a panel of lung squamous tumors, L523S was found to be expressed in 4/7 lung squamous tumors, 2/3 head and neck squamous tumors and 2/2 lung adenocarcinomas, with low level expression being observed in skeletal muscle, soft palate and tonsil. In a second study using a lung adenocarcinoma panel, expression of L523S was observed in 4/9 primary adenocarcinomas, 2/2 lung pleural effusions, 1/1 metastatic lung adenocarcinomas and 2/2 lung squamous tumors, with little expression being observed in normal tissues.

Expression of L523S in lung tumors and various normal tissues was also examined by Northern blot analysis, using standard techniques. In a first study, L523S was found to be expressed in a number of lung adenocarcinomas and squamous cell carcinomas, as well as normal tonsil. No expression was observed in normal lung. In a second study using a normal tissue blot (HB-12) from Clontech, no expression was observed in brain, skeletal muscle, colon, thymus, spleen, kidney, liver, small intestine, lung or PBMC, although there was strong expression in placenta.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF LUNG TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

Eight hundred and fifty seven clones from a cDNA subtraction library, containing cDNA from a pool of two human lung squamous tumors subtracted against eight normal human tissue cDNAs including lung, PBMC, brain, heart, kidney, liver, pancreas, and skin, (Clontech, Palo Alto, CA) were derived and submitted to a first
5 round of PCR amplification. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector P7- Adv vector (Clontech, Palo Alto, CA) and transformed into DH5 α *E. coli* (Gibco, BRL). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated
10 Sequencer Model 373A.

One hundred and sixty two positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the the EMBL and GenBank databases, as described above, revealed no significant homologies to 13 of these clones, hereinafter referred to as Contigs 13, 16, 17, 19, 22, 24, 29, 47, 49, 56-59. The
15 determined cDNA sequences for these clones are provided in SEQ ID NO: 125, 127-129, 131-133, 142, 144, 148-150, and 157, respectively. Contigs 1, 3-5, 7-10, 12, 11, 15, 20, 31, 33, 38, 39, 41, 43, 44, 45, 48, 50, 53, 54 (SEQ ID NO: 115-124, 126, 130, 134-141, 143, 145-147, respectively) were found to show some degree of homology to previously identified DNA sequences. Contig 57 (SEQ ID NO: 149) was found to
20 represent the clone L519S (SEQ ID NO: 94) disclosed in US. Patent Application No. 09/123,912, filed July 27, 1998. To the best of the inventors' knowledge, none of these sequences have been previously shown to be differentially over-expressed in lung tumors.

mRNA expression levels for representative clones in lung tumor tissues,
25 normal lung tissues (n=4), resting PBMC, salivary gland, heart, stomach, lymph nodes, skeletal muscle, soft palate, small intestine, large intestine, bronchial, bladder, tonsil, kidney, esophagus, bone marrow, colon, adrenal gland, pancreas, and skin, (all derived from human) were determined by RT-PCR as described above. Expression levels using microarray technology, as described above, were examined in one sample of each tissue
30 type unless otherwise indicated.

Contig 3 (SEQ ID NO: 116) was found to be highly expressed in all head and neck squamous cell tumors tested (17/17), and expressed in the majority (8/12) of lung squamous tumors, (high expression in 7/12, moderate in 2/12, and low in 2/12), while showing negative expression for 2/4 normal lung tissues and low expression in the remaining two samples. Contig 3 showed moderate expression in skin and soft palate, and lowered expression levels in resting PBMC, large intestine, salivary gland, tonsil, pancreas, esophagus, and colon. Contig 11 (SEQ ID NO: 124) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 14/17, and moderately expressed in 3/17. Additionally, expression in lung squamous tumors showed high expression in 3/12 and moderate in 4/12. Contig 11 was negative for 3/4 normal lung samples, with the remaining sample having only low expression. Contig 11 showed low to moderate reactivity to salivary gland, soft palate, bladder, tonsil, skin, esophagus, and large intestine. Contig 13 (SEQ ID NO: 125) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 12/17, and moderately expressed in 5/17. Contig 13 was expressed in 7/12 lung squamous tumors, with high expression in 4/12 and moderate expression in three samples. Analysis of normal lung samples showed negative expression for 2/4 and low to moderate expression in the remaining two samples. Contig 13 did show low to moderate reactivity to resting PBMC, salivary gland, bladder, pancreas, tonsil, skin, esophagus, and large intestine, as well as high expression in soft palate. Contig 16 (SEQ ID NO: 127) was found to be moderately expressed in some head and neck squamous cell tumors (6/17) and one lung squamous tumor; while showing no expression in any normal lung samples tested. Contig 16 did show low reactivity to resting PBMC, large intestine, skin, salivary gland, and soft palate. Contig 17 (SEQ ID NO: 128) was shown to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 5/17, and moderately expressed in 12/17. Expression levels in lung squamous tumors showed one tumor sample with high expression and 3/12 with moderate levels. Contig 17 was negative for 2/4 normal lung samples, with the remaining samples having only low expression. Additionally, low level expression was found in esophagus and soft palate. Contig 19 (SEQ ID NO: 129) was found to be expressed in most head and neck squamous cell tumors tested (11/17); with two

samples having high levels, 6/17 showing moderate expression, and low expression being found in 3/17. Testing in lung squamous tumors revealed only moderate expression in 3/12 samples. Expression levels in 2/4 of normal lung samples were negative, the two other samples having only low expression. Contig 19 showed low expression levels in esophagus, resting PBMC, salivary gland, bladder, soft palate and pancreas.

Contig 22 (SEQ ID NO: 131), was shown to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in four of these samples, moderate expression in 6/17, and low expression in 3/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression in two normal lung samples and low expression in two other samples (n=4). Contig 22 showed low expression in skin, salivary gland and soft palate. Similarly, Contig 24 (SEQ ID NO: 132) was found to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in three of these samples, moderate expression in 6/17, and low expression in 4/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression for three normal lung samples and low expression in one sample (n=4). Contig 24 showed low expression in skin, salivary gland and soft palate. Contig 29 (SEQ ID NO: 133) was expressed in nearly all head and neck squamous cell tumors tested (16/17): highly expressed in 4/17, moderately expressed in 11/17, with low expression in one sample. Also, it was moderately expressed in 3/12 lung squamous tumors, while being negative for 2/4 normal lung samples. Contig 29 showed low to moderate expression in large intestine, skin, salivary gland, pancreas, tonsil, heart and soft palate. Contig 47 (SEQ ID NO: 142) was expressed in most head and neck squamous cell tumors tested (12/17): moderate expression in 10/17, and low expression in two samples. In lung squamous tumors, it was highly expressed in one sample and moderately expressed in two others (n=13). Contig 47 was negative for 2/4 normal lung samples, with the remaining two samples having moderate expression. Also, Contig 47 showed moderate expression in large intestine, and pancreas, and low expression in skin, salivary gland, soft palate, stomach, bladder, resting PBMC, and tonsil.

Contig 48 (SEQ ID NO: 143) was expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 8/17 and moderately expressed in 7/17, with low expression in two samples. Expression levels in lung squamous tumors were high to moderate in three samples (n=13). Contig 48 was negative for one out of four normal lung samples, the remaining showing low or moderate expression. Contig 48 showed moderate expression in soft palate, large intestine, pancreas, and bladder, and low expression in esophagus, salivary gland, resting PBMC, and heart. Contig 49 (SEQ ID NO: 144) was expressed at low to moderate levels in 6/17 head and neck squamous cell tumors tested. Expression levels in lung squamous tumors were moderate in three samples (n=13). Contig 49 was negative for 2/4 normal lung samples, the remaining samples showing low expression. Moderate expression levels in skin, salivary gland, large intestine, pancreas, bladder and resting PBMC were shown, as well as low expression in soft palate, lymph nodes, and tonsil. Contig 56 (SEQ ID NO: 148) was expressed in low to moderate levels in 3/17 head and neck squamous cell tumors tested, and in lung squamous tumors, showing low to moderate levels in three out of thirteen samples. Notably, low expression levels were detected in one adenocarcinoma lung tumor sample (n=2). Contig 56 was negative for 3/4 normal lung samples, and showed moderate expression levels in only large intestine, and low expression in salivary gland, soft palate, pancreas, bladder, and resting PBMC. Contig 58, also known as L769P, (SEQ ID NO: 150) was expressed at moderate levels in 11/17 head and neck squamous cell tumors tested and low expression in one additional sample. Expression in lung squamous tumors showed low to moderate levels in three out of thirteen samples. Contig 58 was negative for 3/4 normal lung samples, with one sample having low expression. Moderate expression levels in skin, large intestine, and resting PBMC were demonstrated, as well as low expression in salivary gland, soft palate, pancreas, and bladder. Contig 59 (SEQ ID NO: 157) was expressed in some head, neck, and lung squamous tumors. Low level expression of Contig 59 was also detected in salivary gland and large intestine.

The full-length cDNA sequence for Contig 22, also referred to as L763P, is provided in SEQ ID NO: 158, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 159. Real-time RT-PCR analysis of L763P revealed

that it is highly expressed in 3/4 lung squamous tumors as well as 4/4 head and neck squamous tumors, with low level expression being observed in normal brain, skin, soft pallet and trachea. Subsequent database searches revealed that the sequence of SEQ ID NO: 158 contains a mutation, resulting in a frameshift in the corresponding protein sequence. A second cDNA sequence for L763P is provided in SEQ ID NO: 345, with the corresponding amino acid sequence being provided in SEQ ID NO: 346. The sequences of SEQ ID NO: 159 and 346 are identical with the exception of the C-terminal 33 amino acids of SEQ ID NO: 159.

The full-length cDNA sequence incorporating Contigs 17, 19, and 24, referred to as L762P, is provided in SEQ ID NO: 160, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 161. Further analysis of L762P has determined it to be a type I membrane protein and two additional variants have been sequenced. Variant 1 (SEQ ID NO: 167, with the corresponding amino acid sequence in SEQ ID NO: 169) is an alternatively spliced form of SEQ ID NO: 160 resulting in deletion of 503 nucleotides, as well as deletion of a short segment of the expressed protein. Variant 2 (SEQ ID NO: 168, with the corresponding amino acid sequence in SEQ ID NO: 170) has a two nucleotide deletion at the 3' coding region in comparison to SEQ ID NO: 160, resulting in a secreted form of the expressed protein. Real-time RT-PCR analysis of L762P revealed that is over-expressed in 3/4 lung squamous tumors and 4/4 head & neck tumors, with low level expression being observed in normal skin, soft pallet and trachea.

The full-length cDNA sequence for contig 56 (SEQ ID NO: 148), also referred to as L773P, is provided in SEQ ID NO: 171, with the predicted amino acid sequence in SEQ ID NO: 172. L773P was found to be identical to dihydroxyl dehydrogenase at the 3' portion of the gene, with divergent 5' sequence. As a result, the 69 N-terminal amino acids are unique. The cDNA sequence encoding the 69 N-terminal amino acids is provided in SEQ ID NO: 349, with the N-terminal amino acid sequence being provided in SEQ ID NO: 350. Real-time PCR revealed that L773P is highly expressed in lung squamous tumor and lung adenocarcinoma, with no detectable expression in normal tissues. Subsequent Northern blot analysis of L773P demonstrated that this transcript is differentially over-expressed in squamous tumors

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and detected at approximately 1.6 Kb in primary lung tumor tissue and approximately 1.3 Kb in primary head and neck tumor tissue.

Subsequent microarray analysis has shown Contig 58, also referred to as L769S (SEQ ID NO: 150), to be overexpressed in breast tumors in addition to lung
5 squamous tumors.

EXAMPLE 4

SYNTHESIS OF POLYPEPTIDES

10 Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide.
15 Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse
20 phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

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EXAMPLE 5

PREPARATION OF ANTIBODIES AGAINST LUNG CANCER ANTIGENS

Polyclonal antibodies against the lung cancer antigens L514S, L528S and L531S (SEQ ID NO: 155, 225 and 112, respectively) were prepared as follows.

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Rabbits were immunized with recombinant protein expressed in and purified from *E. coli* as described above. For the initial immunization, 400 µg of

antigen combined with muramyl dipeptide (MDP) was injected subcutaneously (S.C.). Animals were boosted S.C. 4 weeks later with 200 µg of antigen mixed with incomplete Freund's Adjuvant (IFA). Subsequent boosts of 100 µg of antigen mixed with IFA were injected S.C. as necessary to induce high antibody titer responses. Serum bleeds
5 from immunized rabbits were tested for antigen-specific reactivity using ELISA assays with purified protein. Polyclonal antibodies against L514S, L528S and L531S were affinity purified from high titer polyclonal sera using purified protein attached to a solid support.

Immunohistochemical analysis using polyclonal antibodies against
10 L514S was performed on a panel of 5 lung tumor samples, 5 normal lung tissue samples and normal colon, kidney, liver, brain and bone marrow. Specifically, tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with antibody for 1 hr. HRP-labeled anti-mouse followed by incubation with DAB
15 chromogen was used to visualize L514S immunoreactivity. L514S was found to be highly expressed in lung tumor tissue with little or no expression being observed in normal lung, brain or bone marrow. Light staining was observed in colon and kidney. Staining was seen in normal liver but no mRNA has been detected in this tissue making this result suspect.

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EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

Immunogenic peptides from the lung cancer antigen L762P (SEQ ID
25 NO: 161) for HLA-A2/K^b-restricted CD8⁺ T cells were identified as follows.

The location of HLA-A2 binding peptides within the lung cancer antigen L762P (SEQ ID NO: 161) was predicted using a computer program which predicts peptides sequences likely to being to HLA-A*0201 by fitting to the known peptide binding motif for HLA-A*0201 (Rupert *et al.* (1993) *Cell* 74:929; Rammensee *et al.*
30 (1995) *Immunogenetics* 41:178-228). A series of 19 synthetic peptides corresponding to a selected subset of the predicted HLA-A*0201 binding peptides was prepared as described above.

Mice expressing the transgene for human HLA A2/K^b (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with the synthetic peptides, as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with
5 50µg of L726P peptide and 120µg of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared. Cells were then resuspended at 7×10^6 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL),
10 non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) L762P peptide- (5µg/ml) and 10mg/ml B₂-microglobulin- (3 µg/ml) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). After six days, cells (5×10^5 /ml) were restimulated with 2.5×10^6 /ml
15 peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 5×10^6 /ml irradiated (3000 rads) A2/K^b-transgenic spleen feeder cells. Cells were cultured in the presence of 10U/ml IL-2. Cells were restimulated on a weekly basis as described, in preparation for cloning the line.

Peptide-specific cell lines were cloned by limiting dilution analysis with
20 irradiated (20,000 rads) L762P peptide-pulsed EL4 A2Kb tumor cells (1×10^4 cells/well) as stimulators and irradiated (3000 rads) A2/K^b-transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 10U/ml IL-2. On day 7, cells were restimulated as before. On day 14, clones that were growing were isolated and maintained in culture.

25 Cell lines specific for L762P-87 (SEQ ID NO: 226; corresponding to amino acids 87-95 of SEQ ID NO: 161), L726P-145 (SEQ ID NO: 227; corresponding to amino acids 145-153 of SEQ ID NO: 161), L726P-585 (SEQ ID NO: 228; corresponding to amino acids 585-593 of SEQ ID NO: 161), L762P-425 (SEQ ID NO: 229; corresponding to amino acids 425-433 of SEQ ID NO: 161), L762P(10)-424 (SEQ
30 ID NO: 230; corresponding to amino acids 424-433 of SEQ ID NO: 161) and L762P(10)-458 (SEQ ID NO: 231; corresponding to amino acids 458-467 of SEQ ID

NO: 161) demonstrated significantly higher reactivity (as measured by percent specific lysis) against L762P peptide-pulsed EL4-A2/K^b tumor target cells than control peptide-pulsed EL4-A2/K^b tumor target cells.

5

EXAMPLE 7

IDENTIFICATION OF CD4 IMMUNOGENIC T CELL EPITOPES DERIVED
FROM THE LUNG CANCER ANTIGEN L762P

CD4 T cell lines specific for the antigen L762P (SEQ ID NO: 161) were
10 generated as follows.

A series of 28 overlapping peptides were synthesized that spanned approximately 50% of the L762P sequence. For priming, peptides were combined into pools of 4-5 peptides, pulsed at 20 micrograms/ml into dendritic cells for 24 hours. The dendritic cells were then washed and mixed with positively selected CD4⁺ T cells in 96
15 well U-bottomed plates. Forty cultures were generated for each peptide pool. Cultures were restimulated weekly with fresh dendritic cells loaded with peptide pools. Following a total of 3 stimulation cycles, cells were rested for an additional week and tested for specificity to antigen presenting cells (APC) pulsed with peptide pools using interferon-gamma ELISA and proliferation assays. For these assays, adherent
20 monocytes loaded with either the relevant peptide pool or an irrelevant peptide were used as APC. T cell lines that appeared to specifically recognize L762P peptide pools both by cytokine release and proliferation were identified for each pool. Emphasis was placed on identifying T cells with proliferative responses. T cell lines that demonstrated either both L762P-specific cytokine secretion and proliferation, or strong proliferation
25 alone were further expanded to be tested for recognition of individual peptides from the pools, as well as for recognition of recombinant L762P. The source of recombinant L762P was *E. coli*, and the material was partially purified and endotoxin positive. These studies employed 10 micrograms of individual peptides, 10 or 2 micrograms of an irrelevant peptide, and 2 or 0.5 micrograms of either L762P protein or an irrelevant,
30 equally impure, *E. coli* generated recombinant protein. Significant interferon-gamma production and CD4 T cell proliferation was induced by a number of L762P-derived

peptides in each pool. The amino acid sequences for these peptides are provided in SEQ ID NO: 232-251. These peptides correspond to amino acids 661-680, 676-696, 526-545, 874-893, 811-830, 871-891, 856-875, 826-845, 795-815, 736-755, 706-725, 706-725, 691-710, 601-620, 571-590, 556-575, 616-635, 646-665, 631-650, 541-560
5 and 586-605, respectively, of SEQ ID NO: 161.

CD4 T cell lines that demonstrated specificity for individual L762P-derived peptides were further expanded by stimulation with the relevant peptide at 10 micrograms/ml. Two weeks post-stimulation, T cell lines were tested using both proliferation and IFN-gamma ELISA assays for recognition of the specific peptide. A
10 number of previously identified T cells continued to demonstrate L762P-peptide specific activity. Each of these lines was further expanded on the relevant peptide and, following two weeks of expansion, tested for specific recognition of the L762P-peptide in titration experiments, as well as for recognition of recombinant *E. coli*-derived L762P protein. For these experiments, autologous adherent monocytes were pulsed with either
15 the relevant L762P-derived peptide, an irrelevant mammaglobin-derived peptide, recombinant *E. coli*-derived L762P (approx. 50% pure), or an irrelevant *E. coli*-derived protein. The majority of T cell lines were found to show low affinity for the relevant peptide, since specific proliferation and IFN-gamma ratios dramatically decreased as L762P peptide was diluted. However, four lines were identified that demonstrated
20 significant activity even at 0.1 micrograms/ml peptide. Each of these lines (referred to as A/D5, D/F5, E/A7 and E/B6) also appeared to specifically proliferate in response to the *E. coli*-derived L762P protein preparation, but not in response to the irrelevant protein preparation. The amino acid sequences of the L762P-derived peptides recognized by these lines are provided in SEQ ID NO: 234, 249, 236 and 245,
25 respectively. No protein specific IFN-gamma was detected for any of the lines. Lines A/D5, E/A7 and E/B6 were cloned on autologous adherent monocytes pulsed with the relevant peptide at 0.1 (A/D5 and E/A7) or 1 (D/F5) microgram/ml. Following growth, clones were tested for specificity for the relevant peptide. Numerous clones specific for the relevant peptide were identified for lines A/D5 and E/A7.

EXAMPLE 8

PROTEIN EXPRESSION OF LUNG TUMOR-SPECIFIC ANTIGENS

5 a) Expression of L514S in *E. coli*

The lung tumor antigen L514S (SEQ ID NO: 89) was subcloned into the expression vector pE32b at NcoI and NotI sites, and transformed into *E. coli* using standard techniques. The protein was expressed from residues 3-153 of SEQ ID NO: 89. The expressed amino acid sequence and the corresponding DNA sequence are
10 provided in SEQ ID NO: 252 and 253, respectively.

b) Expression of L762P

Amino acids 32-944 of the lung tumor antigen L762P (SEQ ID NO: 161), with a 6X His Tag, were subcloned into a modified pET28 expression vector,
15 using kanamycin resistance, and transformed into BL21 CodonPlus using standard techniques. Low to moderate levels of expression were observed. The determined DNA sequence of the L762P expression construct is provided in SEQ ID NO: 254.

From the foregoing it will be appreciated that, although specific
20 embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

SEQUENCE LISTING

<110> Corixa Corporation et al.

<120> COMPOUNDS AND METHODS FOR THERAPY
AND DIAGNOSIS OF LUNG CANCER

<130> 210121.45501PC

<140> PCT

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3

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7

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tctncanaaa	cttcctggcc	acnattcnaa	ttnanggnca	cgnacanatn	ccttccatna	480
ancncacccc	acntttgana	gccangacaa	tgactgcntn	aantgaaggc	ntgaaggaan	540
aactttgaaa	ggaaaaaaa	ctttgtttcc	ggcccccttc	aacncttctg	tgtnnancac	600
tgctttctng	naaccctgga	agcccnngna	cagtgttaca	tgttgttcta	nnaaacngac	660
ncttnaatnt	cnatcttccc	nanaacgatt	ncncc			695

<210> 16

<211> 669

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(669)

<223> n = A,T,C or G

<400> 16

cgccgaagca	gcagcgcagg	ttgtccccgt	ttccccctccc	ccttcccttc	tccggttgcc	60
ttccccgggcc	ccttacactc	cacagtccccg	gtccccgcat	gtcccagaaa	caagaagaag	120
agaaccctgc	ggaggagacc	ggcgaggaga	agcaggacac	gcaggagaaa	gaaggtattc	180
tgcttgagag	agctgaagag	gcaaagctaa	aggccaaata	cccaagccta	ggacaaaagc	240
ctggaggctc	cgacttcctc	atgaagagac	tccagaaaagg	gcaaaaagtac	tttgactcng	300
gagactacaa	catggccaaa	gccaacatga	agaataagca	gctgccaagt	gcangaccag	360
acaagaacct	ggtgactggt	gatcacatcc	ccaccccaca	ggatctgccc	agagaaagtc	420
ctcgctcgtc	accagcaagc	ttgcgggtgg	ccaagttgaa	tgatgctgcc	ggggctctgc	480
canatctgag	acgtttccct	ccctgccccca	cccgggtcct	gtgctggctc	ctgcccttcc	540
tgcttttgca	gccanggggc	aggaagtggc	ncnggtngtg	gctggaaagc	aaaacccttt	600
cctgttggtg	tcccacccat	ggagcccctg	gggcgagccc	angaacttga	ncctttttgt	660
tntcttncc						669

<210> 17

<211> 697

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(697)

<223> n = A,T,C or G

<400> 17

gcaagatatg	gacaactaag	tgagaaggta	atnctctact	gctctagntn	ctcnggcnn	60
gacgcgctga	ggagannnac	gctggcccan	ctgccggcca	cacacgggga	tcntggtnat	120
gcctgcccan	gggancccca	ncnctcggan	cccatntcac	accggnncn	tncgcccacn	180
ncctggctcn	cncngcccng	nccagctcnc	gnccccctcc	gcnnnctcn	ttnnctctc	240
cncnccctcc	nacnacnct	cctaccncng	gtccctctcc	cagccccccc	ccgcaancct	300
ccacnacncc	ntcnnncnga	ancnccnctc	genctcngcc	ccngccccct	gccccccgcc	360
cncnacnncg	cgntcccccg	cgcnccngc	ctnccccct	cccacnacag	ncncacccgc	420
agnacgcnc	tccgcccnc	gacgcccnn	cccgcgcgc	tcacctcat	ggncnncng	480
ccccgctcnc	nccnctgcnc	gccgnccngg	cgccccgcgc	cnnccngntn	ccnccngng	540

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ccccngcngn angcngtgcg cnnccangncc gngccggnncn ncaccctccg nccnccgccc      600
cgcccgcgtgg gggctcccgc cncgcggntc antcccccnc ctnccgccc ctntccgntc      660
cnnnctcnc gctcngcgcn cgcccnccnc cccccc      697

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<210> 18
<211> 670
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (670)
<223> n = A,T,C or G

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<400> 18
ctcgtgtgaa ggggtgcagta cctaagccgg agcggggtag aggcggggccg gcaccccctt      60
ctgacctcca gtgccgccgg cctcaagatc agacatggcc cagaacttga acgacttggc      120
gggacggctg cccgccgggc cccggggcat gggcacggcc ctgaagctgt tgctgggggc      180
cggcgccgtg gcctacgggtg tgcgcgaatc tgtgttcacc gtggaaggcg ggcncagagc      240
catcttcttc aatcggatcg gtggagtgc caggacacta tcctggggccg anggccttca      300
cttcaggatc cttgggtcca gtaccccanc atctatgaca ttcggggccag acctcgaaaa      360
aatctcctcc ctacaggctc caaagaccta cagatgggtga atatctccct gcgagtgttg      420
tctcgaccaa tgctcangaa cttcctaaca tgttccancg cctaagggct ggactacnaa      480
gaacgantgt tgccgtccat tgtcacgaag tgctcaagaa tttnggtggc caagttcaat      540
gncctcacnn ctgatcnccc agcggggcca agttanccct gggtgatccc cgggganctg      600
acnnaaaagg gccaaggact tcccctcatc ctggataatg tggccntcac aaagctcaac      660
tttanccacc      670

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<210> 19
<211> 606
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (606)
<223> n = A,T,C or G

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<400> 19
actagtgcc aacctcagctc ccaggccagt tctctgaatg tcgaggagtt ccaggatctc      60
tggcctcagt tgctccttggg tattgatggg ggacaaattg gggatggcca gagccccgag      120
tgctgccttg gctcaactgt ggttgatttg tctgtgcccc gaaagtgttg catcattcgt      180
ccaggctgtg ccctggaaag tactacagcc atcctccaac agaagtacgg actgctcccc      240
tcacatgcgt cctacctgtg aaactctggg aagcaggaag gccaagacc tgggtgctgga      300
tactatgtgt ctgtccactg acgactgtca aggccctatt tgcagaggcc accggagcta      360
gggcactagc ctgactttta aggcagtgtg tctttctgag cactgtagac caagcccttg      420
gagctgctgg tttagccttg cacctgggga aaggatgtat ttatttgtat tttcatatat      480
cagccaaaag ctgaatggaa aagtnagaa cattcctagg tggccttatt ctaataagtt      540
tcttctgtct gttttgtttt tcaattgaaa agttattaaa taacagattt agaatctagt      600
gagacc      606

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<210> 20
<211> 449
<212> DNA
<213> Homo sapien

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<400> 20

actagtaa	aacagcag	ca gaaacat	cag tatcag	cagc gtcgcc	agca ggagaat	atg	60
cagcgcca	gagagaga	accccc	gctc cctgag	gagg acctgt	ccaa actctt	caaa	120
ccaccaca	gcgctgcc	ag gatgg	actcg ctgctc	attg caggcc	agat aaacac	ttac	180
tgccaga	aaca tcaagg	agtt cactgc	ccaa aactta	ggca agctct	tcac ggccc	aggct	240
cttcaaga	at acaaca	acta agaaa	aggaa gtttcc	agaa aagaag	ttaa catga	actct	300
tgaagtc	aca ccaggg	caac tcttg	gaaga aatat	atttg catatt	gaaa agcac	agagg	360
atttctt	tag tgtcatt	gcc gatttt	ggct ataac	agtgt ctttct	agcc ataata	aaat	420
aaaacaaa	at cttgact	gct tgctca	aaaa				449

<210> 21

<211> 409

<212> DNA

<213> Homo sapien

<400> 21

tatcaat	caa ctggt	gaata attaa	acaat gtgtg	gtgtg atcata	caa gggta	ccact	60
caatgata	aaa aggaaca	agc tgcct	tatatg tggaaca	aca tggat	gcatt tcagaa	actt	120
tatgttg	agtgaa	acaa acacg	gagaa catact	atgt ggttct	cttt atgta	acatt	180
acagaaa	ataa aaacag	aggc aaccac	cttt gaggc	agtat ggagt	gagat agact	ggaaa	240
aaggaagg	aa ggaaact	cta cgctg	atgga aatgt	ctgtg tcttc	attgg gtggt	agtta	300
tgtgggg	ata tacatt	tgtc aaaat	tttatt gaact	atata ctaaag	aact ctgcatt	ttta	360
ttgggat	gtataa	taacct caatt	aaaaa gacaaa	aaaaa aaaaaa			409

<210> 22

<211> 649

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(649)

<223> n = A,T,C or G

<400> 22

acaatttt	tca ttatct	taag cacatt	gtac atttct	acag aacct	gtgat tattct	cgca	60
tgataagg	at ggtact	tgca tatggt	gaat tactact	gtt gacag	tttcc gcagaa	atcc	120
tattttc	agtg gacca	acatt gtggc	atggc agcaa	atgcc aacatt	tttgt ggaat	agcag	180
caaatct	aca agagac	cttg gttgg	ttttt cgtttt	gtttt tcttt	gtttt ttcccc	cttc	240
tcctga	atca gcagg	gatgg aang	agggt gggaa	ggttat gaatt	actcc ttccag	tagt	300
agctct	gaag tgtcac	attt aatat	cagtt ttttt	taaac atgatt	cttag ttnaat	gtag	360
aagagag	aag aaagag	gaag tgttc	acttt tttaata	cac tgattt	tagaa atttg	atgct	420
ttatat	cagt agttct	gagg tattg	atagc ttgctt	tatt tctgc	cttta cgttg	acagt	480
gttgaag	cag ggtga	ataac taggg	gcata tatatt	ttttt ttttt	gttaa gctgt	ttcat	540
gatgttt	tct ttgga	atttc cggata	agtt caggaa	aaaca tctgc	atgtt gttat	ctagt	600
ctgaagt	tcn tatcc	atctc attaca	aaa aaacn	cccag aacgg	nttg		649

<210> 23

<211> 669

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

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<222> (1)...(669)

<223> n = A,T,C or G

<400> 23

actagtgccg	tactggctga	aatccctgca	ggaccaggaa	gagaaccagt	tcagactttg	60
tactctcagt	caccagctct	ggaattagat	aaattccttg	aagatgtcag	gaatgggatc	120
tatcctctga	cagcctttgg	gctgcctcgg	ccccagcagc	cacagcagga	ggaggtgaca	180
tcacctgtcg	tgccccctc	tgtcaagact	ccgacacctg	aaccagctga	ggtggagact	240
cgcaaggtgg	tgctgatgca	gtgcaacatt	gagtcggtgg	aggagggagt	caaacaccac	300
ctgacacttc	tgctgaagtt	ggaggacaaa	ctgaaccggc	acctgagctg	tgacctgatg	360
ccaaatgaga	atatccccga	gttggcggct	gagctggtgc	agctgggctt	cattagttag	420
gctgaccaga	gccggttgac	ttctctgcta	gaagagactt	gaacaagtcc	aattttgcca	480
ggaacagtac	cctcaactca	gccgctgtca	ccgtctcctc	ttagagctca	ctcgggccag	540
gccctgatct	gcgctgtggc	tgtcctggac	gtgctgcacc	ctctgtcctt	ccccccagtc	600
agtattacct	gtgaagccct	tccctccttt	attattcagg	anggctgggg	gggctccttg	660
nttctaacc						669

<210> 24

<211> 442

<212> DNA

<213> Homo sapien

<400> 24

actagtacca	tcttgacaga	ggatacatgc	tcccaaaacg	tttgttacca	cacttaaaaa	60
tcactgccat	cattaagcat	cagtttcaaa	attatagcca	ttcatgattt	actttttcca	120
gatgactatc	attattctag	tcctttgaat	ttgtaagggg	aaaaaaaaaca	aaaacaaaaa	180
cttacgatgc	actttttctc	agcacatcag	atttcaaatt	gaaaatttaa	gacatgctat	240
ggtaatgcac	ttgctagtac	tacacacttt	ggtacaacaa	aaaacagagg	caagaaacaa	300
cggaaagaga	aaagccttcc	tttgttggcc	cttaaactga	gtcaagatct	gaaatgtaga	360
gatgatctct	gacgatacct	gtatgttctt	attgtgtaaa	taaaattgct	ggtatgaaat	420
gacctaaaaa	aaaaaaaaaga	aa				442

<210> 25

<211> 656

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(656)

<223> n = A,T,C or G

<400> 25

tgcaagtacc	acacactggt	tgaattttgc	acaaaaagtg	actgtaggat	caggtgatag	60
ccccggaatg	tacagtgtct	tggtgcacca	agatgccttc	taaaggctga	cataccttgg	120
accctaattg	ggcagagagt	atagccctag	cccagtgggtg	acatgaccac	tccctttggg	180
aggcctgagg	tagaggggag	tggtatgtgt	tttctcagtg	gaagcagcac	atgagtgggt	240
gacaggatgt	tagataaagg	ctctagttag	ggtgtcattg	tcatttgaga	gactgacaca	300
ctcctagcag	ctggtaaagg	ggtgctggan	gccatggagg	anctctagaa	acattagcat	360
gggctgatct	gattacttcc	tggcatcccc	ctcactttta	tgggaagtct	tattagangg	420
atgggacagt	tttccatata	cttgctgtgg	agctctggaa	cactctctaa	atttcctctt	480
attaaaaatc	actgccctaa	ctacacttcc	tccttgaagg	aatagaaatg	gaactttctc	540
tgacatantt	cttggcatgg	ggagccagcc	acaaatgana	atctgaacgt	gtccaggttt	600
ctcctganac	tcatctacat	agaattgggt	aaaccctccc	ttggaataag	gaaaaa	656

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<210> 26
 <211> 434
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(434)
 <223> n = A,T,C or G

<400> 26
 actagttcag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60
 ctaggtgttt ccatctatgt ttcaatctgt ccatctacca ggctcgcga taaaaacaaa 120
 acaaaaaaac gctgccaggt tttagaagca gttctggtct caaaaccatc aggatcctgc 180
 caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcatct 240
 aataactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttgtgg 300
 gaataagtta taatcagtat tcatctcttt gttttttgtc actcttttct ctctaattgt 360
 gtcatttgta ctgtttgaaa aatatttctt ctatnaaatt aaactaacct gccttaaaaa 420
 aaaaaaaaaa aaaa 434

<210> 27
 <211> 654
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(654)
 <223> n = A,T,C or G

<400> 27
 actagtccaa cacagtcaga aacattgttt tgaatcctct gtaaaccaag gcattaatct 60
 taataaacca ggatccattt aggtaccact tgatataaaa aggatatcca taatgaatat 120
 ttataactgc atcctttaca ttagccacta aatacgttat tgcttgatga agacctttca 180
 cagaatccta tggattgcag catttcactt ggctacttca taccatgcc ttaaagaggg 240
 gcagtttctc aaaagcagaa acatgccgcc agttctcaag ttttcctcct aactccattt 300
 gaatgtaagg gcagctggcc cccaatgtgg ggaggtccga acattttctg aattcccatt 360
 ttcttgttcg cggctaaatg acagtttctg tcattactta gattccgac tttcccaaag 420
 gtgttgattt acaaagaggc cagctaatag cagaaatcat gacctgaaa gagagatgaa 480
 attcaagctg tgagccaggc agganctcag tatggcaaag gtcttgagaa tcngccattt 540
 ggtacaaaaa aaatttttaa gcntttatgt tataccatgg aaccatagaa anggcaaggg 600
 aattgttaag aanaatttta agtgtccaga cccanaanga aaaaaaaaaa aaaa 654

<210> 28
 <211> 670
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(670)
 <223> n = A,T,C or G

<400> 28
 cgtgtgcaca tactgggagg atttccacag ctgcacggtc acagccctta cggattgcc 60

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ggaaggggcg aaagatatgt gggataaact gagaaaagaa nccaaaaacc tcaacatcca      120
aggcagctta ttcgaactct gcggcagcgg caacggggcg gcgggggtccc tgctcccggc      180
gttcccgggtg ctcttggtgt ctctctcggc agcttttagcg acctgncttt ccttctgagc      240
gtggggccag ctccccccgc ggcgcccacc cacnctcact ccatgctccc ggaaatcgag      300
aggaagatca ttagttcttt ggggacgtn gtgattctct gtgatgctga aaaacactca      360
tatagggaat gtgggaaatc ctganctctt tnttatntcg tntgatttct tgtgttttat      420
ttgccaaaat gttaccaatc agtgaccaac cnagcacagc caaaaatcgg acntcngctt      480
tagtccgtct tcacacacag aataagaaaa cggcaaacc accccacttt tnantttnat      540
tattactaan ttttttctgt tgggcaaaag aatctcagga acngccctgg ggccnccgta      600
ctanagttaa ccnagctagt tncatgaaaa atgatgggct ccnctcaat gggaaagcca      660
agaaaaagnc                                     670

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<210> 29

<211> 551

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(551)

<223> n = A,T,C or G

<400> 29

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actagtcttc cacagcctgt gaatccccct agacctttca agcatagtga gcggagaaga      60
agatctcagc gtttagccac cttacccatg cctgatgatt ctgtagaaaa ggtttcttct      120
ccctctccag ccactgatgg gaaagtattc tccatcagtt ctcaaaatca gcaagaatct      180
tcagtaccag aggtgcctga tgttgacat ttgccacttg agaagctggg accctgtctc      240
cctcttgact taagtcgtgg ttcagaagtt acagcaccgg tagcctcaga ttctctttac      300
cgtaatgaat gtcccagggc agaaaaagag gatacncaga tgcttccaaa tccttcttcc      360
aaagcaatag ctgatgggaa gaggagctcc agcagcagca ggaatatcga aaacagaaaa      420
aaaagtgaaa ttgggaagac aaaagctcaa cagcatttgg taaggagaaa aganaagatg      480
aggaaggaag agagaagaga gacnaagatc nctacggacc gnnncggaag aagaagaagn      540
aaaaaanaaa a                                     551

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<210> 30

<211> 684

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(684)

<223> n = A,T,C or G

<400> 30

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actagttcta tctggaaaaa gcccgggttg gaagaagctg tggagagtgc gtgtgcaatg      60
cgagactcat ttcttggaag catccctggc aaaaatgcag ctgagtacaa ggttatcact      120
gtgatagaac ctggactgct ttttgagata atagagatgc tgcagtctga agagacttcc      180
agcacctctc agttgaatga attaatgatg gcttctgagt caactttact ggctcaggaa      240
ccacgagaga tgactgcaga tgtaatcgag cttaaaggga aattcctcat caacttagaa      300
ggtggtgata ttcgtgaaga gtcttcctat aaagtaattg tcatgccgac tacgaaagaa      360
aatgcccc gttgttgga gtatacagcg ggagtcttca gatacactgt gtctcgtatg      420
tgcagaagtt gtcagtggga aaatagtatt aacagctcac tcgagcaaga accctcctga      480
cagtactggg ctagaagttt ggatggatta tttacaatat aggaaagaaa gccaaagaatt      540
aggtnatgag tggatgagta aatggtgga gatggggaat tcaaatacaga attatggaag      600

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aagttnttcc tggtactata gaaaggaatt atgtttatatt acatgcagaa aatatanatg 660
 tgtgggtgtgt accgtggatg gaan 684

<210> 31
 <211> 654
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(654)
 <223> n = A,T,C or G

<400> 31
 gcgcagaaaa ggaaccaata tttcagaaac aagcttaata ggaacagctg cctgtacatc 60
 aacatcttct cagaatgacc cagaagttat catcgtggga gctggcgtgc ttggctctgc 120
 tttggcagct gtgctttcca gagatggaag aaaggtgaca gtcattgaga gagacttaaa 180
 agagcctgac agaatagttg gagaattcct gcagccgggt gggtatcatg ttctcaaaga 240
 ccttggctct ggagatacag tggaaggtct tgatgccag gttgtaaata gttacatgat 300
 tcatgatcag ggaaagcaaa tcagangttc agattcctta ccctctgtca gaaaacaatc 360
 aagtgcagag tggaagagct ttccatcacg gaagattcat catgagtctc cggaaagcag 420
 ctatggcaga gcccaatgca aagtttattg aaggtgttgt gttacagtta ttagaggaag 480
 atgatgttgt gatgggagtt cagtacaagg ataaagagac tgggagatat caaggaactc 540
 catgctccac tgactgttgt tgcagatggg cttttctcca anttcaggaa aagcctggtc 600
 tcaataaagt ttctgtatca ctcatgttgt tggcttctta tgaagaatgc nccc 654

<210> 32
 <211> 673
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(673)
 <223> n = A,T,C or G

<400> 32
 actagtgaag aaaaagaaat tctgatacgg gacaaaaatg ctcttcaaaa catcattctt 60
 tatcacctga caccaggagt tttcattgga aaaggatttg aacctgggtg tactaacatt 120
 ttaaagacca cacaaggaag caaaatcttt ctgaaagaag taaatgatac acttctgggtg 180
 aatgaattga aatcaaaaaga atctgacatc atgacaacaa atgggtgtaat tcatgttgta 240
 gataaactcc tctatccagc agacacacct gttggaaatg atcaactgct ggaaataactt 300
 aataaattaa tcaaatacat ccaaattaag tttgttcgtg gtagcacctt caaagaaatc 360
 cccgtgactg tctatnagcc aattattaaa aaatacacca aaatcattga tgggagtgcc 420
 tgtgggaaat aactgaaaaa gagaccgaga agaacgaatc attacaggtc ctgaaataaa 480
 atacctagga tttctactgg aggtggagaa acagaagaac tctgaagaaa ttgttacaag 540
 aagangtccc aaggtcacca aattcattga aggtgggtgat ggtctttatt tgaagatgaa 600
 gaaattaaaa gacgcttcag ggagacnccc catgaaggaa ttgccagcca caaaaaaatt 660
 cagggattag aaa 673

<210> 33
 <211> 673
 <212> DNA
 <213> Homo sapien

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<220>
 <221> misc_feature
 <222> (1)...(673)
 <223> n = A,T,C or G

<400> 33
 actagttatt tactttcctc cgcttcagaa ggtttttcag actgagagcc taagcatact 60
 ggatctgttg tttcttttgg gtctcacctc atcagtgtgc atagtggcag aaattataaa 120
 gaaggttgaa aggagcaggg aaaagatcca gaagcatgtt agttcgacat catcatcttt 180
 tcttgaagta tgatgcatat tgcattattht tatttgcaaa ctaggaattg cagtctgagg 240
 atcatttaga agggcaagtt caagaggata tgaagatttg agaacttttt aactattcat 300
 tgactaaaaa tgaacattaa tgttnaagac ttaagacttt aacctgctgg cagtcccaaa 360
 tgaaattatg caactttgat atcatattcc ttgattttaa ttgggctttt gtgattgant 420
 gaaactttat aaagcatatg gtcagttatt tnattaaaaa ggcaaaacct gaaccacctt 480
 ctgcacttaa agaagtctaa cagtacaaat acctatctat cttagatgga tntatttntt 540
 tntattttta aatattgtac tattttatggg nggtggggct ttcttactaa tacacaaatn 600
 aatttatcat ttcaanggca ttctatttgg gtttagaagt tgattccaag nantgcatat 660
 ttcgctactg tnt 673

<210> 34
 <211> 684
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(684)
 <223> n = A,T,C or G

<400> 34
 actagtttat tcaagaaaag aacttactga ttcctctgtt cctaaagcaa gagtggcagg 60
 tgatcagggc tgggtgtagca tccggttcct ttagtgcagc taactgcatt tgtcactgat 120
 gaccaaggag gaaatcacta agacatttga gaagcagtgg tatgaacggt cttggacaag 180
 ccacagttct gagccttaac cctgtagttt gcacacaaga acgagctcca cctccccttc 240
 ttcaggagga atctgtgcgg atagattggc tggacttttc aatggttctg gggtgcaagt 300
 gggcactgtt atggctgggt atggagcgga cagccccagg aatcagagcc tcagcccggc 360
 tgcctgggtg gaaggtacag gtgttcagca ccttcggaaa aagggcataa agtngtgggg 420
 gacaattctc agtccaagaa gaatgcattg accattgctg gctatttgct tncctagtan 480
 gaattggatn catttttgac cangatnntt ctncctatgct ttnttgcaat gaaatcaaat 540
 cccgcattat ctacaagtgg tatgaagtcc tgcnncccc agagaggctg ttcaggcnat 600
 gtcttccaag ggcagggtgg gttacaccat tttacctccc ctctcccccc agattatgna 660
 cncagaagga atttntttcc tccc 684

<210> 35
 <211> 614
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(614)
 <223> n = A,T,C or G

<400> 35
 actagtccaa cgcgttngcn aatattcccc tggtagccta ctcccttacc cccgaatatt 60

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ggtaagatcg	agcaatggct	tcaggacatg	ggttctcttc	tcctgtgatc	attcaagtgc	120
tcactgcatg	aagactggct	tgtctcagtg	tntcaacctc	accagggctg	tctcttggtc	180
cacacctcgc	tcctgttag	tgccgtatga	cagcccccat	canatgacct	tggccaagtc	240
acggtttctc	tgtggtcaat	gttggtnggc	tgattggtgg	aaagtanggt	ggaccaaagg	300
aagnncgtg	agcagncanc	nccagttctg	caccagcagc	gcctccgtcc	tactnggggtg	360
ttccngtttc	tcctggccct	gngtgggcta	nggcctgatt	cgggaaanag	cctttgcang	420
gaaggganga	taantgggat	ctaccaattg	attctggcaa	aacnatntct	aagattnttn	480
tgctttatgt	ggganacana	tctanctctc	atttnntgct	gnanatnaca	ccctactcgt	540
gntcgancnc	gtcttcgatt	ttcgganaca	cnccantnaa	tactggcggt	ctgttggttaa	600
aaaaaaaaaa	aaaa					614

<210> 36

<211> 686

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(686)

<223> n = A,T,C or G

<400> 36

gtggctggcc	cggttctccg	cttctcccca	tcccctactt	tcctccctcc	ctccctttcc	60
ctccctcgtc	gactgttgct	tgctggtcgc	agactccctg	acccctccct	caccctcccc	120
taacctcggg	gccaccggat	tgcccttctt	ttcctgttgc	ccagcccagc	cctagtgtca	180
gggcgggggc	ctggagcagc	ccgaggcact	gcagcagaag	ananaaaaga	cacgacnaac	240
ctcagctcgc	cagtccgggc	gctngcttcc	cgccgcatgg	caatnagaca	gacgcccgtc	300
acctgctctg	ggcacacgcg	accggtgggt	gatttggcct	tcagtggcat	cacccttatg	360
ggtatttctt	aatcagcgtc	tgcaaagatg	gttaacctat	gctacgccag	ggagatacag	420
gagactggat	tggaacattt	ttgggggtcta	aaggtctgtt	tgggggtgcaa	cactgaataa	480
ggatgccacc	aaagcagcta	cagcagctgc	agatttcaca	gcccaggtgt	gggatgctgt	540
ctcagganat	naattgataa	cctgggtcat	aacacattgt	caagaatgtg	gatttcccca	600
ggatattatt	atttgtttac	cgggggganag	gataactgtt	tcnctntattt	taattgaaca	660
aactnaaaca	aanctaagg	aatcc				686

<210> 37

<211> 681

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(681)

<223> n = A,T,C or G

<400> 37

gagacanacn	naacgtcang	agaanaaaag	angcatggaa	cacaanccag	gcncgatggc	60
caccttccca	ccagcancca	gcgcccccca	gcngccccca	ngnccggang	accangactc	120
cancctgnat	caatctganc	tctattcctg	gcccattncct	acctcggagg	tggangccgn	180
aaaggtcgca	cnnncagaga	agctgctgcc	ancaccancc	gccccnnccc	tgncgggctn	240
nataggaaac	tggtgaccnn	gctgcanaat	tcatacagga	gcacgcgang	ggcacnnnct	300
cacactgagt	tnnngatgan	gcctnaccan	ggacctnccc	cagcnnattg	annacnggac	360
tgcgaggagg	ggaagacccc	gnacnggatc	ctggccggcn	tgccaccccc	ccacccttag	420
gattatnccc	cttgactgag	tctctgaggg	gctacccgaa	ccgcctcca	ttccctacca	480
natnntgctc	natcgggact	gacangctgg	ggatngggagg	ggctatcccc	cancatcccc	540

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tnanaccaac agcnacngan natnggggct ccccnngggtc ggngcaacnc tcctncaccc	600
cggcgenggc cttegggtgnt gtcctccntc aacnaattcc naaanggcgg gccccccngt	660
ggactcctcn ttgttccctc c	681

<210> 38
 <211> 687
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(687)
 <223> n = A,T,C or G

<400> 38						
canaaaaaaaa	aaaacatggc	cgaaccagn	aagctgcgcg	atggcgccac	ggccccctctt	60
ctcccggcct	gtgtccggaa	ggtttccctc	cgaggcgccc	cggctcccgc	aagcggagga	120
gagggcgggg	cntgccgggg	cggagctca	naggccctgg	ggccgctctg	ctctcccgcc	180
atcgcaagg	cggcgctaac	ctnaggcctc	cccgcaaagg	tccccnangc	ggnggcggcg	240
gggggctgtg	anaaccgcaa	aaanaacgct	gggcgcgcng	cgaaccgcgc	cacccccgcg	300
aaggananac	ttccacagan	gcagcgtttc	cacagcccan	agccacnttt	ctaggggtgat	360
gcaccccagt	aagttcctgn	cggggaagct	caccgctgtc	aaaaaanctc	ttcgctccac	420
cggcgacna	agggggangan	ggcangangc	tgccgcccgc	acaggtcac	tgatcacgtc	480
gcccgccta	ntctgctttt	gtgaatctcc	actttgttca	accccacccg	ccgttctctc	540
ctccttgcc	cttccctcna	ccttaanaac	cagcttcctc	taccnratng	tanttnctct	600
gcncnngtng	aaattaattc	ggtcnccgg	aacctcttnc	ctgtggcaac	tgctnaaaga	660
aactgctgtt	ctgnttactg	cngtccc				687

<210> 39
 <211> 695
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(695)
 <223> n = A,T,C or G

<400> 39						
actagtctgg	cctacaatag	tgtgattcat	gtaggacttc	tttcatcaat	tcaaaacccc	60
tagaaaaacg	tatacagatt	atataagtag	ggataagatt	tctaacattt	ctgggctctc	120
tgaccctgc	gctagactgt	ggaaaggagg	tattattata	gtatacaaca	ctgctgttgc	180
cttattagtt	ataacatgat	aggtgctgaa	ttgtgattca	caatttaaaa	acactgtaat	240
ccaaactttt	ttttttaact	gtagatcatg	catgtgaatg	ttaatgttaa	tttgttcaan	300
gttgttatgg	gtagaaaaaa	ccacatgcct	taaaatttta	aaaagcaggg	cccaaactta	360
ttagtttaaa	attaggggta	tgtttccagt	ttgttattaa	ntggttatag	ctctgttttag	420
aanaaatcna	ngaacangat	ttngaaantt	aagntgacat	tatttnccag	tgacttggtta	480
atgtgaaatc	anacacggca	ccttccgttt	tggtntctatt	ggnttttgaa	tccaancngg	540
ntccaaatct	tnttggaac	ngtcnttta	acttttttac	nanatcttat	ttttttat	600
tggaatggcc	ctatttaang	ttaaaagggg	ggggnccac	naccattent	gaataaaact	660
naatatatat	ccttggtccc	ccaaaattta	aggng			695

<210> 40
 <211> 674
 <212> DNA

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<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(674)

<223> n = A,T,C or G

<400> 40

actagtagtc	agttgggagt	ggttgctata	ccttgacttc	atztatatga	atttccactt	60
tattaaataa	tagaaaagaa	aatcccgggtg	cttgccagtag	agttatagga	cattctatgc	120
ttacagaaaa	tatagccatg	attgaaatca	aatagtaaag	gctgttctgg	ctttttatct	180
tcttagctca	tcttaaataa	gtagtacact	tgggatgcag	tgcgtctgaa	gtgctaata	240
gttgtaacaa	tagcacaaat	cgaacttagg	atgtgtttct	tctcttctgt	gtttcgattt	300
tgatcaattc	tttaattttg	ggaacctata	atacagtttt	cctattcttg	gagataaaaa	360
ttaaattgat	cactgatatt	taagtcattc	tgcttctcat	ctnaatattc	catattctgt	420
attagganaa	antacctccc	agcacagccc	cctctcaaac	cccacccaaa	accaagcatt	480
tggaatgagt	ctcctttatt	tccgaantgt	ggatgggtata	acccatatcn	ctccaatttc	540
tgnttgggtt	gggtattaat	ttgaactgtg	catgaaaagn	ggnaatcttt	nctttgggtc	600
aaantttncc	ggttaatttg	nctngncaaa	tccaatttnc	tttaagggtg	tctttataaa	660
atttgctatt	cngg					674

<210> 41

<211> 657

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(657)

<223> n = A,T,C or G

<400> 41

gaaacatgca	agtaccacac	actgtttgaa	ttttgcacaa	aaagtgactg	tagggatcag	60
gtgatagccc	cggaatgtac	agtgtcttgg	tgcaccaaga	tgccttctaa	aggctgacat	120
accttgggac	cctaattggg	cagagagtat	agccctagcc	cagtgggtgac	atgaccactc	180
cctttgggag	gctgaagtta	aagggaatgg	tatgtgtttt	ctcatggaag	cagcacatga	240
atnggtnaca	ngatgttaaa	ntaaggntct	antttgggtg	tcttgtcatt	tgaaaaantg	300
acacactcct	ancanctggt	aaaggggtgc	tggaagccat	ggaagaactc	taaaaacatt	360
agcatgggct	gatctgatta	cttcctggca	tcccgcctcac	ttttatggga	agtcttatta	420
naaggatggg	ananttttcc	atatccttgc	tggttggaaact	ctggaacact	ctctaaattt	480
ccctctatta	aaaatcactg	nccttactac	acttcctcct	tganggaata	gaaatggacc	540
ttctcttgac	ttagtctctg	gcatggganc	cagcccaaatt	taaaatctga	cttntccggt	600
ttctccngaa	ctcacctact	tgaattggta	aaacctcctt	tggaattagn	aaaaacc	657

<210> 42

<211> 389

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(389)

<223> n = A,T,C or G

<400> 42

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actagtgtctg	aggaatgtaa	acaagtttgc	tgggccttgc	gagacttcac	caggttgttt	60
cgatagctca	cactcctgca	ctgtgcctgt	cacccaggaa	tgtctttttt	aattagaaga	120
caggaagaaa	acaaaaacca	gactgtgtcc	cacaatcaga	aacctccgtt	gtggcagang	180
ggccttcacc	gccaccaggg	tgtcccgcga	gacagggaga	gactccagcc	ttctgaggcc	240
atcctgaaga	attcctgttt	gggggttgtg	aaggaaaatc	acccggattt	aaaaagatgc	300
tgttgcttgc	ccgcgtngtn	gggaagggac	tggtttcctg	gtgaatttct	taaaagaaaa	360
atattttaag	ttaagaaaaa	aaaaaaaaaa				389

<210> 43

<211> 279

<212> DNA

<213> Homo sapien

<400> 43

actagtgtgaca	agctcctgggt	cttgagatgt	cttctcgtta	aggagatggg	cctttttggag	60
gtaaaggata	aatgaatga	gttctgtcat	gattcactat	tctagaactt	gcatgacctt	120
tactgtgtta	gctctttgaa	tggtcttgaa	atttttagact	ttctttgtaa	acaaataata	180
tgctccttatc	attgtataaa	agctgttatg	tgcaacagtg	tggagatcct	tgtctgattt	240
aataaaatac	ttaaactctg	aaaaaaaaaa	aaaaaaaaaa			279

<210> 44

<211> 449

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (449)

<223> n = A,T,C or G

<400> 44

actagtagca	tctttttctac	aacgttaaaa	ttgcagaagt	agcttatcat	taaaaaacia	60
caacaacaac	aataacaata	aatcctaagt	gtaaatcagt	tattctaccc	cctaccaagg	120
atatcagcct	gttttttccc	ttttttctcc	tggaataaat	tgtgggcttc	ttcccaaatt	180
tctacagcct	ctttcctctt	ctcatgcttg	agcttccctg	tttgacgca	tgcgttgtgc	240
aagantgggc	tgtttngctt	ggantncggg	ccnagtggaa	ncatgctttc	ccttgttact	300
gttggaagaa	actcaaactt	tcnanccta	ggtgttncca	ttttgtcaag	tcatcactgt	360
atttttgtac	tggcattaac	aaaaaaagaa	atnaaatatt	gttccattaa	actttaataa	420
aactttaaaa	gggaaaaaaa	aaaaaaaaaa				449

<210> 45

<211> 559

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (559)

<223> n = A,T,C or G

<400> 45

actagtgtgg	gggaatcacg	gacacttaaa	gtcaatctgc	gaaataattc	ttttattaca	60
cactcactga	agttttttgag	tcccagagag	ccattctatg	tcaaacattc	caagtactct	120
ttgagagccc	agcattacat	caacatgccc	gtgcagttca	aaccgaagtc	cgcaggcaaa	180
tttgaagctt	tgcttgtcat	tcaaacagat	gaaggcaaga	gtattgctat	tcgactaatt	240

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ggtgaagctc ttggaaaaaa ttnactagaa tactttttgt gttaagttaa ttacataagt 300
tgtattttgt taactttatc tttctacact acaattatgc ttttgtatat atattttgta 360
tgatggatat ctataattgt agattttggt tttacaagct aatactgaag actcgactga 420
aatattatgt atctagccca tagtattgta cttaactttt acagggtgaa aaaaaaattc 480
tgtgtttgca ttgattatga tattctgaat aaatatggga atatatattta atgtgggtaa 540
aaaaaaaaaa aaaaaggaa 559

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<210> 46
 <211> 731
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(731)
 <223> n = A,T,C or G

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<400> 46
actagttcta gtaccatggc tgtcatagat gcaaccatta tattccattt agtttcttcc 60
tcaggttccc taacaattgt ttgaaactga atatatatgt ttatgtatgt gtgtgtgttc 120
actgtcatgt atatggtgta tatgggatgt gtgcagtttt cagttatata tatattcata 180
tatacatatg catatatatg tataatatac atatatacat gcatacactt gtataatata 240
catatatata cacatatatg cacacatatn atcactgagt tccaaagtga gtctttattt 300
ggggcaattg tattctctcc ctctgtctgc tcaactgggc tttgcaagac atagcaattg 360
cttgatttcc tttggataag agtcttatct tcggcactct tgactctagc cttaacttta 420
gatttctatt ccagaatacc tctcatatct atcttaaaac ctaaganggg taaagangtc 480
ataagattgt agtatgaaag antttgctta gttaaattat atctcaggaa actcattcat 540
ctacaaatta aattgtaaaa tgatgggttg ttgtatctga aaaaatgttt agaacaagaa 600
atgtaactgg gtacctgtta tatcaaagaa cctcnattta ttaagtctcc tcatagccan 660
atccttatat ngccctctct gacctgantt aatananact tgaataatga atagttaatt 720
taggnttggg c 731

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<210> 47
 <211> 640
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(640)
 <223> n = A,T,C or G

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<400> 47
tgcgngccgg tttggccctt ctttgtanga cactttcate cgccctgaaa tcttcccgat 60
cgttaataac tcctcaggtc cctgcctgca cagggttttt tcttantttg ttgcctaaca 120
gtacaccaaa tgtgacatcc tttcaccaat atngattnct tcataccaca tcntcnatgg 180
anacgactnc aacaattttt tgatnaccn aanactggg ggctnnaana agtacantct 240
ggagcagcat ggacctgtcn gcnactaang gaacaanagt nntgaacatt tacacaacct 300
ttggtatgtc ttactgaaag anagaaacat gcttctnncc ctagaccacg aggncaaccg 360
caganattgc caatgccaaag tccgagcggg tagatcaggg aatacattcc atggatgcat 420
tacatacntt gtccccgaaa nanaagatgc cctaanggct tcttcanact ggtccngaaa 480
acanctacac ctgggtgcttg ganaacanac tctttggaag atcatctggc acaagttccc 540
cccagtgggt tttnccttgg cacctanctt accanatcna ttcggaancc attctttgcc 600
ntggcnttnt nttgggacca ntcttctcac aactgnacc 640

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<210> 48
 <211> 257
 <212> DNA
 <213> Homo sapien

<400> 48
 actagtatat gaaaatgtaa atatcacttg tgtactcaaa caaaagttgg tcttaagctt 60
 ccaccttgag cagccttgga aacctaacct gcctctttta gcataatcac attttctaaa 120
 tgattttctt tgttcctgaa aaagtgattt gtattagttt tacatttggt ttttggaaga 180
 ttatatttgt atatgtatca tcataaaata tttaaataaa aagtatcttt agagtgaaaa 240
 aaaaaaaaaa aaaaaaa 257

<210> 49
 <211> 652
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(652)
 <223> n = A,T,C or G

<400> 49
 actagttcag atgagtggct gctgaagggg ccccttggtc attttcatta taaccaatt 60
 tccacttatt tgaactctta agtcataaat gtataatgac ttatgaatta gcacagttaa 120
 gttgacacta gaaactgccc atttctgtat tacactatca aataggaaac attggaaaga 180
 tggggaaaaa aatcttattt taaaatggct tagaaagttt tcagattact ttgaaaattc 240
 taaacttctt tctgtttcca aaacttgaaa atatgtagat ggactcatgc attaagactg 300
 ttttcaaagc tttcctcaca tttttaaagt gtgattttcc ttttaatatata catatttatt 360
 ttcttttaaag cagctatatc ccaacccatg actttggaga tatacctatn aaaccaatat 420
 aacagcangg ttattgaagc agctttctca aatgttgctt cagatgtgca agttgcaaatt 480
 ttatttgtat ttgtanaata caatttttgt tttaaactgt atttcaatct atttctccaa 540
 gatgcttttc atatagagtg aaatatccca ngataactgc ttctgtgtcg tcgcatttga 600
 cgcataactg cacaaatgaa cagtgtatac ctcttggttg tgcattnacc cc 652

<210> 50
 <211> 650
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(650)
 <223> n = A,T,C or G

<400> 50
 ttgcgctttg atttttttag ggcttgtgcc ctgtttcact tatagggctc agaatgcttg 60
 tgttgagtaa aaaggagatg cccaatatcc aaagctgcta aatgttctct ttgccataaa 120
 gactccgtgt aactgtgtga acacttgga tttttctcct ctgtcccgag gtcgtcgtct 180
 gctttctttt ttgggttctt tctagaagat tgagaaatgc atatgacagg ctgagancac 240
 ctccccaac acacaagctc tcagccacan gcagcttctc cacagcccca gcttcgcaca 300
 ggctcctgga nggctgcctg ggggaggcag acatgggagt gccaaagggtg ccagatgggt 360
 ccaggactac aatgtcttta tttttaactg tttgccactg ctgccctcac ccctgcccgg 420
 ctctggagta ccgtctgccc canacaagtg ggantgaaat ggggggtgggg gggaacactg 480
 attcccantt aggggggtgcc taactgaaca gtagggatan aaggtgtgaa cctgngaant 540

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gcttttataa attatnttcc ttgttanatt tatttttttaa tttaattctct gttnaactgc 600
 ccngggaaaaa ggggaaaaaaa aaaaaaaaaat tctnttttaaa cacatgaaca 650

<210> 51
 <211> 545
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (545)
 <223> n = A,T,C or G

<400> 51
 tggcgtgcaa ccagggtagc tgaagtttgg gtctgggact ggagattggc cattaggcct 60
 cctganattc cagctccctt ccaccaagcc cagtcttgct acgtggcaca gggcaaacct 120
 gactcccttt gggcctcagt tccccctccc cttcatgana tgaaaagaat actacttttt 180
 cttgttggtc taacnttgct ggacncaaag tgtngtcatt attgttgatg tgggtgatgt 240
 gtncaaaaact gcagaagctc actgcctatg agaggaanta agagagatag tggatganag 300
 ggacanaagg agtcattatt tggatatagat ccaccntcc caacctttct ctcctcagtc 360
 cctgcncctc atgtntctgg tntgggtgagt cctttgtgcc accanccatc atgctttgca 420
 ttgctgccat cctgggaagg gggtnatcg tctcacaact tgttgatcgc gtttganatg 480
 catgctttct tnatnaaaca aanaaannaa tgtttgacag ngtttaaaat aaaaaanaaa 540
 caaaa 545

<210> 52
 <211> 678
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (678)
 <223> n = A,T,C or G

<400> 52
 actagtagaa gaactttgcc gcttttgtgc ctctcacagg cgcctaaagt cattgccatg 60
 ggaggaagac gatttggggg gggagggggg gggggcangg tccgtggggc tttccctant 120
 ntatctccat ntccantggn cnntgtcgcc tcttccctcg tcn cattnga anttantccc 180
 tggnccccnn nccctctccn nctnncct cccccctccg ncnctccnn cttttntan 240
 ncttcccat ctcntcccc cctnanngtc ccaacnccgn cagcaatnnc ncaactnctc 300
 nctcncnc ctcnncggt cttctnttct cnaentntnc ncnntnccn tgcnnntnaa 360
 annctctccc cnctgcaanc gattctctcc ctcnncnnan ctntccactc cntncttctc 420
 ncnctctcc ntntentnnc ccacctctcn ccttcgnccc cantacnctc ncnccectn 480
 cgnntenttn nnntcctcnn acnccccnc tcccttnc cctcttctcc ccggtntntc 540
 tctctccnc ncnncnnc cncnccntcc nngcgnccnt ttcgccccn cncncntt 600
 ccttctcnc cantccatcn cntntnccat nctnccntcc nctcacnccc gctnccccn 660
 ntctctttca cacngtcc 678

<210> 53
 <211> 502
 <212> DNA
 <213> Homo sapien

<220>

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<221> misc_feature
 <222> (1)...(502)
 <223> n = A,T,C or G

<400> 53
 tgaagatcct ggtgtcgcca tgggcccgcg ccccgcccgt tgttaccggt attgtaagaa 60
 caagccgtac ccaaagtctc gcttctgccg aggtgtccct gatgccaaaa ttcgcattht 120
 tgacctgggg cggaaaaang caaaantgga tgagtctccg ctttgtggcc acatggtgtc 180
 agatcaatat gagcagctgt cctctgaagc cctgnangct gcccgaattt gtgccaataa 240
 gtacatggta aaaagtngtg gcnaagatgc ttccatatcc ggggtgcggnt ccacccttc 300
 cacgtcatcc gcatacaaa gatgttggtc tgtgctgggg ctgacaggct cccaacaggc 360
 atgcgaagtg cctttggaaa acccanggca ctgtggccag ggttcacatt gggccaattn 420
 atcatgttca tccgcaccaa ctgcagaaca angaacntgt naattnaagc cctgcccagg 480
 gncaanttca aatttcccgg cc 502

<210> 54
 <211> 494
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(494)
 <223> n = A,T,C or G

<400> 54
 actagtccaa gaaaaatatg cttaatgtat attacaaagg ctttgtatat gttaacctgt 60
 tttaatgcca aaagtttgct ttgtccacaa tttccttaag acctcttcag aaagggattt 120
 gtttgcctta atgaatactg ttgggaaaaa acacagtata atgagtgaag agggcagaag 180
 caagaaattt ctacatctta ggcactccaa gaagaatgag tatccacatt tagatggcac 240
 attatgagga ctttaattctt tccttaaaca caataatgtt ttcttttttc ttttattcac 300
 atgattttcta agtatatttt tcatgcagga cagtttttca accttgatgt acagtgactg 360
 tgttaaattt ttctttcagt ggcaacctct ataatcttta aaatatggtg agcatcttgt 420
 ctgttttgaa ngggatatga cnatnaatct atcagatggg aaatcctgtt tccaagttag 480
 aaaaaaaaaa aaaa 494

<210> 55
 <211> 606
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(606)
 <223> n = A,T,C or G

<400> 55
 actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataataaat 60
 gatgttaagc tttttgaaaa gtttaggtta aacctactgt tgtagatta atgtatttgt 120
 tgcttccctt tatctggaat gtggcattag cttttttatt ttaaccctct ttaattctta 180
 ttcaattcca tgacttaagg ttggagagct aaacactggg atttttggat aacagactga 240
 cagttttgca taattataat cggcattgta catagaaagg atatggctac cttttgttaa 300
 atctgcactt tctaaatatc aaaaaaggga aatgaagtat aaatcaattt ttgtataatc 360
 tgtttgaaac atgantttta tttgcttaat attanggctt tgcccttttc tgtagtctc 420
 ttgggatacct gtgtaaaact gttctcatta aacaccaaac agttaagtcc attctctggt 480

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actagctaca aattccgttt catattctac ntaacaattt aaattaactg aaatattttct 540
 anatggtcta cttctgtent ataaaaacna aacttgantt nccaaaaaaa aaaaaaaaaa 600
 aaaaaa 606

<210> 56
 <211> 183
 <212> DNA
 <213> Homo sapien

<400> 56
 actagtatat ttaaacttac aggcttattt gtaatgtaaa ccaccatttt aatgtactgt 60
 aattaacatg gttataatac gtacaatcct tccctcatcc catcacacaa ctttttttgt 120
 gtgtgataaa ctgatttttg tttgcaataa aaccttgaaa aataaaaaaa aaaaaaaaaa 180
 aaa 183

<210> 57
 <211> 622
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (622)
 <223> n = A,T,C or G

<400> 57
 actagtcact actgtcttct ccttgtagct aatcaatcaa tattcttccc ttgcctgtgg 60
 gcagtggaga gtgctgctgg gtgtacgctg cacctgcca ctgagttggg gaaagaggat 120
 aatcagtgag cactgttctg ctgagagctc ctgatctacc ccaccccta ggatccagga 180
 ctgggtcaaa gctgcatgaa accaggccct ggcagcaacc tgggaatggc tggaggtggg 240
 agagaacctg acttctcttt ccctctccct cctccaacat tactggaact ctatcctgtt 300
 agggatcttc tgagcttggt tccctgctgg gtgggacaga agacaaagga gaagggangg 360
 tctacaanaa gcagcccttc tttgtcctct ggggttaatg agcttgacct ananttcagt 420
 gaganaccan aagcctctga tttttaattt ccntnaaatg tttgaagtnt atatntacat 480
 atatatatatt cttttnaatnt ttgagtcttt gatatgtctt aaaatccant ccctctgccn 540
 gaaacctgaa ttaaaacat gaanaaaaat gtttncctta aagatgttan taattaattg 600
 aaacttgaaa aaaaaaaaaa aa 622

<210> 58
 <211> 433
 <212> DNA
 <213> Homo sapien

<400> 58
 gaacaaattc tgattgggta tgtaccgtca aaagacttga agaaatttca tgattttgca 60
 gtgtggaagc gttgaaaatt gaaagttact gcttttccac ttgctcatat agtaaaggga 120
 tcctttcagc tgccagtgtt gaataatgta tcatccagag tgatgttatc tgtgacagtc 180
 accagcttta agctgaacca ttttatgaat accaaataaa tagacctctt gtactgaaaa 240
 catatttgtg actttaatcg tgctgcttgg atagaaatat ttttactggg tcttctgaat 300
 tgacagtaaa cctgtccatt atgaatggcc tactgttcta ttatttggtt tgacttgaat 360
 ttatccacca aagacttcat ttgtgtatca tcaataaagt tgtatgtttc aactgaaaaa 420
 aaaaaaaaaa aaa 433

<210> 59
 <211> 649

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<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(649)
 <223> n = A,T,C or G

<400> 59
 actagttatt atctgacttt cnggttataa tcatttctaag gagtgtgaag tagcctctgg 60
 tgtcatttgg atttgcattt ctctgatgag tgatgctatc aagcaccttt gctgggtgctg 120
 ttggccatat gtgtatgttc cctggagaag tgtctgtgct gagccttggc ccacttttta 180
 attaggcgtn tgtcttttta ttactgagtt gtaaganttc ttatatatt ctggattcta 240
 gacccttatac agatacatgg tttgcaaata ttttctccca ttctgtgggt tgtgttttca 300
 ctttatcgat aatgtcctta gacatataat aaatttgtat tttaaaagtg acttgatttg 360
 ggctgtgcaa ggtgggctca cgcttgtaat ccagcactt tgggagactg aggtgggtgg 420
 atcatatgan gangctagga gtctgaggtc agcctggcca gcatagcgaa aacttgtctc 480
 tacnaaaaat acaaaaatta gtcaggcatg gtgggtgcacg tctgtaatac cagcttctca 540
 ggangctgan gcacaaggat cacttgaacc ccagaangaa gangttgcag tganctgaag 600
 atcatgccag ggcaacaaaa atgagaactt gtttaaaaaa aaaaaaaaaa 649

<210> 60
 <211> 423
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(423)
 <223> n = A,T,C or G

<400> 60
 actagttcag gccttccagt tcaactgacaa acatggggaa gtgtgcccag ctggctggaa 60
 acctggcagt gataccatca agcctgatgt ccaaaagagc aaagaatatt tctccaagca 120
 gaagtgagcg ctgggctggt ttagtgccag gctgcggtgg gcagccatga gaacaaaacc 180
 tcttctgtat tttttttttc cattagatana acacaagact cngattcagc cgaattgtgg 240
 tgtcttacaa ggcagggctt tctacaggg ggtgganaaa acagcctttc ttccttttgt 300
 agaatggcc tgagttggcg ttgtgggcag gctactgggt tgtatgatgt attagtagag 360
 caaccatta atctttttgta gtttgtatna aacttganct gagaccttaa acaaaaaaaa 420
 aaa 423

<210> 61
 <211> 423
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(423)
 <223> n = A,T,C or G

<400> 61
 cgggactgga atgtaaagtg aagttcggag ctctgagcac gggctcttcc cgccgggtcc 60
 tccctcccca gacccagag ggagaggccc accccgcccc gccccgcccc agcccctgct 120
 caggtctgag tatggctggg agtcgggggc cacaggcctc tagctgtgct gctcaagaag 180

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actggatcag	ggtanctaca	agtggccggg	ccttgccctt	gggattctac	cctgttccta	240
atttggtgtt	gggggtgcgg	gtccctggcc	cccttttcca	cactncctcc	ctccngacag	300
caacctccct	tggggcaatt	gggcctggnt	ctccncccg	tgttgcnacc	ctttgttggt	360
ttaaggncct	taaaaatggt	annttttccc	ntgccnggg	taaaaaagga	aaaaactnaa	420
aaa						423

<210> 62

<211> 683

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(683)

<223> n = A,T,C or G

<400> 62

gctggagagg	ggtacggact	ttcttggagt	tgtcccaggt	tggaatgaga	ctgaactcaa	60
gaagagaccc	taagagactg	gggaatgggt	cctgccttca	ggaaagtgaa	agacgcttag	120
gctgtcaaca	cttaaaggaa	gtccccctga	agcccagagt	ggacagacta	gacccattga	180
tggggccact	ggccatggtc	cgtggacaag	acattccngt	gggccatggc	acaccggggg	240
ggatcaaaat	gtgtacttgt	ggggctctgc	cccttgccaa	aaccaaacca	ntcccactcc	300
tgtcnttgga	ctttcttccc	attccctcct	ccccaaatgc	acttcccctc	ctccctctgc	360
ccctcctgtg	tttttggaat	tctgtttccc	tcaaaattgt	taatttttta	nttttngacc	420
atgaacttat	gtttggggtc	nangttcccc	ttnccaatgc	atactaatat	attaatgggt	480
atztattttt	gaaatatatt	ttaatgaact	tggaaaaaat	tnntggaatt	tccttncttc	540
cntttntttt	gggggggggtg	gggggntggg	ttaaaatttt	tttgggaancc	cnatnggaaa	600
ttnttacttg	gggccccctt	naaaaaantn	anttccaatt	cttnnatngc	ccctnttccn	660
ctaaaaaaaa	ananannaaa	aan				683

<210> 63

<211> 731

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(731)

<223> n = A,T,C or G

<400> 63

actagtcata	aagggtgtgc	gcgtcttcga	cgtggcggtc	ttggcgccac	tgctgcgaga	60
cccggccctg	gacctcaagg	tcatccactt	ggtgcgtgat	ccccgcgcgg	tggcgagtgc	120
acggatccgc	tcgcgccacg	gcctcatccg	tgagagccta	caggtgggtgc	gcagccgaga	180
ccgcgagctc	accgcatgcc	cttcttggag	gccgcggggc	acaagcttgg	cgcccanaaa	240
gaaggcgtng	ggggcccgcg	aantaccacg	ctctgggcgc	tatggaangt	cctcttgcaa	300
taatattggt	tnaaaanctg	canaanagcc	cctgcancec	cctgaactgg	gntgcagggc	360
cncttacctn	gtttggntgc	ggttacaaag	aacctgtttn	ggaaaaccct	nccnaaaacc	420
ttccgggaaa	attntncaaa	ttttntttgg	ggaattnttg	ggtaaaccct	ccnaaaatgg	480
gaaacntttt	tgccctnnaa	antaaaccat	tnggttccgg	gggccccccc	ncaaaaccct	540
ttttnttttt	ttntgcccc	cantnncccc	ccggggcccc	tttttttngg	ggaaaanccc	600
ccccctncc	nanantttta	aaagggnngg	anaatttttn	nttncccccc	gggncccccn	660
ggngntaaaa	nggtttcncc	cccccgaggg	gnggggnnnc	ctcnnaaacc	cntntcnna	720
ccnctttttn	n					731

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<210> 64
 <211> 313
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(313)
 <223> n = A,T,C or G

<400> 64
 actagttgtg caaaccacga ctgaagaaag acgaaaagtg ggaaataact tgcaacgtct 60
 gttagagatg gttgctacac atgttgggtc tgtagagaaa catcttgagg agcagattgc 120
 taaagttgat agagaatatg aagaatgcat gtcagaagat ctctcggaaa atattaaaga 180
 gattagagat aagtatgaga agaaagctac tctaattaag tcttctgaag aatgaagatn 240
 aaatgttgat catgtatata tatccatagt gaataaaatt gtctcagtaa agttgtaaaa 300
 aaaaaaaaaa aaa 313

<210> 65
 <211> 420
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(420)
 <223> n = A,T,C or G

<400> 65
 actagttccc tggcaggcaa gggcttccaa ctgaggcagt gcatgtgtgg cagagagagg 60
 caggaagctg gcagtggcag cttctgtgtc tagggagggg tgtggctccc tccttccttg 120
 tctgggaggt tggagggaag aatctaggcc ttagcttgcc ctectgccac ccttcccctt 180
 gtagatactg ccttaacact ccctcctctc tcagctgtgg ctgccacca agccaggttt 240
 ctccgtgctc actaatttat ttccaggaaa ggtgtgtgga agacatgagc cgtgtataat 300
 atttgtttta acattttcat tgcaagtatt gaccatcatc cttggttgtg tatcgttgta 360
 acacaaatta atgatattaa aaagcatcca aacaaagccn annnnnaana nnannngaaa 420

<210> 66
 <211> 676
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(676)
 <223> n = A,T,C or G

<400> 66
 actagtttcc tatgatcatt aaactcattc tcagggttaa gaaaggaatg taaatttctg 60
 cctcaatttg tacttcatca ataagttttt gaagagtgcg gattttttagt caggtcttaa 120
 aaataaactc acaaatctgg atgcatttct aaattctgca aatgtttcct ggggtgactt 180
 aacaaggaat aatcccacaa tatacctagc tacctaatac atggagctgg ggctcaaccc 240
 actgttttta aggatttgcg cttacttgty gctgaggaaa aataagtagt tccgagggaa 300
 gtagttttta aatgtgagct tatagatngg aacagaata tcaacttaat tatggaaatt 360
 gttagaaacc tgttctcttg ttatctgaat cttgattgca attactattg tactggatag 420

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actccagccc attgcaaagt ctcagatata ttanctgtgt agttgaattc cttggaaatt 480
ctttttaaga aaaaattgga gtttnaaaga aataaacccc tttgttaaata gaagcttggc 540
tttttggtga aaaanaatca tccgcgagg cttattgttt aaaaanggaa ttttaagcct 600
ccctggaaaa anttgtaaata taaatgggga aaatgntggg naaaaattat ccgttagggt 660
ttaaagggaa aactta 676

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<210> 67
<211> 620
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(620)
<223> n = A,T,C or G

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<400> 67
caccattaaa gctgcttacc aagaacttcc ccagcatttt gacttccttg tttgatagct 60
gaattgtgag caggtgatag aagagccttt ctagttgaac atacagataa tttgctgaat 120
acattccatt taatgaagggt gttacatctg ttacgaagct actaagaagg agcaagagca 180
taggggaaaa aaatctgatc agaacgcac aaactcacat gtgccccctc tactacaaac 240
agattgtagt gctgtggtgg tttattccgt tgtgcagaac ttgcaagctg agtcactaaa 300
cccaaagaga ggaaattata ggtagttaa acattgtaac cccaggaact aagtttaatt 360
cacttttgaa gtgttttggt ttttattttt ggtttgtctg atttactttg ggggaaaang 420
ctaaaaaaaa agggatatca atctctaatt cagtgcccac taaaagttgt ccctaaaaag 480
tctttactgg aanttatggg actttttaag ctccaggtn tttggtcctc caaattaacc 540
ttgcatgggc cccttaaaat tgttgaangg cattcctgcc tctaagtttg gggaaaattc 600
ccccnttttn aaaatttgga 620

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<210> 68
<211> 551
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(551)
<223> n = A,T,C or G

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<400> 68
actagtagct ggtacataat cactgaggag ctattttctta acatgctttt atagaccatg 60
ctaagtctag accagtattt aagggtctaat ctacacctc cttagctgta agagtctggc 120
ttagaacaga cctctctgtg caataacttg tggccactgg aaatccctgg gccggcattt 180
gtattgggggt tgcaatgact cccaagggcc aaaagagtta aaggcacgac tgggatttct 240
tctgagactg tggtgaaact ccttccaagg ctgaggggggt cagtangtgc tctgggaggg 300
actcggcacc actttgatata tcaacaagcc acttgaagcc caattataaa attgttattt 360
tacagctgat ggaactcaat ttgaaccttc aaaactttgt tagtttatcc tattatattg 420
ttaaacctaa ttacatttgt ctagcatttg atttggttcc tgtngcatat gtttttttcn 480
cctatgtgct cccctcccc nnatcttaat ttaaaccnca attttgcnat tcncnnnnnn 540
nannnannna a 551

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<210> 69
<211> 396
<212> DNA
<213> Homo sapien

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<220>
 <221> misc_feature
 <222> (1)...(396)
 <223> n = A,T,C or G

<400> 69
 cagaaatgga aagcagagtt ttcatttctg tttataaacg tctccaaaca aaaatggaaa 60
 gcagagtttt cattaaatcc ttttaccttt tttttttctt ggtaatcccc tcaaataaca 120
 gtatgtggga tattgaatgt taaagggata tttttttcta ttatttttat aattgtacaa 180
 aattaagcaa atgttaaaag ttttatatgc tttattaatg ttttcaaaag gtatnatata 240
 tgtgatacat tttttaagct tcagttgctt gtcttctggc actttctggt atgggctttt 300
 ggggagccan aaaccaatct acnatctctt tttgtttgcc aggacatgca ataaaattta 360
 aaaaataaat aaaaactatt nagaaattga aaaaaa 396

<210> 70
 <211> 536
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(536)
 <223> n = A,T,C or G

<400> 70
 actagtgcaa aagcaaatat aaacatcgaa aaggcgttcc tcacgttagc tgaagatatc 60
 cttcgaaaga cccctgtaaa agagcccaac agtgaaaatg tagatatcag cagtggagga 120
 ggcgtgacag gctggaagag caaatgctgc tgagcattct cctgttccat cagttgccat 180
 ccactacccc gttttctctt cttgctgcaa aataaaccac tctgtccatt tttaactcta 240
 aacagatatt tttgtttctc atcttaacta tccaagccac ctattttatt tgttctttca 300
 tctgtgactg cttgctgact ttatcataat tttcttcaaa caaaaaaatg tatagaaaaa 360
 tcatgtctgt gacttcattt ttaaatgnta cttgctcagc tcaactgcat ttcagttggt 420
 ttatagtcca gttcttatca acattnaaac ctatngcaat catttcaaat ctattctgca 480
 aattgtataa gaataaaagt tagaatttaa caattaaaaa aaaaaaaaaa aaaaaa 536

<210> 71
 <211> 865
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(865)
 <223> n = A,T,C or G

<400> 71
 gacaaagcgt taggagaaga anagaggcag ggaanactnc ccaggcacga tggccncctt 60
 cccaccagca accagcgccc cccaccagcc cccaggcccg gacgacgaag actccatcct 120
 ggattaatct nacctctntc gcctgnccca ttcctacctc ggaggtggag gccggaaagg 180
 tcncaccaag aganaanctg ctgccaacac caaccgcccc agccctggcg ggcacganag 240
 gaaactggtg accaatctgc agaattctna gaggaanaag cnaggggccc cgcgctnaga 300
 cagagctgga tatgangcca gaccatggac nctacncccn ncaatncana cgggactgcy 360
 gaagatggan gaccncgcac nngatcaggc cngctnncca nccccccacc cctatgaatt 420
 attcccgcgtg aangaatctc tgannggctt ccannaaagc gcctccccnc cnaacgnaan 480

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tncaacatng	ggattanang	ctgggaactg	naaggggcaa	ancctnnaat	atccccagaa	540
acaanctctc	ccnaanaaac	tggggcncct	catnggtggn	accaactatt	aactaaaccg	600
cacgccaaagn	aantataaaa	ggggggcccc	tcnccggng	accccccttt	gtcccttaat	660
ganggttatc	cnccttgct	accatggtnc	ccnnttctgt	ntgnatgttt	ccnctcccc	720
ccncttatnt	cnagccgaac	tcnnatttnc	ccgggggtgc	natchantng	tncnctttt	780
ttngttgncc	cngccctttc	cgncggaacn	cgtttccccg	ttantaacgg	cacccggggn	840
aagggtgntt	ggccccctcc	ctccc				865

<210> 72

<211> 560

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (560)

<223> n = A,T,C or G

<400> 72

cctggacttg	tcttggttcc	agaacctgac	gacccggcga	cggcgacgtc	tcttttgact	60
aaaagacagt	gtccagtgt	ccngcctagg	agtctacggg	gaccgcctcc	cgcgccgcca	120
ccatgcccga	cttctctggc	aactggaaaa	tcacccgatc	ggaaaacttc	gangaattgc	180
tcnaantgct	gggggtgaat	gtgatgctna	ngaanattgc	tgtggctgca	gcgtccaagc	240
cagcagtggg	gacnaacag	gagggagaca	ctttctacat	caaaacctcc	accaccgtgc	300
gcaccacaaa	gattaacttc	nnngttgggg	aggantttga	ggancaaact	gtggatngga	360
ngcctgtnaa	aacctggtga	aatgggagaa	tganaataaa	atggtctgtg	ancanaaact	420
cctgaaagga	gaaggcccc	anaactcctg	gaccngaaaa	actgaccnc	cnatngggga	480
actgatnctt	gaaccctgaa	cgggcgggat	ganccttttt	tnttgcnc	naanggggtc	540
tttccntttc	ccccaaaaaa					560

<210> 73

<211> 379

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (379)

<223> n = A,T,C or G

<400> 73

ctgggggancc	ggcggtnngc	nccatntcnn	gncgcgaagg	tggcaataaa	aanccnctga	60
aaccgcncaa	naaacatgcc	naagatatgg	acgaggaaga	tnngnctttc	nngnacaanc	120
gnanngagga	acanaacaaa	ctcnangagc	tctcaagcta	atgccgcggg	gaagggggccc	180
ttggccacnn	gtggaattaa	gaaatctggc	aaanngtann	tgttccttgt	gcctnangag	240
ataagngacc	ctttatttca	tctgtattta	aacctctctn	ttccctgnca	taacttcttt	300
tnccacgtan	agntggaant	anttgttggt	ttggactggt	gtncatttta	gannaaactt	360
ttgttcaaaa	aaaaaataa					379

<210> 74

<211> 437

<212> DNA

<213> Homo sapien

<220>

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<221> misc_feature
 <222> (1)...(437)
 <223> n = A,T,C or G

<400> 74
 actagttcag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60
 ctaggtgttt ccatctatgt ttcaatctgt ccatctacca ggcctcgcga taaaaacaaa 120
 acaaaaaaac gctgccaggt tttanaagca gttctgggtct caaaaccatc aggatcctgc 180
 caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcatct 240
 aatcactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttgtgg 300
 gaataagtta taatcagtat tcatctcttt gttttttgtc actcttttct ctctnattgt 360
 gtcatttgta ctgtttgaaa aatattttct ctataaaatt aaactaacct gccttaaaaa 420
 aaaaaaaaaa aaaaaaa 437

<210> 75
 <211> 579
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(579)
 <223> n = A,T,C or G

<400> 75
 ctccgtcgcc gccaaagatga tgtgcggggc gccctccgcc acgcagccgg ccaccgccga 60
 gaccagcac atcgccgacc aggtgaggct ccagcttgaa gagaaagaaa acaagaagtt 120
 ccctgtgttt aaggccgtgt cattcaagag ccagggtggtc gcggggacaa actacttcat 180
 caagggtcac gtcggcgacg aggacttcgt acacctgcga gtgttccaat ctctccctca 240
 tgaaaacaag cccttgacct tatctaacta ccagaccaac aaagccaagc atgatgagct 300
 gacctatttc tgatcctgac ttgggacaag gcccttcagc cagaagactg acaaagtcac 360
 cctccgtcta ccagagcgtg cacttgtgat cctaaaataa gtttcatctc cgggctgtgc 420
 ccttgggggtg gaaggggcan gatctgcact gcttttgcac ttctcttctt aaatttcatt 480
 gtgttgattc tttccttcca ataggatgat ttnattactt tcagaatatt ttccaaatna 540
 gatatatattt naaaatcctt aaaaaaaaaa aaaaaaaaaa 579

<210> 76
 <211> 666
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(666)
 <223> n = A,T,C or G

<400> 76
 gtttatacta tcttccaac cagattgtca gctccttgag ggcaagagcc acagtatatt 60
 tccctgtttc ttccacagtg cctaataata ctgtggaact aggttttaata aatttttta 120
 ttgatgttgt tatgggcagg atggcaacca gaccattgtc tcagagcagg tgctggctct 180
 ttctggcta ctccatgttg gctagcctct ggtaacctct tacttattat cttcaggaca 240
 ctactacag ggaccaggga tgatgcaaca tccttgtctt tttatgacag gatgtttgct 300
 cagcttctcc aacaataaaa agcacgtggg aaaacacttg cggatattct ggactgtttt 360
 taaaaaatat acagtttacc gaaaatcata ttatcttaca atgaaaagga ntttatagat 420
 cagccagtga acaacctttt cccaccatac aaaaattcct tttcccgaan gaaaanggct 480

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ttctcaataa ncctcacttt cttaanatct tacaagatag ccccganatc ttatcgaaac	540
tcatttttagg caaatatgan ttttattgtn cgttacttgt ttcaaaattt ggtattgtga	600
atatcaatta ccacccccat ctcccatgaa anaaanggga aanggtgaan ttentaancg	660
cttaaa	666

<210> 77
 <211> 396
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(396)
 <223> n = A,T,C or G

<400> 77					
ctgcagcccg ggggatccac taatctacca ngggtatttg gcagctaatt ctanatttgg	60				
atcattgccc aaagttgcac ttgctggtct cttgggattt ggccttggaagggtatcata	120				
catanganta tgccanaata aattccattt ttttgaaaat canctccttg gggctgggtt	180				
tggtccacag cataacangc actgcctcct tacctgtgag gaatgcaaaa taaagcatgg	240				
attaagtgag aaggagact ctcagccttc agcttcctaa attctgtgtc tgtgactttc	300				
gaagtttttt aaacctctga atttgtacac atttaaaatt tcaagtgtac tttaaaataa	360				
aatacttcta atgggaacaa aaaaaaaaaa aaaaaa	396				

<210> 78
 <211> 793
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(793)
 <223> n = A,T,C or G

<400> 78					
gcacccctagc cgccgactca cacaaggcag gtgggtgagg aaatccagag ttgccatgga	60				
gaaaattcca gtgtcagcat tcttgctcct tgtggccctc tcctacactc tggccagaga	120				
taccacagtc aaacctggag ccaaaaagga cacaaggac tctcgacca aactgcccc	180				
gacctctctc agaggttggg gtgaccaact catctggact cagacatatg aagaagctct	240				
atataaatcc aagacaagca acaaaccctt gatgattatt catcacttgg atgagtgc	300				
acacagtcna gctttaaaga aagtgtttgc tgaaaataaa gaaatccaga aattggcaga	360				
gcagtttgtc ctctcaatc tggtttatga aacaactgac aaacacctt ctctgatgg	420				
ccagtatgtc ccaggattat gtttggtgac ccattctctga cagttgaagc cgatatcctg	480				
ggaagatatt cnaaccgtct ctatgcttac aaactgcaga tacgctctgt tgcttgacac	540				
atgaaaaagc tctcaagttg ctnaaaatga attgtaagaa aaaaaatctc cagccttctg	600				
tctgtcggct tgaaaattga aaccagaaaa atgtgaaaaa tggctattgt ggaacanatn	660				
gacacctgat taggttttgg ttatgttcac cactattttt aanaaaanan nttttaaaat	720				
ttggttcaat tntctttttt aaacaatntg tttctacntt gnganctgat ttctaaaaaa	780				
aataatnttt ggc	793				

<210> 79
 <211> 456
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (456)

<223> n = A,T,C or G

<400> 79

actagtatgg	ggtgggaggg	cccacccttc	tcccctaggg	gctgttcttg	ctccaaaggg	60
ctccgtggag	agggactggc	agagctgang	ccacctgggg	ctggggatcc	cactcttctt	120
gcagctgttg	agcgcaccta	accactggtc	atgccccccac	ccctgctctc	cgcacccgct	180
tcctcccgac	cccangacca	ggctacttct	cccctcctct	tgctccctc	ctgcccctgc	240
tgctctgat	cgtangaatt	gangantgtc	ccgccttggt	gctganaatg	gacagtggca	300
ggggctggaa	atgggtgtgt	gtgtgtgtgt	gtgtgtgtgt	gtgtgtgtgt	gcnecccccc	360
tgcaagaccg	agattgaggg	aaancatgtc	tgctgggtgt	gaccatgttt	cctctccata	420
aantncccct	gtgacnctca	naaaaaaaaa	aaaaaa			456

<210> 80

<211> 284

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (284)

<223> n = A,T,C or G

<400> 80

ctttgtacct	ctagaaaaga	taggtattgt	gtcatgaaac	ttgagtttaa	attttatata	60
taaaactaaa	agtaatgctc	actttagcaa	cacatactaa	aattggaacc	atactgagaa	120
gaatagcatg	acctccgtgc	aaacaggaca	agcaaatttg	tgatgtgttg	attaaaaaga	180
aataaataaa	tgtgtatatg	tgtaacttgt	atgttttatgt	ggaatacaga	ttgggaaata	240
aatgtatttt	cttactgtga	aaaaaaaaaa	aaaaaaaaaa	aana		284

<210> 81

<211> 671

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (671)

<223> n = A,T,C or G

<400> 81

gccaccaaca	ttccaagcta	ccctgggtac	ctttgtgcag	tagaagctag	tgagcatgtg	60
agcaagcggg	gtgcacacgg	agactcatcg	ttataattta	ctatctgcc	agagtagaaa	120
gaaaggctgg	ggatatttgg	gttggcttgg	ttttgatttt	ttgcttgttt	gtttgttttg	180
tactaaaaca	gtattatctt	ttgaatatcg	tagggacata	agtatataca	tgttatccaa	240
tcaagatggc	tagaatgggt	cctttctgag	tgtctaaaac	ttgacacccc	tggtaaatct	300
ttcaacacac	ttccactgcc	tgcgtaatga	agtttttgatt	cattttttaac	cactggaatt	360
tttcaatgcc	gtcattttca	gttagatnat	tttgcacttt	gagattaaaa	tgccatgtct	420
at ttgattag	tcttattttt	ttattttttac	aggcttatca	gtctcactgt	tggtgtcat	480
tgtgacaaag	tcaaataaac	ccccnaggac	aacacacagt	atgggatcac	atattgtttg	540
acattaagct	ttggccaaaa	aatgttgcac	gtgtttttacc	tcgacttgct	aatcaatan	600
canaaaggct	ggctnataat	gttggtggtg	aaataattaa	tnantaacca	aaaaaaaaan	660
aaaaaaaaaa	a					671

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<210> 82
 <211> 217
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(217)
 <223> n = A,T,C or G

<400> 82
 ctgcagatgt ttcttgaatg ctttgtcaaa ttaanaaagt taaagtgcaa taatgtttga 60
 agacaataag tgggtggtgta tcttgtttct aataagataa actttttttgt ctttgcttta 120
 tcttattagg gagttgtatg tcagtgtata aaacatactg tgtggtataa caggcttaat 180
 aaattcttta aaaggaaaaa aaaaaaaaaa aaaaaaa 217

<210> 83
 <211> 460
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(460)
 <223> n = A,T,C or G

<400> 83
 cgcgagtggg agcaccagga tctcgggctc ggaacgagac tgcacggatt gttttaagaa 60
 aatggcagac aaaccagaca tgggggaaat cgccagcttc gatnaggcca agctgaanaa 120
 aacggagacg caggagaaga acaccctgcc gaccaaagag accattgagc angagaagcg 180
 gagtgaaatt tcctaagatc ctggaggatt tcctaccccc gtccctcttcg agaccccagt 240
 cgtgatgtgg aggaagagcc acctgcaaga tggacacgag ccacaagctg cactgtgaac 300
 ctgggcactc cgcgccgatg ccaccggcct gtgggtctct gaagggaccc cccccaatcg 360
 gactgccaaa ttctccggtt tgccccggga tattatacaa nattatttgt atgaataatg 420
 annataaaac acacctcgtg gcancaaana aaaaaaaaaa 460

<210> 84
 <211> 323
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(323)
 <223> n = A,T,C or G

<400> 84
 tgggtggatct tggctctgtg gagctgctgg gacgggatct aaaagactat tctggaagct 60
 gtgggtccaan gcattttgct ggcttaacgg gtcccgaac aaaggacacc agctctctaa 120
 aattgaagtt taccganat aacaatcttt tgggcagaga tgcctatttt aacaaacncc 180
 gtccctgcgc aacaacnaac aatctctggg aaataccggc catgaacntg ctgtctcaat 240
 cnancatctc tctagctgac cgatcatatc gtcccagatt actacanatc ataataattg 300
 atttcctgta naaaaaaaaa aaa 323

<210> 85
 <211> 771
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(771)
 <223> n = A,T,C or G

<400> 85
 aaactgggta ctcaacactg agcagatctg ttctttgagc taaaaacccat gtgctgtacc 60
 aanagtttgc tcctggctgc tttgatgtca gtgctgctac tccacctctg cggcgaatca 120
 gaagcaagca actttgactg ctgtcttgga tacacagacc gtattcttca tcctaaattt 180
 attgtgggct tcacacggca gctggccaat gaaggctgtg acatcaatgc tatcatcttt 240
 cacacaaaga aaaagttgtc tgtgtgcgca aatccaaaac agacttgggt gaaatatatt 300
 gtgcgtctcc tcagtataaa agtcaagaac atgtataaac tgtggctttt ctggaatgga 360
 attggacata gcccaagaac agaaagaact tgctgggggt ggagggttca cttgcacatc 420
 atgganggtt tagtgcttat cttatttgtg cctcctggac ttgtccaatt natgaagtta 480
 atcatattgc atcatanttt gctttgttta acatcacatt naaattaaac tgtattttat 540
 gttatttata gctntagggt ttctgtgttt aactttttat acnaantttc cttaaactatt 600
 ttggtntant gcaanttaaa aattatatatt ggggggggaa taaatattgg antttctgca 660
 gccacaagct ttttttataaa aaccantaca nccnngttaa atggtnggtc ccnaatggtt 720
 tttgcttttn antagaaaat ttnttagaac natttgaaaa aaaaaaaaaa a 771

<210> 86
 <211> 628
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(628)
 <223> n = A,T,C or G

<400> 86
 actagtttgc tttacatttt tgaaaagtat tatttttgtc caagtgccta tcaactaaac 60
 cttgtgttag gtaagaatgg aatttattaa gtgaatcagt gtgacccttc ttgtcataag 120
 attatcttaa agctgaagcc aaaatatgct tcaaaaagaaa angactttat tgttcattgt 180
 agttcataca ttcaaagcat ctgaactgta gtttctatag caagccaatt acatccataa 240
 gtggagaang aaatagatta atgtcnaagt atgattgggt gagggagcaa ggttgaagat 300
 aatctgggggt tgaaattttc tagttttcat tctgtacatt tttagttnga catcagattt 360
 gaaatattaa tgtttacctt tcaatgtgtg gtatcagctg gactcantaa caccctttc 420
 ttccctnggg gatggggaat ggattattgg aaaatggaaa gaaaaaagta cttaaagcct 480
 tcctttcnca gtttctggct cctaccctac tgatttancc agaataagaa aacattttat 540
 catcntctgc tttattccca ttaatnaant tttgatgaat aaatctgctt ttatgcnnac 600
 ccaaggaatt nagtggnttc ntenttgt 628

<210> 87
 <211> 518
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

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<222> (1) . . . (518)

<223> n = A,T,C or G

<400> 87

tttttttattt	tttttagaga	gtagttcagc	ttttatttat	aaattttattg	cctgtttttat	60
tataacaaca	ttatactggt	tatggtttaa	tacatatggt	tcaaaatgta	taatacatca	120
agtagtacag	ttttaaaatt	ttatgcttaa	aacaagtttt	gtgtaaaaaa	tgacagataca	180
ttttacatgg	caaatcaatt	tttaagtcac	cctaaaaatt	gattttttttt	tgaaattttaa	240
aaacacattt	aattttcaatt	tctctcttat	ataaccttta	ttactatagc	atggttttcca	300
ctacagttta	acaatgcagc	aaaattccca	tttcacggta	aattgggttt	taagcggcaa	360
ggttaaaatg	ctttgaggat	cctnaatacc	ctttgaactt	caaatgaagg	ttatggttgt	420
naatttaacc	ctcatgccat	aagcagaagc	acaagtttag	ctgcattttg	ctctaaactg	480
taaaancgag	ccccccgttg	aaaaagcaaa	agggaccc			518

<210> 88

<211> 1844

<212> DNA

<213> Homo sapien

<400> 88

gagacagtga	atcctagtat	caaaggattt	ttggcctcag	aaaaagttgt	tgattattttt	60
tatttttattt	tattttttcga	gactccgtct	caaaaaaaaaa	aaaaaaaaaaa	agaatcacaa	120
ggtattttgct	aaagcatttt	gagctgcttg	gaaaaaggga	agtagttgca	gtagagtttc	180
ttccatcttc	ttgggtgctgg	gaagccatat	atgtgtcttt	tactcaagct	aaggggtata	240
agcttatgtg	ttgaatttgc	tacatctata	tttcacatat	tctcacaata	agagaattttt	300
gaaatagaaa	tatcatagaa	cattttaagaa	agttttagtat	aaataatatt	ttgtgtgtttt	360
taatcccttt	gaagggatct	atccaaagaa	aatatttttac	actgagctcr	ttcctacacg	420
tctcagtaac	agatcctgtg	ttagtctttg	aaaatagctc	atttttttaa	tgctcagtga	480
tagatgtagc	atacatatga	tgtataatga	cgtgtattat	gttaacaatg	tctgcagatt	540
ttgtaggaat	acaaaacatg	gcctttttta	taagcaaaac	gggccaatga	ctagaataac	600
acatagggca	atctgtgaat	atgtattata	agcagcattc	cagaaaagta	gttgggtgaa	660
taattttcaa	gtcaaaaagg	gatattggaa	gggaattatg	agtaacctct	atttttttaag	720
ccttgctttt	aaattaaacg	ctacagccat	ttaagccttg	aggataataa	agcttgagag	780
taataatgtt	aggtttagca	aggtttagat	gtatcacttc	atgcatgcta	ccatgatagt	840
aatgcagctc	ttcgagtcac	ttctgggtcat	tcaagatatt	cacccttttg	cccatagaaa	900
gcaccctacc	tcacctgctt	actgacattg	tcttagctga	tcacaagatc	attatcagcc	960
tccattattc	cttactgtat	ataaaataca	gagttttata	ttttcctttc	ttcgttttttc	1020
accatattca	aaacctaata	ttgttttttg	agatgggaat	caaagtaatc	aagtgttcgt	1080
gctttcacct	agaagggtgt	ggtcctgaag	gaaagaggtc	cctaaatatc	ccccaccctg	1140
ggtgctcctc	cttccttggt	accctgacta	ccagaagtca	ggtgctagag	cagctggaga	1200
agtgcagcag	cctgtgcttc	cacagatggg	ggtgctgctg	caacaaggct	ttcaatgtgc	1260
ccatcttagg	gggagaagct	agatcctgtg	cagcagcctg	gtaagtcctg	aggaggttcc	1320
attgctcttc	ctgctgctgt	cctttgcttc	tcaacggggc	tcgctctaca	gtctagagca	1380
catgcagcta	acttgtgcct	ctgcttatgc	atgagggtta	aattaacaac	cataaccttc	1440
atttgaagtt	caaagggtga	ttcaggatcc	tcaaagcatt	ttaaccttgc	cgcttaaaac	1500
ccaatttacc	gtgaaatggg	aattttgctg	cattgtttaa	ctgtagtgga	aaccatgcta	1560
tagtaataaa	ggttatataa	gagagaaatt	gaaattaaat	gtgtttttta	atttcaaaaa	1620
aaaatcaatc	tttaggatga	cttaaaaatt	gatttgccat	gtaaaatgta	tctgcattttt	1680
ttacacaaaa	cttgttttta	gcataaaatt	ttaaaactgt	actacttgat	gtattatata	1740
ttttgaacca	tatgtattaa	accataaaca	gtataatgtt	gttataataa	aacaggcaat	1800
aaatttataa	ataaaagctg	aaaaaaaaaa	aaaaaaaaaa	aaaa		1844

<210> 89

<211> 523

<212> DNA

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<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(523)

<223> n = A,T,C or G

<400> 89

tttttttttt	tttttttagt	caatccacat	ttattgatca	cttattatgt	accaggcact	60
gggataaaga	tgactgtag	tcactcacag	taaggaagaa	aactagcaaa	taagacgatt	120
acaatatgat	gtagaaaatg	ctaagccaga	gatatagaaa	ggtcctattg	ggtccttctg	180
tcacctgtgc	tttccacatc	cctacccttc	acaggccttc	cctccagctt	cctgcccccg	240
ctccccactg	cagatcccct	gggattttgc	ctagagctaa	acgagganat	gggccccctg	300
gccctggcat	gacttgaacc	caaccacaga	ctgggaaagg	gagcctttcg	anagtggatc	360
actttgatna	gaaaacacat	agggaattga	agagaaantc	cccaaattggc	cacccgtgct	420
ggtgctcaag	aaaagtttgc	agaatggata	aatgaaggat	caaggggaatt	aatanaatgaa	480
taattgaatg	gtggctcaat	aagaatgact	ncnttgaatg	acc		523

<210> 90

<211> 604

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(604)

<223> n = A,T,C or G

<400> 90

ccagtgtggt	ggaatgcaaa	gattacccccg	gaagcttttcg	agaagctggg	attccctgca	60
gcaaaggaaa	tagccaatat	gtgtcgtttc	tatgaaatga	agccagaccg	agatgtcaat	120
ctcaccacc	aactaaatcc	caaagtcaaa	agcttcagcc	agtttatctc	agagaaccag	180
gggagccttc	aagggcattg	agaaaatcag	ctgttcagat	aggcctctgc	accacacagc	240
ctctttcctc	tctgacctt	ttcctcttta	cggcacaaca	ttcatgtttg	acagaacatg	300
ctggaatgca	attgtttgca	acaccgaagg	atttcctgcg	gtcgcctctt	cagtaggaag	360
cactgcattg	gtgataggac	acggtaattt	gattcacatt	taacttgcta	gttagtgata	420
aggggtggta	cacctgtttg	gtaaaatgag	aagcctcgga	aacttgggag	cttctctcct	480
accactaatg	gggagggcag	attattactg	ggattttctcc	tgggggtgaat	taatttcaag	540
ccctaattgc	tgaaattccc	ctnggcaggc	tccagttttc	tcaactgcat	tgcaaaattc	600
cccc						604

<210> 91

<211> 858

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(858)

<223> n = A,T,C or G

<400> 91

tttttttttt	ttttttttta	tgattattat	tttttttatt	gatctttaca	tcctcagtgt	60
tggcagagtt	tctgatgctt	aataaacatt	tgttctgatc	agataagtgg	aaaaaattgt	120
catttcctta	ttcaagccat	gcttttctgt	gatattctga	tcctagttga	acatacagaa	180

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ataaatgtct	aaaacagcac	ctcgattctc	gtctataaca	ggactaagtt	cactgtgatc	240
ttaaataagc	ttggctaaaa	tgggacatga	gtggaggtag	tcacacttca	gcgaagaaag	300
agaatctcct	gtataatctc	accaggagat	tcaacgaatt	ccaccacact	ggactagtgg	360
atcccccg	ctgcaggaat	tcgatatcaa	gcttatcgat	accgtcgacc	tcgagggggg	420
gcccgggtacc	caattcgccc	tatagtgagt	cgtattacgc	gcgctcactg	gccgtcgttt	480
tacaacgtcg	tgactgggaa	aaccctggcg	ttaccctaact	taatcgctt	gcagcacatc	540
cccctttcgc	cagctggcgt	aatagcgaan	agcccgcacc	gatcgccctt	ncaacagttg	600
cgcagcctga	atggcgaatg	ggacgcgccc	tgtagcggcg	cattaaagcg	cggcnggggtg	660
tggnggntcc	cccacgtgac	cgntacactt	ggcagcgcct	tacgccggtc	nttcgctttc	720
ttcccttcct	ttctcgcacc	gttcgcggcg	tttccccggn	agctnttaat	cgggggnctc	780
cctttanggg	tncnaattaa	nggnnttacng	gaccttngan	cccaaaaact	ttgattaggg	840
ggaagggtccc	cgaagggg					858

<210> 92

<211> 585

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 92

gttgaatctc	ctggtgagat	tatacaggag	attctctttc	ttcgctgaag	tgtgactacc	60
tccactcatg	tcccatttta	gccaagctta	tttaagatca	cagtgaactt	agtcctgtta	120
tagacgagaa	tcgaggtgct	gttttagaca	tttatttctg	tatgttcaac	taggatcaga	180
atatcacaga	aaagcatggc	ttgaataagg	aaatgacaat	tttttccact	tatctgatca	240
gaacaaatgt	ttattaagca	tcagaaactc	tgccaacact	gaggatgtaa	agatcaataa	300
aaaaaataat	aatcatnann	naaanannan	nngaagggcg	gccgccaccg	cgggtggagct	360
ccagcttttg	ttcccttttag	tgagggttaa	ttgcgcgctt	ggcgtaatac	atgggtcatag	420
ctgttttctg	tgtgaaattg	ttatccggct	cacaattccn	cncaacatac	gagccgggaa	480
gcntnangtg	taaaagcctg	ggggtgccta	attgagttag	ctnactcaca	ttaattgngt	540
tgcgctccac	ttgcccgcct	ttccantccg	ggaaacctgt	tcgnc		585

<210> 93

<211> 567

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(567)

<223> n = A,T,C or G

<400> 93

cggcagtggt	gctgtctgcg	tgtccacctt	ggaatctggc	tgaactggct	gggaggacca	60
agactgcggc	tgggggtggc	anggaaggga	accgggggct	gctgtgaagg	atcttggaac	120
ttccctgtac	ccaccttccc	cttgcttcat	gtttgtanag	gaaccttggt	ccggccaagc	180
ccagtttctt	tgtgtgatac	actaatgtat	ttgctttttt	tgggaaatan	anaaaaatca	240
attaaattgc	tantgtttct	ttgaannnnn	nnnnnnnnnn	nnnnnnnggg	ggggnccgcc	300
ccnccgngga	aacnccccct	tttgcttccct	ttaattgaaa	ggttaattng	cncncttggc	360
gttaancnt	gggccaanc	tngttncccg	tgntgaaatt	gttnatcccc	tcccaaattc	420
ccccccncc	ttccaaaccc	ggaaancctn	annntgttna	ancccggggg	gttgcctaan	480
ngnaattnaa	ccnaaccccc	ntttaaatng	nntttgcncn	ccacnngccc	cnccttccca	540

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nttcggggaa aaccctntcc gtgccca

567

<210> 94
 <211> 620
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(620)
 <223> n = A,T,C or G

<400> 94
 actagtcaaa aatgctaaaa taatttgggga gaaaatattt tttaagtagt gttatagttt 60
 catgtttatc ttttattatg ttttgtgaag ttgtgtcttt tcactaatta cctatactat 120
 gccaatattt ccttatatct atccataaca tttatactac atttgtaana naatatgcac 180
 gtgaaactta acactttata aggtaaaaat gaggtttcca anatttaata atctgatcaa 240
 gttcttggtta tttccaaata gaatggactt ggtctgttaa gggctaagga gaagaggaag 300
 ataagggttaa aagttgttaa tgaccaaaaca ttctaaaaga aatgcaaaaa aaaagtttat 360
 tttcaagcct tcgaactatt taaggaaagc aaaatcattt cctaaatgca tatcatttgt 420
 gagaatttct cattaatatc ctgaatcatt catttcacta aggctcatgt tnactccgat 480
 atgtctctaa gaaagtacta tttcatgggc caaacctggg tgccatantt gggtaaaggc 540
 tttcccttaa gtgtgaaant atttaaaatg aaattttcct ctttttataaa attctttana 600
 aggggttaagg gtgttgggga 620

<210> 95
 <211> 470
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(470)
 <223> n = A,T,C or G

<400> 95
 ctcgaccttc tctgcacagc ggatgaaccc tgagcagctg aagaccagaa aagccactat 60
 nactttntgc ttaattcang agcttacang attcttcaaa gagtgngtcc agcatccttt 120
 gaaacatgag ttcttaccag cagaagcaga cttttacccc accacctcag cttcaacagc 180
 agcaggtgaa acaacccatc cagcctccac ctnaggaaat atttggtccc acaaccaagg 240
 agccatgcca ctcaaagggt ccacaacctg naaacacaaa nattccagag ccaggctgta 300
 ccaagggtccc tgagccaggg ctgtaccaan gtccctgagc cagggtgtac caangtcct 360
 gagccaggat gtaccaaggc ccctgancca gggtgtccaa gggtccctgag ccaggctaca 420
 ccaagggcct gngccaggca gcatcaangt ccctgaccaa ggcttatcaa 470

<210> 96
 <211> 660
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(660)
 <223> n = A,T,C or G

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<400> 96

tttttttttt	tttttttttt	ggaattaaaa	gcaatttaaat	gagggcagag	caggaaacat	60
gcatttcctt	tcattcgaat	cttcagatga	accctgagca	gccgaagacc	agaaaagcca	120
tgaagacttt	ctgcttaatt	caggggctta	caggattctt	cagagtgtgt	gtgaacaaaa	180
gctttatagt	acgtattttt	aggatacaaa	taagagagag	actatggctt	ggggtgagaa	240
tgtactgatt	acaaggtcta	cagacaatta	agacacagaa	acagatggga	agagggtgnc	300
cagcatctgg	nggttggctt	ctcaagggct	tgtctgtgca	ccaaattact	tctgcttggn	360
cttctgctga	gctgggcctg	gagtgaccgt	tgaaggacat	ggctctggta	cctttgtgta	420
gcctgncaca	ggaacttttg	tgtatccttg	ctcaggaact	ttgatggcac	ctggctcagg	480
aaacttgatg	aagccttggt	caagggacct	tgatgcttgc	tggctcaggg	accttggnngn	540
ancctgggct	canggacctt	tgncncaacc	ttggcttcaa	gggacccttg	gnacatcctg	600
gcnnagggac	ccttgggncc	aaccctgggc	ttnagggacc	ccttggntnc	nanccttggc	660

<210> 97

<211> 441

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(441)

<223> n = A,T,C or G

<400> 97

gggaccatac	anagtattcc	tctcttcaca	ccaggaccag	ccactgttgc	agcatgagtt	60
cccagcagca	gaagcagccc	tgcattccac	cccctcagct	tcagcagcag	caggtgaaac	120
agccttgcca	gcctccacct	caggaaccat	gcattcccaa	aaccaaggag	ccctgccacc	180
ccaaggtgcc	tgagccctgc	caccccaaag	tgcctgagcc	ctgccagccc	aaggttccag	240
agccatgcca	ccccaaggtg	cctgagccct	gcccttcaat	agtcactcca	gcaccagccc	300
agcagaanac	caagcagaag	taatgtgggt	cacagccatg	cccttgagga	gccggccacc	360
agatgctgaa	tcccctatcc	cattctgtgt	atgagtccca	tttgccttgc	aattagcatt	420
ctgtctcccc	caaaaaaaaa	a				441

<210> 98

<211> 600

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(600)

<223> n = A,T,C or G

<400> 98

gtattcctct	cttcacacca	ggaccagcca	ctggtgcagc	atgagttccc	agcagcagaa	60
gcagccctgc	atcccacccc	ctcagcttca	gcagcagcag	gtgaaacagc	cttgccagcc	120
tccacctcag	gaaccatgca	tccccaaaac	caaggagccc	tgccacccca	aggtgcctga	180
gccctgccac	cccaaagtgc	ctgagccctg	ccagcccaag	gttccagagc	catgccaccc	240
caaggtgcct	gagccctgcc	cttcaatagt	cactccagca	ccagcccagc	agaanaccaa	300
gcagaagtaa	tgtggtccac	agccatgccc	ttgaggagcc	ggccaccana	tgctgaatcc	360
cctatcccat	tctgtgtatg	agtcccatct	gccttgcaat	tagcattctg	tctcccccaa	420
aaaagaatgt	gctatgaagc	tttctttcct	acacactctg	agtctctgaa	tgaagctgaa	480
ggtcttaant	acaganctag	ttttcagctg	ctcagaattc	tctgaagaaa	agatttaaga	540
tgaaaggcaa	atgattcagc	tccttattac	cccattaaat	tcnctttcaa	ttccaaaaaa	600

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<210> 99
 <211> 667
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(667)
 <223> n = A,T,C or G

<400> 99
 actagtgact gagttcctgg caaagaaatt tgacctggac cagttgataa ctcattgtttt 60
 accatttaaa aaaatcagtg aaggatttga gctgctcaat tcaggacaaa gcattcgaac 120
 ggtcctgacg ttttgagatc caaagtggca ggaggtctgt gttgtcatgg tgaactggag 180
 tttctcttgt gagagttccc tcatctgaaa tcatgtatct gtctcacaaa tacaagcata 240
 agtagaagat ttgttgaaga catagaaccc ttataaagaa ttattaacct ttataaacat 300
 ttaaagtctt gtgagcacct gggaattagt ataataacaa tgtnnatatt ttgattttac 360
 attttgtaag gctataattg tatcttttaa gaaaacatac cttggatttc tatgttgaaa 420
 tggagatttt taagagtttt aaccagctgc tgcagatata ttactcaaaa cagatatagc 480
 gtataaagat atagtaaatt catctcctag agtaatatcc acttaacaca ttggaaacta 540
 ttatttttta gatttgaata tnaatgttat tttttaaaca cttgttatga gttacttggg 600
 attacatttt gaaatcagtt cattccatga tgcanattac tgggattaga ttaagaaaga 660
 cggaataa 667

<210> 100
 <211> 583
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(583)
 <223> n = A,T,C or G

<400> 100
 gttttgtttg taagatgatc acagtcattgt tacactgatc taaaggacat atatataacc 60
 ctttaaaaaa aaaatcactg cctcattctt atttcaagat gaatttctat acagactaga 120
 tgtttttctg aagatcaatt agacattttg aaaatgattt aaagtgtttt ccttaatgtt 180
 ctctgaaaac aagtttcttt tgtagtttta accaaaaaag tgcccttttt gtcactggat 240
 tctcctagca ttcattgattt ttttttcata caatgaaatt aaaattgcta aaatcatgga 300
 ctggctttct ggttggattt caggtaagat gtgtttaagg ccagagcttt tctcagtatt 360
 tgattttttt cccaatatt tgatttttta aaaatataca catnggtgct gcattttatat 420
 ctgctggttt aaaattctgt catatttcac ttctagcctt ttagttatgg caaatcatat 480
 ttacttttta cttaaagcat ttggtnattt ggantatctg gttctannct aaaaaaanta 540
 attctatnaa ttgaantttt ggtactcnnn catatttgga tcc 583

<210> 101
 <211> 592
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(592)
 <223> n = A,T,C or G

<400> 101

gtggagacgt	acaaagagca	gccgctcaag	acacctggga	agaaaaagaa	aggcaagccc	60
gggaaacgca	aggagcagga	aaagaaaaaa	cggcgaactc	gctctgcctg	gtagactct	120
ggagtgactg	ggagtgggct	agaaggggac	cacctgtctg	acacctccac	aacgtcgctg	180
gagctcgatt	cacggaggca	ttgaaatfff	cagcaganac	cttccaagga	catattgcag	240
gattctgtaa	tagtgaacat	atggaaagta	ttagaaatat	ttattgtctg	taaatactgt	300
aaatgcattg	gaataaaaact	gtctcccca	ttgctctatg	aaactgcaca	ttggtcattg	360
tgaatattff	tttttttgcc	aaggctaata	caattattat	tatcacattt	accataattt	420
attttgtcca	ttgatgtatt	tattttgtaa	atgtatcttg	gtgctgctga	atttctatat	480
tttttgtaca	taatgcntff	anatatacct	atcaagtttg	ttgataaatg	acncaatgaa	540
gtgnncnana	ttggngggtg	aatttaatga	atgcctaatt	ttattatccc	aa	592

<210> 102
 <211> 587
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(587)
 <223> n = A,T,C or G

<400> 102

cgtcctaagc	acttagacta	catcagggaa	gaacacagac	cacatccctg	tcctcatgcg	60
gcttatgtff	tctggaagaa	agtggagacc	nagtccttgg	ctttagggct	ccccggctgg	120
gggctgtgca	ntccggtcag	ggcgggaagg	gaaatgcacc	gctgcatgtg	aacttacagc	180
ccaggcggat	gccccctccc	ttagcactac	ctggcctcct	gcacccctc	gcctcatgtt	240
cctcccacct	tcaaanaatg	aanaacccca	tgggcccagc	cccttgccct	ggggaaccaa	300
ggcagccttc	caaaactcag	gggctgaagc	anactattag	ggcaggggct	gactttgggt	360
gacactgccc	attccctctc	agggcagctc	angtcaccn	ggncctctga	accagcctg	420
ttcctttgaa	aaagggcaaa	actgaaaagg	gcttttccta	naaaaagaaa	aaccagggaa	480
ctttgccagg	gcttcnntnt	taccaaaca	ncttctcnng	gatttttaat	tccccattng	540
gcctccactt	accnggggcn	atgccccaaa	attaanaatt	tcccatc		587

<210> 103
 <211> 496
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(496)
 <223> n = A,T,C or G

<400> 103

anaggactgg	ccctacntgc	tctctctcgt	cctacctatc	aatgcccaac	atggcagaac	60
ctgcancctt	tggncactgc	anatggaaac	ctctcagtgt	cttgacatca	ccctaccnt	120
gcggtgggct	tccaccacaa	ccactttgac	tctgtggtcc	ctgnanggtg	gnttctcctg	180
actggcagga	tggaccttan	ccnacatata	cctctgttcc	ctctgctnag	anaaagaatt	240
cccttaacat	gatataatcc	acccatgcaa	ntngctactg	gcccagctac	catttaccat	300
ttgcctacag	aatttcattc	agtctacact	ttggcattct	ctctggcgat	agagtgtggc	360
tgggctgacc	gcaaaagggtg	ccttacacac	tggccccac	cctcaaccgt	tgacncatca	420
gangcttgcc	tctctcttct	gattnncccc	catgttggat	atcaggggtg	tcnagggtt	480
ggaaaagaaa	caaaac					496

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<210> 104
 <211> 575
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (575)
 <223> n = A,T,C or G

<400> 104
 gcacctgctc tcaatccnnc tctcaccatg atcctccgcc tgcanaaact cctctgccaa 60
 ctatggangt ggtttcnngg gtggctcttg ccaactggga agaagccgtg gtgtctctac 120
 ctgttcaact cngtttgtgt ctgggggatc aactnngggc tatggaagcg gctnaactgt 180
 tgttttggtg gaagggctgg taattggctt tgggaagtng cttatngaag ttggcctnng 240
 gaagttgcta ttgaaagtng cnttggaagt ngntttggtg ggggggttttg ctggtggcct 300
 ttgttnaatt tgggtgcttt gtnaatggcg gccccctcnc ctgggcaatg aaaaaaatca 360
 ccnatgcngn aaacctcnac nnaacagcct gggcttcctt cacctcgaaa aaagttgctc 420
 cccccccaaa aaaggncaan cccctcaann tggaangttg aaaaaatcct cgaatgggga 480
 nccnnaaaac aaaaancccc cntttcccn gnaanggggg aaataccncc cccccactta 540
 cnaaaaccct tntaaaaaac cccccgggaa aaaaa 575

<210> 105
 <211> 619
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (619)
 <223> n = A,T,C or G

<400> 105
 cactagtagg atagaaacac tgtgtcccga gagtaaggag agaagctact attgattaga 60
 gcctaaccce ggttaactgc aagaagaggc gggatacttt cagctttcca tgtaactgta 120
 tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaact gaatcccact 180
 tcaatacaca ctcatagaact cctgatggaa caataacagg cccaagcctg tggatgatg 240
 tgcacacttg ctagactcan aaaaaatact actctcataa atgggtggga gtattttggt 300
 gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg 360
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata 420
 tttccaaatt tttgtacagt cgctgcacat atttgaaatc atatattaag acttccaaaa 480
 aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcncct ctggttggtg 540
 cttaaaacat ctactatatn gttanatga aattcctttt cccncctcc cgaaaaana 600
 aagtgggtggg gaaaaaaaaa 619

<210> 106
 <211> 506
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (506)
 <223> n = A,T,C or G

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<400> 106

cattggtnct	ttcatttgct	ntggaagtgt	nnatctctaa	cagtggacaa	agttcccngt	60
gccttaaact	ctgtnacact	tttgggaant	gaaaanttnng	tantatgata	ggttattctg	120
angtanagat	gttctggata	ccattanatn	tgccccngt	gtcagaggct	catattgtgt	180
tatgtaaagt	gtatntcatt	cgctactatn	antcaattng	aaatanggtc	tttgggttat	240
gaatanntng	cagcncanct	nanangctgt	ctgtngtatt	cattgtggtc	atagcacctc	300
acancattgt	aacctcnatc	nagttagaca	nactagnaan	ttcctagtga	tggctcanga	360
ttccaaatgg	ntcatntcn	aatgtttaaa	agttanttaa	gtgtaagaaa	tacagactgg	420
atgttccacc	aactagtacc	tgtaatgacn	ggcctgtccc	aacacatctc	ccttttccat	480
gactgtggta	ncccgcacgc	gaaaaa				506

<210> 107

<211> 452

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (452)

<223> n = A,T,C or G

<400> 107

gttgagtctg	tactaaacag	taagatatct	caatgaacca	taaattcaac	tttgtaaaaa	60
tcttttgaag	catagataat	attgtttggg	aatgttttct	tttgtttggg	aatgttttct	120
tttaaagacc	ctcctattct	ataaaactct	gcatgtagag	gcttgtttac	ctttctctct	180
ctaagggtta	caataggagt	ggtgatttga	aaaatataaa	attatgagat	tggttttcct	240
gtggcataaa	ttgcatcact	gtatcatttt	cttttttaac	cggtaagant	ttcagtttgt	300
tggaaagtaa	ctgtganaac	ccagtttccc	gtccatctcc	cttagggact	acccatagaa	360
catgaaaagg	tccccacnga	agcaagaaga	taagtctttc	atggctgctg	gttgcttaaa	420
ccacttttaa	accaaaaaat	tccccttgga	aa			452

<210> 108

<211> 502

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (502)

<223> n = A,T,C or G

<400> 108

atcttcttcc	cttaattagt	tnttatattat	ntattaaatt	ttattgcatg	tcctggcaaa	60
caaaaagaga	ttgtagattg	gcttctggct	ccccaaaagc	ccataacaga	aagtaccaca	120
agaccncaac	tgaagcttaa	aaaatctatc	acatgtataa	tacctttnga	agaacattaa	180
tanagcatat	aaaactttta	acatntgctt	aatgttgtnc	aattataaaa	ntaatngaaa	240
aaaatgtccc	tttaacatnc	aatatcccac	atagtgttat	ttnaggggat	taccnngnaa	300
naaaaaaagg	gtagaaggga	tttaatgaaa	actctgcttn	ccatttctgt	ttanaaacgt	360
ctccagaaca	aaaacttntc	aantctttca	gctaaccgca	tttgagctna	ggccactcaa	420
aaactccatt	agncccactt	tctaanggtc	tctanagctt	actaancctt	ttgacccctt	480
accctggnta	ctcctgccct	ca				502

<210> 109

<211> 1308

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PCT/US00/08896

44

<212> DNA

<213> Homo sapien

<400> 109

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<210> 110

<211> 391

<212> PRT

<213> Homo sapien

<400> 110

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              20              25              30
Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
              35              40              45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
              50              55              60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Ile Glu Asn Thr Glu
65              70              75              80
Ala Val His Gln Gln Phe Gln Lys Phe Leu Thr Glu Ile Ser Lys Leu
              85              90              95
Thr Asn Asp Tyr Glu Leu Asn Ile Thr Asn Arg Leu Phe Gly Glu Lys
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Thr Tyr Leu Phe Leu Gln Lys Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr
              115             120             125
His Ala Ser Leu Glu Pro Val Asp Phe Val Asn Ala Ala Asp Glu Ser
              130             135             140
Arg Lys Lys Ile Asn Ser Trp Val Glu Ser Lys Thr Asn Glu Lys Ile
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Lys Asp Leu Phe Pro Asp Gly Ser Ile Ser Ser Ser Thr Lys Leu Val
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 Lys Glu Asn Thr Lys Glu Glu Lys Phe Trp Met Asn Lys Ser Thr Ser
 195 200 205
 Lys Ser Val Gln Met Met Thr Gln Ser His Ser Phe Ser Phe Thr Phe
 210 215 220
 Leu Glu Asp Leu Gln Ala Lys Ile Leu Gly Ile Pro Tyr Lys Asn Asn
 225 230 235 240
 Asp Leu Ser Met Phe Val Leu Leu Pro Asn Asp Ile Asp Gly Leu Glu
 245 250 255
 Lys Ile Ile Asp Lys Ile Ser Pro Glu Lys Leu Val Glu Trp Thr Ser
 260 265 270
 Pro Gly His Met Glu Glu Arg Lys Val Asn Leu His Leu Pro Arg Phe
 275 280 285
 Glu Val Glu Asp Ser Tyr Asp Leu Glu Ala Val Leu Ala Ala Met Gly
 290 295 300
 Met Gly Asp Ala Phe Ser Glu His Lys Ala Asp Tyr Ser Gly Met Ser
 305 310 315 320
 Ser Gly Ser Gly Leu Tyr Ala Gln Lys Phe Leu His Ser Ser Phe Val
 325 330 335
 Ala Val Thr Glu Glu Gly Thr Glu Ala Ala Ala Thr Gly Ile Gly
 340 345 350
 Phe Thr Val Thr Ser Ala Pro Gly His Glu Asn Val His Cys Asn His
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<210> 111

<211> 1419

<212> DNA

<213> Homo sapien

<400> 111

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PCT/US00/08896

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<210> 112
 <211> 400
 <212> PRT
 <213> Homo sapien

<400> 112
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 35 40 45
 Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
 50 55 60
 Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Val Arg Ile Lys Ala
 65 70 75 80
 Glu Gly Lys Glu Ile Glu Asn Thr Glu Ala Val His Gln Gln Phe Gln
 85 90 95
 Lys Phe Leu Thr Glu Ile Ser Lys Leu Thr Asn Asp Tyr Glu Leu Asn
 100 105 110
 Ile Thr Asn Arg Leu Phe Gly Glu Lys Thr Tyr Leu Phe Leu Gln Lys
 115 120 125
 Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr His Ala Ser Leu Glu Pro Val
 130 135 140
 Asp Phe Val Asn Ala Ala Asp Glu Ser Arg Lys Lys Ile Asn Ser Trp
 145 150 155 160
 Val Glu Ser Lys Thr Asn Glu Lys Ile Lys Asp Leu Phe Pro Asp Gly
 165 170 175
 Ser Ile Ser Ser Ser Thr Lys Leu Val Leu Val Asn Met Val Tyr Phe
 180 185 190
 Lys Gly Gln Trp Asp Arg Glu Phe Lys Lys Glu Asn Thr Lys Glu Glu
 195 200 205
 Lys Phe Trp Met Asn Lys Ser Thr Ser Lys Ser Val Gln Met Met Thr
 210 215 220
 Gln Ser His Ser Phe Ser Phe Thr Phe Leu Glu Asp Leu Gln Ala Lys
 225 230 235 240
 Ile Leu Gly Ile Pro Tyr Lys Asn Asn Asp Leu Ser Met Phe Val Leu
 245 250 255
 Leu Pro Asn Asp Ile Asp Gly Leu Glu Lys Ile Ile Asp Lys Ile Ser
 260 265 270
 Pro Glu Lys Leu Val Glu Trp Thr Ser Pro Gly His Met Glu Glu Arg
 275 280 285
 Lys Val Asn Leu His Leu Pro Arg Phe Glu Val Glu Asp Ser Tyr Asp
 290 295 300
 Leu Glu Ala Val Leu Ala Ala Met Gly Met Gly Asp Ala Phe Ser Glu
 305 310 315 320
 His Lys Ala Asp Tyr Ser Gly Met Ser Ser Gly Ser Gly Leu Tyr Ala
 325 330 335
 Gln Lys Phe Leu His Ser Ser Phe Val Ala Val Thr Glu Glu Gly Thr
 340 345 350

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Glu Ala Ala Ala Thr Gly Ile Gly Phe Thr Val Thr Ser Ala Pro
 355 360 365
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 370 375 380
 His Asn Glu Ser Asn Ser Ile Leu Phe Phe Gly Arg Phe Ser Ser Pro
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 <211> 957
 <212> DNA
 <213> Homo sapien

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<210> 114
 <211> 161
 <212> PRT
 <213> Homo sapien

<400> 114
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 Phe Val Pro Thr Thr Lys Glu Pro Cys His Ser Lys Val Pro Gln Pro
 35 40 45
 Gly Asn Thr Lys Ile Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro
 50 55 60
 Gly Cys Thr Lys Val Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro
 65 70 75 80
 Gly Cys Thr Lys Val Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro
 85 90 95
 Gly Tyr Thr Lys Val Pro Glu Pro Gly Ser Ile Lys Val Pro Asp Gln
 100 105 110
 Gly Phe Ile Lys Phe Pro Glu Pro Gly Ala Ile Lys Val Pro Glu Gln
 115 120 125
 Gly Tyr Thr Lys Val Pro Val Pro Gly Tyr Thr Lys Val Pro Glu Pro
 130 135 140
 Cys Pro Ser Thr Val Thr Pro Gly Pro Ala Gln Gln Lys Thr Lys Gln

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48

145
Lys

150

155

160

<210> 115
 <211> 506
 <212> DNA
 <213> Homo sapien

<220>
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 <223> n = A,T,C or G

<400> 115

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 <213> Homo sapien

<400> 116

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<210> 117

<211> 6921

<212> DNA

<213> Homo sapien

<400> 117

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PCT/US00/08896

50

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ggcactag

8948

<210> 120
 <211> 587
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(587)
 <223> n = A,T,C or G

<400> 120
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 gggctgtgca ntccggtcag ggcgggaagg gaaatgcacc gctgcatgtg aacttacagc 180
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 gcctccactt accnggggcn atgccccaaa attaanaatt tcccatc 587

<210> 121
 <211> 619
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(619)
 <223> n = A,T,C or G

<400> 121
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 tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaact gaatcccact 180
 tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tggtagtgatg 240
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 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata 420
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 aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcncct ctgtttggtg 540
 cttaaaacat ctactatatn gttnanatga aattcctttt ccccnctcc cgaaaaaana 600
 aagtggtagg gaaaaaaaaa 619

<210> 122
 <211> 1475
 <212> DNA
 <213> Homo sapien

<400> 122
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<210> 123

<211> 2294

<212> DNA

<213> Homo sapien

<400> 123

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<210> 124

<211> 956

<212> DNA

<213> Homo sapien

<400> 124

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<210> 125

<211> 486

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(486)

<223> n = A,T,C or G

<400> 125

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<210> 126

<211> 3552

<212> DNA

<213> Homo sapien

<400> 126

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59

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<210> 127

<211> 754

<212> DNA

<213> Homo sapien

<400> 127

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<210> 128

<211> 374

<212> DNA

<213> Homo sapien

<400> 128

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<210> 129

<211> 546

<212> DNA

<213> Homo sapien

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60

<400> 129

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<210> 130

<211> 5156

<212> DNA

<213> Homo sapien

<400> 130

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<210> 131

<211> 671

<212> DNA

<213> Homo sapien

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62

<400> 131

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<210> 132

<211> 590

<212> DNA

<213> Homo sapien

<400> 132

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<210> 133

<211> 581

<212> DNA

<213> Homo sapien

<400> 133

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<210> 134

<211> 4797

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (4797)

<223> n = A,T,C or G

<400> 134

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<210> 135

<211> 2856

<212> DNA

<213> Homo sapien

<400> 135

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<210> 136

<211> 356

<212> DNA

<213> Homo sapien

<400> 136

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agtgtacttt	cagacaacca	caaggatgac	tgatgtagac	agaaatggca	ccactgctta	240
tgaaggaaac	tggaacccag	aagcacaccc	tcccctcatt	caccatgagc	atcatgagga	300
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<210> 137

<211> 356

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (356)

<223> n = A,T,C or G

<400> 137

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66

gtcactggct	gcccccgga	cagggcgctg	ctccatggct	ctgcttgtgg	tagtctgtgg	120
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cgctaaggcc	aaanttccag	acanayggcc	gggccggtn	nataggggan	cccaacttgg	300
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<210> 138

<211> 353

<212> DNA

<213> Homo sapien

<400> 138

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<210> 139

<211> 371

<212> DNA

<213> Homo sapien

<400> 139

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actagtggat	c					371

<210> 140

<211> 370

<212> DNA

<213> Homo sapien

<400> 140

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aggagctgcc	tgagtggtag	tttctcttcc	tggtaatcct	ctggcccagc	ctcatggcag	180
aatagaggta	tttttaggct	atttttgtaa	tatggcttct	ggtcaaaatc	cctgtgtagc	240
tgaattccca	agccctgcat	tgtacagccc	cccactcccc	tcaccaccta	ataaaggaat	300
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gcacactggc						370

<210> 141

<211> 371

<212> DNA

<213> Homo sapien

<400> 141

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67

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<210> 142

<211> 343

<212> DNA

<213> Homo sapien

<400> 142

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gtcttcattg	gaaacgggat	acctttacat	aaaaactaga	cagtagcatt	ctcagaaatt	240
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<210> 143

<211> 354

<212> DNA

<213> Homo sapien

<400> 143

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gtggtggagt	gtgtcatgaa	caatgtcacc	tgtactcgga	tctatgaaaa	agtagaataa	180
aaattccatc	atcactttgg	acaggagtta	attaagagaa	tgaccaagct	cagttcaatg	240
agcaaactctc	catactgttt	ctttcttttt	tttttcatta	ctgtgttcaa	ttatctttat	300
cataaacatt	ttacatgcag	ctatttcaaa	gtgtgttgga	ttaattagga	tcat	354

<210> 144

<211> 353

<212> DNA

<213> Homo sapien

<400> 144

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aagatgacag	actaagtagg	attctgccat	ttagaataat	tctgggtatcc	tgggcgttgc	180
gttaagtgtc	ttacttttca	ttctgtctta	cgatagtctt	cagaggtggg	aacagatgaa	240
gaaaccatgc	cccagagaag	gttaagtgc	ttcctcttta	tggagccagt	gttccaacct	300
aggtttgcct	gataccagac	ctgtggcccc	acctcccatg	caggtctctg	tgg	353

<210> 145

<211> 371

<212> DNA

<213> Homo sapien

<400> 145

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attgccactg	ttgatcacta	gctttttctt	ctgccacac	cttcttcgac	tggtgactgc	180
aatgcaaact	gcaagaatca	aagccaaggc	caagagggat	gccaagatga	tcagccattc	240

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68

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<210> 146
 <211> 355
 <212> DNA
 <213> Homo sapien

<400> 146	
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<210> 147
 <211> 355
 <212> DNA
 <213> Homo sapien

<400> 147	
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<210> 148
 <211> 369
 <212> DNA
 <213> Homo sapien

<400> 148	
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<210> 149
 <211> 620
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(620)
 <223> n = A,T,C or G

<400> 149

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69

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catgtttatc	ttttattatg	ttttgtgaag	ttgtgtcttt	tcactaatta	cctatactat	120
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<210> 150

<211> 371

<212> DNA

<213> Homo sapien

<400> 150

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<212> DNA

<213> Homo sapien

<400> 151

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70

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PCT/US00/08896

71

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 <212> PRT
 <213> Homo sapien

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 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
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 Glu Gly Gln Ile Ala Pro Ser Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
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 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
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 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
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 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
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 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
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 Glu Leu Val Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
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 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu
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 355 360 365
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val
 370 375 380

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 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
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 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys
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 465 470 475 480
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 485 490 495
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
 500 505 510
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
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 530 535 540
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
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<210> 153

<211> 2007

<212> DNA

<213> Homo sapien

<400> 153

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<210> 154

<211> 2148

<212> DNA

<213> Homo sapien

<400> 154

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WO 00/61612

PCT/US00/08896

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 <211> 153
 <212> PRT
 <213> Homo sapien

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 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr
 85 90 95
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala
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 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu
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 <211> 128
 <212> PRT
 <213> Homo sapien

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 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Thr Ile
 85 90 95
 Cys Ala Ile Asp Asp Gln Lys Thr Val Glu Glu Gly Phe Met Glu Asp
 100 105 110
 Val Gly Leu Ser Trp Ser Leu Arg Glu His Asp His Val Ala Gly Ala
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<210> 157
 <211> 424
 <212> DNA
 <213> Homo sapien

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75

<220>

<221> misc_feature

<222> (1)...(424)

<223> n = A,T,C or G

<400> 157

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<210> 158

<211> 2099

<212> DNA

<213> Homo sapien

<400> 158

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<210> 159
 <211> 291
 <212> PRT
 <213> Homo sapien

<400> 159
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 65 70 75 80
 Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala
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 Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
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 Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys Gln Lys Val Arg Ile
 115 120 125
 Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile
 130 135 140
 Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly
 145 150 155 160
 Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn
 165 170 175
 Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr
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 Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
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 Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile
 245 250 255
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<210> 160
 <211> 3951
 <212> DNA
 <213> Homo sapien

<400> 160
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<210> 161

<211> 943

<212> PRT

<213> Homo sapien

<400> 161

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Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn
          35          40          45
Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
          50          55          60
Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
65          70          75          80
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
          85          90          95
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
          100          105          110
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
          115          120          125
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
          130          135          140
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
145          150          155          160
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu
          165          170          175
Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
          180          185          190
Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
          195          200          205
Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
          210          215          220
Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
225          230          235          240
Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser
          245          250          255
Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu
          260          265          270
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Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu
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Phe	Tyr	Leu	Met	Gln	Ile	Val	Glu	Ile	His	Thr	Phe	Val	Gly	Ile	Ala	340	345	350	
Ser	Phe	Asp	Ser	Lys	Gly	Glu	Ile	Arg	Ala	Gln	Leu	His	Gln	Ile	Asn	355	360	365	
Ser	Asn	Asp	Asp	Arg	Lys	Leu	Leu	Val	Ser	Tyr	Leu	Pro	Thr	Thr	Val	370	375	380	
Ser	Ala	Lys	Thr	Asp	Ile	Ser	Ile	Cys	Ser	Gly	Leu	Lys	Lys	Gly	Phe	385	390	395	400
Glu	Val	Val	Glu	Lys	Leu	Asn	Gly	Lys	Ala	Tyr	Gly	Ser	Val	Met	Ile	405	410	415	
Leu	Val	Thr	Ser	Gly	Asp	Asp	Lys	Leu	Leu	Gly	Asn	Cys	Leu	Pro	Thr	420	425	430	
Val	Leu	Ser	Ser	Gly	Ser	Thr	Ile	His	Ser	Ile	Ala	Leu	Gly	Ser	Ser	435	440	445	
Ala	Ala	Pro	Asn	Leu	Glu	Glu	Leu	Ser	Arg	Leu	Thr	Gly	Gly	Leu	Lys	450	455	460	
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Ser	Arg	Ile	Ser	Ser	Gly	Thr	Gly	Asp	Ile	Phe	Gln	Gln	His	Ile	Gln	485	490	495	
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Thr	Trp	Gln	Ala	Ser	Gly	Pro	Pro	Glu	Ile	Ile	Leu	Phe	Asp	Pro	Asp	530	535	540	
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Tyr	Thr	Leu	Asn	Asn	Thr	His	His	Ser	Leu	Gln	Ala	Leu	Lys	Val	Thr	580	585	590	
Val	Thr	Ser	Arg	Ala	Ser	Asn	Ser	Ala	Val	Pro	Pro	Ala	Thr	Val	Glu	595	600	605	
Ala	Phe	Val	Glu	Arg	Asp	Ser	Leu	His	Phe	Pro	His	Pro	Val	Met	Ile	610	615	620	
Tyr	Ala	Asn	Val	Lys	Gln	Gly	Phe	Tyr	Pro	Ile	Leu	Asn	Ala	Thr	Val	625	630	635	640
Thr	Ala	Thr	Val	Glu	Pro	Glu	Thr	Gly	Asp	Pro	Val	Thr	Leu	Arg	Leu	645	650	655	
Leu	Asp	Asp	Gly	Ala	Gly	Ala	Asp	Val	Ile	Lys	Asn	Asp	Gly	Ile	Tyr	660	665	670	
Ser	Arg	Tyr	Phe	Phe	Ser	Phe	Ala	Ala	Asn	Gly	Arg	Tyr	Ser	Leu	Lys	675	680	685	
Val	His	Val	Asn	His	Ser	Pro	Ser	Ile	Ser	Thr	Pro	Ala	His	Ser	Ile	690	695	700	
Pro	Gly	Ser	His	Ala	Met	Tyr	Val	Pro	Gly	Tyr	Thr	Ala	Asn	Gly	Asn	705	710	715	720
Ile	Gln	Met	Asn	Ala	Pro	Arg	Lys	Ser	Val	Gly	Arg	Asn	Glu	Glu	Glu	725	730	735	
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			770				775					780					
Trp	Thr	Ala	Pro	Gly	Glu	Asp	Phe	Asp	Gln	Gly	Gln	Ala	Thr	Ser	Tyr		
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Glu	Ile	Arg	Met	Ser	Lys	Ser	Leu	Gln	Asn	Ile	Gln	Asp	Asp	Phe	Asn		
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Ile	Arg	Glu	Ile	Phe	Thr	Phe	Ser	Pro	Gln	Ile	Ser	Thr	Asn	Gly	Pro		
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Glu	His	Gln	Pro	Asn	Gly	Glu	Thr	His	Glu	Ser	His	Arg	Ile	Tyr	Val		
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Ala	Ile	Arg	Ala	Met	Asp	Arg	Asn	Ser	Leu	Gln	Ser	Ala	Val	Ser	Asn		
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Ile	Gly	Ile	Ile	Cys	Leu	Ile	Ile	Val	Val	Thr	His	His	Thr	Leu	Ser		
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<210> 162
 <211> 498
 <212> DNA
 <213> Homo sapien

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<210> 163
 <211> 1128
 <212> DNA
 <213> Homo sapien

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<210> 164

<211> 1310

<212> DNA

<213> Homo sapien

<400> 164

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<210> 165

<211> 177

<212> PRT

<213> Homo sapien

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Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
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Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile

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82

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Thr	Tyr	Lys	Glu	Gln	Pro
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Lys	Pro	Gly	Lys	Arg	Lys
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His

<210> 166
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Lys	Pro
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Ser	Ala
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His	Leu
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Val	Gln	Gln	Trp	Ser	Val
10					15
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65				75	80
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		85		90	95
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His

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 <211> 3362
 <212> DNA
 <213> Homo sapien

<400> 167

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<211> 2784

<212> DNA

<213> Homo sapien

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85

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2784

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<211> 592

<212> PRT

<213> Homo sapien

<400> 169

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86

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Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr		415
	420	425
Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser		430
	435	440
Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys		445
	450	455
Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe		460
465	470	475
Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln		480
	485	490
Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn		495
	500	505
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545	550	555
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Tyr Thr Leu Met Cys Phe His His Ala Lys Leu Leu Thr Trp Lys Leu		575
	580	585
		590

<210> 170

<211> 791

<212> PRT

<213> Homo sapien

<400> 170

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Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met	
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Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val	
65	70
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn	
	85
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile	
	100
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln	
	115
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn	
130	135
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg	
145	150
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu	
	155
	160

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				165					170					175			
Tyr	Asn	Asn	Asp	Lys	Pro	Phe	Tyr	Ile	Asn	Gly	Gln	Asn	Gln	Ile	Lys		
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Gly	Pro	Cys	Pro	Gln	Glu	Asn	Cys	Ile	Ile	Ser	Lys	Leu	Phe	Lys	Glu		
	210					215					220						
Gly	Cys	Thr	Phe	Ile	Tyr	Asn	Ser	Thr	Gln	Asn	Ala	Thr	Ala	Ser	Ile		
225					230					235					240		
Met	Phe	Met	Gln	Ser	Leu	Ser	Ser	Val	Val	Glu	Phe	Cys	Asn	Ala	Ser		
			245					250						255			
Thr	His	Asn	Gln	Glu	Ala	Pro	Asn	Leu	Gln	Asn	Gln	Met	Cys	Ser	Leu		
			260					265					270				
Arg	Ser	Ala	Trp	Asp	Val	Ile	Thr	Asp	Ser	Ala	Asp	Phe	His	His	Ser		
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Phe	Pro	Met	Asn	Gly	Thr	Glu	Leu	Pro	Pro	Pro	Pro	Thr	Phe	Ser	Leu		
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Val	Glu	Ala	Gly	Asp	Lys	Val	Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser		
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			325					330						335			
Phe	Tyr	Leu	Met	Gln	Ile	Val	Glu	Ile	His	Thr	Phe	Val	Gly	Ile	Ala		
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Ser	Phe	Asp	Ser	Lys	Gly	Glu	Ile	Arg	Ala	Gln	Leu	His	Gln	Ile	Asn		
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Ser	Asn	Asp	Asp	Arg	Lys	Leu	Leu	Val	Ser	Tyr	Leu	Pro	Thr	Thr	Val		
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Ser	Ala	Lys	Thr	Asp	Ile	Ser	Ile	Cys	Ser	Gly	Leu	Lys	Lys	Gly	Phe		
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Ser	Arg	Ile	Ser	Ser	Gly	Thr	Gly	Asp	Ile	Phe	Gln	Gln	His	Ile	Gln		
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Leu	Glu	Ser	Thr	Gly	Glu	Asn	Val	Lys	Pro	His	His	Gln	Leu	Lys	Asn		
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Thr	Trp	Gln	Ala	Ser	Gly	Pro	Pro	Glu	Ile	Ile	Leu	Phe	Asp	Pro	Asp		
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Gly	Arg	Lys	Tyr	Tyr	Thr	Asn	Asn	Phe	Ile	Thr	Asn	Leu	Thr	Phe	Arg		
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			565					570						575			
Tyr	Thr	Leu	Asn	Asn	Thr	His	His	Ser	Leu	Gln	Ala	Leu	Lys	Val	Thr		
		580						585					590				
Val	Thr	Ser	Arg	Ala	Ser	Asn	Ser	Ala	Val	Pro	Pro	Ala	Thr	Val	Glu		
		595					600					605					

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Ala	Phe	Val	Glu	Arg	Asp	Ser	Leu	His	Phe	Pro	His	Pro	Val	Met	Ile
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Tyr	Ala	Asn	Val	Lys	Gln	Gly	Phe	Tyr	Pro	Ile	Leu	Asn	Ala	Thr	Val
625					630					635					640
Thr	Ala	Thr	Val	Glu	Pro	Glu	Thr	Gly	Asp	Pro	Val	Thr	Leu	Arg	Leu
				645					650					655	
Leu	Asp	Asp	Gly	Ala	Gly	Ala	Asp	Val	Ile	Lys	Asn	Asp	Gly	Ile	Tyr
			660					665					670		
Ser	Arg	Tyr	Phe	Phe	Ser	Phe	Ala	Ala	Asn	Gly	Arg	Tyr	Ser	Leu	Lys
		675					680					685			
Val	His	Val	Asn	His	Ser	Pro	Ser	Ile	Ser	Thr	Pro	Ala	His	Ser	Ile
	690					695					700				
Pro	Gly	Ser	His	Ala	Met	Tyr	Val	Pro	Gly	Tyr	Thr	Ala	Asn	Gly	Asn
705					710					715					720
Ile	Gln	Met	Asn	Ala	Pro	Arg	Lys	Ser	Val	Gly	Arg	Asn	Glu	Glu	Glu
				725						730				735	
Arg	Lys	Trp	Gly	Phe	Ser	Arg	Val	Ser	Ser	Gly	Gly	Ser	Phe	Ser	Val
			740					745					750		
Leu	Gly	Val	Pro	Ala	Gly	Pro	His	Pro	Asp	Val	Phe	Pro	Pro	Cys	Lys
		755					760				765				
Ile	Ile	Asp	Leu	Glu	Ala	Val	Asn	Arg	Arg	Gly	Ile	Asp	Pro	Ile	Leu
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<210> 171

<211> 1491

<212> DNA

<213> Homo sapien

<400> 171

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1491

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<210> 172
<211> 364
<212> PRT
<213> Homo sapien
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<400> 172

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Ser	Pro	Gly	Arg	Pro	Arg	Glu	Leu	Thr	Ile	Pro	Gln	Thr	Ser	Ser	His
	50					55					60				
Gly	Ala	Asn	Arg	Phe	Val	Pro	Lys	Ser	Lys	Ala	Leu	Glu	Ala	Val	Lys
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Leu	Ala	Ile	Glu	Ala	Gly	Phe	His	His	Ile	Asp	Ser	Ala	His	Val	Tyr
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Asn	Asn	Glu	Glu	Gln	Val	Gly	Leu	Ala	Ile	Arg	Ser	Lys	Ile	Ala	Asp
		100					105						110		
Gly	Ser	Val	Lys	Arg	Glu	Asp	Ile	Phe	Tyr	Thr	Ser	Lys	Leu	Trp	Ser
		115					120					125			
Asn	Ser	His	Arg	Pro	Glu	Leu	Val	Arg	Pro	Ala	Leu	Glu	Arg	Ser	Leu
	130					135					140				
Lys	Asn	Leu	Gln	Leu	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Phe	Pro
145				150						155					160
Val	Ser	Val	Lys	Pro	Gly	Glu	Glu	Val	Ile	Pro	Lys	Asp	Glu	Asn	Gly
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Lys	Ile	Leu	Phe	Asp	Thr	Val	Asp	Leu	Cys	Ala	Thr	Trp	Glu	Ala	Met
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Phe	Asn	His	Arg	Leu	Leu	Glu	Met	Ile	Leu	Asn	Lys	Pro	Gly	Leu	Lys
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Tyr	Lys	Pro	Val	Cys	Asn	Gln	Val	Glu	Cys	His	Pro	Tyr	Phe	Asn	Gln
225				230						235					240
Arg	Lys	Leu	Leu	Asp	Phe	Cys	Lys	Ser	Lys	Asp	Ile	Val	Leu	Val	Ala
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Tyr	Ser	Ala	Leu	Gly	Ser	His	Arg	Glu	Glu	Pro	Trp	Val	Asp	Pro	Asn
			260					265					270		
Ser	Pro	Val	Leu	Leu	Glu	Asp	Pro	Val	Leu	Cys	Ala	Leu	Ala	Lys	Lys
		275					280					285			
His	Lys	Arg	Thr	Pro	Ala	Leu	Ile	Ala	Leu	Arg	Tyr	Gln	Leu	Gln	Arg
	290					295					300				
Gly	Val	Val	Val	Leu	Ala	Lys	Ser	Tyr	Asn	Glu	Gln	Arg	Ile	Arg	Gln
305				310						315					320
Asn	Val	Gln	Val	Phe	Glu	Phe	Gln	Leu	Thr	Ser	Glu	Glu	Met	Lys	Ala
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Ile	Asp	Gly	Leu	Asn	Arg	Asn	Val	Arg	Tyr	Leu	Thr	Leu	Asp	Ile	Phe
			340					345					350		
Ala	Gly	Pro	Pro	Asn	Tyr	Pro	Phe	Ser	Asp	Glu	Tyr				

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<210> 173
 <211> 1988
 <212> DNA
 <213> Homo sapiens

<400> 173
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<210> 174
 <211> 238
 <212> PRT
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<400> 174
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Leu Ser Ala Ile Ala Phe Asp Ile Ile Ala Leu Ala Gly Arg Gly Trp		
65	70	75 80
Leu Gln Ser Ser Asp His Gly Gln Thr Ser Ser Leu Trp Trp Lys Cys		
85	90	95
Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly Cys Gln Ser		
100	105	110
Leu Met Glu Tyr Ala Trp Gly Arg Ala Ala Ala Ala Met Leu Phe Cys		
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Gly Phe Ile Ile Leu Val Ile Cys Phe Ile Leu Ser Phe Phe Ala Leu		
130	135	140
Cys Gly Pro Gln Met Leu Val Phe Leu Arg Val Ile Gly Gly Leu Leu		
145	150	155 160
Ala Leu Ala Ala Val Phe Gln Ile Ile Ser Leu Val Ile Tyr Pro Val		
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Lys Tyr Thr Gln Thr Phe Thr Leu His Ala Asn Pro Ala Val Thr Tyr		
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Ile Tyr Asn Trp Ala Tyr Gly Phe Gly Trp Ala Ala Thr Ile Ile Leu		
195	200	205
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<211> 4181

<212> DNA

<213> Homo sapiens

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WO 00/61612

PCT/US00/08896

92

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94

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4181

<210> 176

<211> 580

<212> PRT

<213> Homo sapiens

<400> 176

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Asp	Leu	Glu	Ser	Ile	Phe	Lys	Asp	Ala	Lys	Ile	Pro	Val	Ser	Gly	Pro
			20					25					30		

Phe	Leu	Val	Lys	Thr	Gly	Tyr	Ala	Phe	Val	Asp	Cys	Pro	Asp	Glu	Ser
		35					40					45			

Trp	Ala	Leu	Lys	Ala	Ile	Glu	Ala	Leu	Ser	Gly	Lys	Ile	Glu	Leu	His
	50					55					60				

Gly	Lys	Pro	Ile	Glu	Val	Glu	His	Ser	Val	Pro	Lys	Arg	Gln	Arg	Ile
65					70					75					80

Arg	Lys	Leu	Gln	Ile	Arg	Asn	Ile	Pro	Pro	His	Leu	Gln	Trp	Glu	Val
				85					90					95	

Leu	Asp	Ser	Leu	Leu	Val	Gln	Tyr	Gly	Val	Val	Glu	Ser	Cys	Glu	Gln
			100					105					110		

Val	Asn	Thr	Asp	Ser	Glu	Thr	Ala	Val	Val	Asn	Val	Thr	Tyr	Ser	Ser
		115					120					125			

Lys	Asp	Gln	Ala	Arg	Gln	Ala	Leu	Asp	Lys	Leu	Asn	Gly	Phe	Gln	Leu
	130					135					140				

Glu	Asn	Phe	Thr	Leu	Lys	Val	Ala	Tyr	Ile	Pro	Asp	Glu	Met	Ala	Ala
145					150					155					160

Gln	Gln	Asn	Pro	Leu	Gln	Gln	Pro	Arg	Gly	Arg	Arg	Gly	Leu	Gly	Gln
				165					170					175	

Arg	Gly	Ser	Ser	Arg	Gln	Gly	Ser	Pro	Gly	Ser	Val	Ser	Lys	Gln	Lys
			180					185					190		

Pro	Cys	Asp	Leu	Pro	Leu	Arg	Leu	Leu	Val	Pro	Thr	Gln	Phe	Val	Gly
		195					200					205			

Ala	Ile	Ile	Gly	Lys	Glu	Gly	Ala	Thr	Ile	Arg	Asn	Ile	Thr	Lys	Gln
	210					215					220				

Thr	Gln	Ser	Lys	Ile	Asp	Val	His	Arg	Lys	Glu	Asn	Ala	Gly	Ala	Ala
225					230					235					240

Glu	Lys	Ser	Ile	Thr	Ile	Leu	Ser	Thr	Pro	Glu	Gly	Thr	Ser	Ala	Ala
				245					250					255	

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Cys	Lys	Ser	Ile	Leu	Glu	Ile	Met	His	Lys	Glu	Ala	Gln	Asp	Ile	Lys	260	265	270	
Phe	Thr	Glu	Glu	Ile	Pro	Leu	Lys	Ile	Leu	Ala	His	Asn	Asn	Phe	Val	275	280	285	
Gly	Arg	Leu	Ile	Gly	Lys	Glu	Gly	Arg	Asn	Leu	Lys	Lys	Ile	Glu	Gln	290	295	300	
Asp	Thr	Asp	Thr	Lys	Ile	Thr	Ile	Ser	Pro	Leu	Gln	Glu	Leu	Thr	Leu	305	310	315	320
Tyr	Asn	Pro	Glu	Arg	Thr	Ile	Thr	Val	Lys	Gly	Asn	Val	Glu	Thr	Cys	325	330	335	
Ala	Lys	Ala	Glu	Glu	Glu	Ile	Met	Lys	Lys	Ile	Arg	Glu	Ser	Tyr	Glu	340	345	350	
Asn	Asp	Ile	Ala	Ser	Met	Asn	Leu	Gln	Ala	His	Leu	Ile	Pro	Gly	Leu	355	360	365	
Asn	Leu	Asn	Ala	Leu	Gly	Leu	Phe	Pro	Pro	Thr	Ser	Gly	Met	Pro	Pro	370	375	380	
Pro	Thr	Ser	Gly	Pro	Pro	Ser	Ala	Met	Thr	Pro	Pro	Tyr	Pro	Gln	Phe	385	390	395	400
Glu	Gln	Ser	Glu	Thr	Glu	Thr	Val	His	Gln	Phe	Ile	Pro	Ala	Leu	Ser	405	410	415	
Val	Gly	Ala	Ile	Ile	Gly	Lys	Gln	Gly	Gln	His	Ile	Lys	Gln	Leu	Ser	420	425	430	
Arg	Phe	Ala	Gly	Ala	Ser	Ile	Lys	Ile	Ala	Pro	Ala	Glu	Ala	Pro	Asp	435	440	445	
Ala	Lys	Val	Arg	Met	Val	Ile	Ile	Thr	Gly	Pro	Pro	Glu	Ala	Gln	Phe	450	455	460	
Lys	Ala	Gln	Gly	Arg	Ile	Tyr	Gly	Lys	Ile	Lys	Glu	Glu	Asn	Phe	Val	465	470	475	480
Ser	Pro	Lys	Glu	Glu	Val	Lys	Leu	Glu	Ala	His	Ile	Arg	Val	Pro	Ser	485	490	495	
Phe	Ala	Ala	Gly	Arg	Val	Ile	Gly	Lys	Gly	Gly	Lys	Thr	Val	Asn	Glu	500	505	510	
Leu	Gln	Asn	Leu	Ser	Ser	Ala	Glu	Val	Val	Val	Pro	Arg	Asp	Gln	Thr	515	520	525	
Pro	Asp	Glu	Asn	Asp	Gln	Val	Val	Val	Lys	Ile	Thr	Gly	His	Phe	Tyr	530	535	540	

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96

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

Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser
 565 570 575

Arg Arg Lys

<210> 177
 <211> 401
 <212> DNA
 <213> Homo sapiens

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 cacacagcaa aaaattgttt actttgttgg acaaaccaaa tcagttctca aaaaatgacc 180
 ggtgcttata aaaagttata aatatcgagt agctctaaaa caaaccacct gaccaagagg 240
 gaagtgagct tgtgcttagt atttacattg gatgccagtt ttgtaatcac tgacttatgt 300
 gcaaactggg gcagaaattc tataaactct ttgctgtttt tgatacctgc tttttgtttc 360
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<210> 178
 <211> 561
 <212> DNA
 <213> Homo sapiens

<400> 178
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 agtgagctgg ccactgcggt taaagcacga attgggagct ctcagcgaca tcaccagtca 180
 gcagccaaag acctaaactca gtcccctgag gtctcccca caaccatcca ggtgacatac 240
 ctcccctcca gtcagaagag taaacgtgcc aagcacttcc ttgaattgaa gagctttaag 300
 gataactata acacattgga gagtactctg tgacggagct gaaggactct tgccgtagat 360
 taagccagtc agttgcaatg tgcaagacag gctgcttgcc gggccgcctt cggaacatct 420
 ggcccagcag gccagactg tatccatcca agttcccgtt gtatccagag ttcttagagc 480
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<210> 179
 <211> 521
 <212> DNA
 <213> Homo sapiens

<400> 179
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 gatcgagcaa tggcttcagg acatgggttc tcttctcctg tgatcattca agtgctcact 120
 gcatgaagac tggcttgtct cagtgtttca acctcaccag ggctgtctct tgggtccacac 180
 ctcgctccct gttagtgccg tatgacagcc cccatcaaat gaccttggcc aagtcacggt 240
 ttctctgtgg tcaaggttgg ttggctgatt ggtggaaagt aggggtggacc aaaggaggcc 300
 acgtgagcag tcagcaccag ttctgcacca gcagcgctc cgtcctagtg ggtgttccctg 360
 tttctcctgg ccctgggtgg gctagggcct gattcgggaa gatgccttg cagggagggg 420
 aggataagtg ggatctacca attgattctg gcaaaacaat ttctaagatt tttttgcttt 480

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97

atgtgggaaa cagatctaaa tctcatttta tgctgtatTT t 521

<210> 180
 <211> 417
 <212> DNA
 <213> Homo sapiens

<400> 180
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 cccccagccg catctttctgg cggaccgtgc gaggtatgct gccccacaaa accaagcgag 300
 gccaggccgc tctggaccgt ctcaaggtgt ttgacggcat cccaccgccc tacgacaaga 360
 aaaagcggat ggtggttcct gctgccctca aggtcgtgcg tctgaagcct acaagaa 417

<210> 181
 <211> 283
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (35)
 <223> n=A,T,C or G

<400> 181
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 caagaactca agtgtaactg tgataaaata acctttccca ggtatatagg caggtatgtg 120
 tgtaatctca gaatacacag gtgacataga tatgatatga caactggtaa tgggtggattc 180
 atttacattg ttacacttc tatgaccagg ccttaaggga aggtcagttt tttaaaaaaac 240
 caagtagtgt ctctctacct atctccagat acatgtcaaa aaa 283

<210> 182
 <211> 401
 <212> DNA
 <213> Homo sapiens

<400> 182
 atattcttgc tgcttatgca gctgacattg ttgccctccc taaagcaacc aagtagcctt 60
 tatTTcccac agtgaaagaa aacgctggcc tatcagttac attacaaaag gcagatttca 120
 agaggattga gtaagtagtt ggatggcttt cataaaaaca agaattcaag aagaggattc 180
 atgctttaag aaacatttgt tatacattcc tcacaaatta tacctgggat aaaaactatg 240
 tagcaggcag tgtgttttcc ttccatgtct ctctgcacta cctgcagtgt gtcctctgag 300
 gctgcaagtc tgccttatct gaattcccag cagaagcact aagaagctcc accctatcac 360
 ctagcagata aaactatggg gaaaacttaa atctgtgcat a 401

<210> 183
 <211> 366
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (325)

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<223> n=A,T,C or G

<400> 183

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tttaaggaca aagatgaagt cactgtaaac taatctgtca ttgtttttac cttccttttc 180
tttttcagtg cagaaattaa aagtaagtat aaagcaccgt gattgggagt gtttttgcgt 240
gtgtcggaat cactggtaaa tgttggctga gaacaatccc tccccttgca cttgtgaaaa 300
cactttgagc gctttaagag attancctga gaaataatta aatatctttt ctcttcaaaa 360
aaaaaa                                           366

```

<210> 184

<211> 370

<212> DNA

<213> Homo sapiens

<400> 184

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tcttacttca aaagaaaaat aaacataaaa aataagttgc tggttcctaa caggaaaaat 60
tttaataatt gtactgagag aaactgctta cgtacacatt gcagatcaaa tatttggagt 120
taaaatgtta gtctacatag atgggtgatt gtaactttat tgccattaaa agatttcaaa 180
ttgcattcat gcttctgtgt acacataatg aaaaatgggc aaataatgaa gatctctcct 240
tcagtctgct ctgtttaatt ctgctgtctg ctcttctcta atgctgcgtc cctaattgta 300
cacagtttag tgatatctag gagtataaag ttgtcgccca tcaataaaaa tcacaaagtt 360
ggtttaaaaa                                           370

```

<210> 185

<211> 107

<212> DNA

<213> Homo sapiens

<400> 185

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ctcatattat tttccttttg agaaattgga aactctttct gttgctatta tattaataaa 60
gttggtgttt attttctggt agtcaccttc cccatttaaa aaaaaaa 107

```

<210> 186

<211> 309

<212> DNA

<213> Homo sapiens

<400> 186

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agagggccac aggggtggcc gggagtgtgc agctgatgcc tgctgagagg caggaattgt 120
gccagtgagt gacagtcatt agggagtgtc tcttcttggg gaggaagaa ggtagagcct 180
ttctgtctga atgaaaggcc aaggctacag tacagggccc cgccccagcc aggggtgttaa 240
tgcccacgta gtggaggcct ctggcagatc ctgcattcca aggtcactgg actgtacgtt 300
tttatgggtt                                           309

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<210> 187

<211> 477

<212> DNA

<213> Homo sapiens

<400> 187

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ttcagtccta gcaagaagcg agaattctga gatcctccag aaagtcgagc agcaccacc 60
tccaacctcg ggccagtgtc ttcaggcttt actggggacc tgcgagctgg cctaattgtg 120

```

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99

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tggcctgcaa gccaggccat ccctgggccc cacagacgag ctccgagcca ggtcaggctt 180
cggaggccac aagctcagcc tcaggcccag gcactgattg tggcagaggg gccactaccc 240
aaggtctagc taggcccagg acctagttac ccagacagtg agaagcccct ggaaggcaga 300
aaagttggga gcatggcaga cagggaaggg aaacattttc agggaaaaga catgtatcac 360
atgtcttcag aagcaagtca ggtttcatgt aaccgagtggt cctcttgctg gtccaaaagt 420
agcccagggc tgtagcacag gcttcacagt gattttgtgt tcagccgtga gtcacac 477

```

<210> 188

<211> 220

<212> DNA

<213> Homo sapiens

<400> 188

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ttaaataagt accctgtgag tatgagataa attagtgaca atcagaacaa gtttcagtat 120
cagatgttca agagggaagt gctattgcat tgattttaat atttgtacat aaacactgat 180
ttttttgagc attattttgt atttgttgta ctttaatacc 220

```

<210> 189

<211> 417

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (76)

<223> n=A,T,C or G

<221> unsure

<222> (77)

<223> n=A,T,C or G

<400> 189

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tatcattatt ctagtccttt gaatttgtaa ggggaaaaaa aacaaaaaca aaaacttacg 180
atgcactttt ctccagcaca tcagatttca aattgaaaat taaagacatg ctatggtaat 240
gcacttgcta gtactacaca ctttgtacaa caaaaaacag aggcaagaaa caacggaaag 300
agaaaagcct tcctttgttg gcccttaaac tgagtcaaga tctgaaatgt agagatgatc 360
tctgacgata cctgtatggt cttattgtgt aaataaaatt gctgggtatga aatgaca 417

```

<210> 190

<211> 497

<212> DNA

<213> Homo sapiens

<400> 190

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aacgcaggag ctgtcattga ctggcccaca gaggagggca aggaagtatg ggattatgtg 120
acggctccga aggatgccta catgttctgg tggctctatt atgccaccaa ctctgcaag 180
aacttctcag aactgcccct ggtcatgtgg cttcaggggc gtccaggcgg ttctagcact 240
ggatttgga aacttgagga aattgggccc cttgacagtg atctcaaacc acggaaaacc 300
acctggctcc aggctgccag tctcctatct gtggataatc ccgtgggcac tgggttcagt 360
tatgtgaatg gtagtggtgc ctatgccaa gacctggcta tgggtggctc agacatgatg 420
gttctcctga agaccttctt cagttgccac aaagaattcc agacagttcc attctacatt 480
ttctcagagt cctatgg 497

```

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100

<210> 191
 <211> 175
 <212> DNA
 <213> Homo sapiens

<400> 191
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 ctacttgagt acaaggattt gagcctgtta cattcactgc tgaatttttag gctcctggaa 120
 gataccacgc attcaataga gaccacacaa taaatatatg tcaaataaaa aaaaa 175

<210> 192
 <211> 526
 <212> DNA
 <213> Homo sapiens

<400> 192
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 aagaacagta ttgctgtaat tcctTTTctt ttcttctca tttcctctgc cccttaaaag 120
 attgaagaaa gagaaacttg tcaactcata tccacgttat ctagcaaagt acataagaat 180
 ctatcactaa gtaatgtatc cttcagaatg tggttggttta ccagtgcacac cccatattca 240
 tcacaaaatt aaagcaagaa gtccatagta atttatTTTgc taatagtgga tttttaatgc 300
 tcagagtttc tgaggtcaaa ttttatcttt tcacttacaa gctctatgat cttaaataat 360
 ttacttaatg tattttggtg tattttcttc aaattaatat tgggtgttcaa gactatatct 420
 aattcctctg atcactttga gaaacaaact tttattaat gtaaggcact tttctatgaa 480
 ttttaaatat aaaaataaat attgttctga ttattactga aaaaaa 526

<210> 193
 <211> 553
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (290)
 <223> n=A,T,C or G
 <221> unsure
 <222> (300)
 <223> n=A,T,C or G
 <221> unsure
 <222> (411)
 <223> n=A,T,C or G
 <221> unsure
 <222> (441)
 <223> n=A,T,C or G

<400> 193
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 gctgggatga gccgtgctcc cgggtggaagc aaggagccc agccggagcc atggccagta 120
 cagtggtagc agttggactg accattgctg ctgcaggatt tgcaggccgt tacgttttgc 180
 aagccatgaa gcatatggag cctcaagtaa aacaagtttt tcaaagccta ccaaaatctg 240
 ccttcagtgg tggctattat agaggtgggt ttgaacccaa aatgacaaan cgggaagcan 300
 cattaatact aggtgtaagc cctactgcca ataaaggga aataagagat gctcatcgac 360
 gaattatgct tttaaactcat cctgacaaag gaggatctcc ttatatagca nccaaaatca 420
 atgaagctaa agatttacta naagggtcaag ctaaaaaatg aagtaaatgt atgatgaatt 480

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101

ttaagttcgt attagtttat gtatatgagt actaagtttt tataataaaa tgcctcagag 540
ctacaatttt aaa 553

<210> 194
<211> 320
<212> DNA
<213> Homo sapiens

<400> 194
cccttcccaa tccatcagta aagaccccat ctgccttgtc catgccgttt cccaacaggg 60
atgtcacttg atatgagaat ctcaaattct aatgccttat aagcattcct tcctgtgtcc 120
attaagactc tgataattgt ctccccctcca taggaatttc tcccaggaaa gaaatatatc 180
cccatctccg tttcatatca gaactaccgt ccccgatatt cccttcagag agattaaaga 240
ccagaaaaaa gtgagcctct tcatctgcac ctgtaatagt ttcagttcct attttcttcc 300
attgacccat atttatacct 320

<210> 195
<211> 320
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (203)
<223> n=A,T,C or G
<221> unsure
<222> (218)
<223> n=A,T,C or G

<400> 195
aagcatgacc tggggaaatg gtcagacctt gtattgtgtt tttggccttg aaagtagcaa 60
gtgaccagaa tctgccatgg caacaggctt taaaaaagac ccttaaaaag acactgtctc 120
aactgtggtg ttagcaccag ccagctctct gtacatttgc tagcttgtag ttttctaaga 180
ctgagtaaac ttcttatttt tanaaagggg aggctggntt gtaactttcc ttgtacttaa 240
ttgggtaaaa gtctttttcca caaaccacca tctattttgt gaactttggt agtcattctt 300
tatttggtaa attatgaact 320

<210> 196
<211> 357
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (36)
<223> n=A,T,C or G

<400> 196
atataaaata atacgaaact ttaaaaagca ttggantgtc agtatgttga atcagtagtt 60
tcactttaac tgtaaacaat ttcttaggac accatttggg ctagtttctg tgtaagtgtg 120
aatactacaa aaacttatct atactgttct tatgtcattt gttatattca tagatttata 180
tgatgatatg acatctggct aaaaagaaat tattgcaaaa ctaaccacta tgtacttttt 240
tataaatact gtatggacaa aaaatggcat tttttatatt aaattgttta gctctggcaa 300
aaaaaaaaaa ttttaagagc tgggtactaat aaaggattat tatgactgtt aaaaaaa 357

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102

<210> 197
 <211> 565
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (27)
 <223> n=A,T,C or G

<400> 197
 tcagctgagt accatcagga tatttanccc ttttaagtgc gttttgggag tagaaaacta 60
 aagcaacaat acttcctctt gacagctttg attggaatgg ggttattaga tcattcacct 120
 tggtcctaca ctttttagga tgcttggtga acataacacc acttataatg aacatccctg 180
 gttcctatat tttgggctat gtgggtagga attgttactt gttactgcag cagcagccct 240
 agaaagtaag cccagggcct cagatctaag ttagtccaaa agctaaatga tttaaagtca 300
 agttgtaatg ctaggcataa gcactctata atacattaaa ttataggccg agcaattagg 360
 gaatgtttct gaaacattaa acttgtatct atgtcactaa aattctaaca caaacttaaa 420
 aatgtgtct catacatatg ctgtactagg cttcatcatg catttctaaa tttgtgtatg 480
 atttgaatat atgaaagaat ttatacaaga gtgttattta aaattattaa aaataaatgt 540
 atataatttg tacctattgt aaaaaa 565

<210> 198
 <211> 484
 <212> DNA
 <213> Homo sapiens

<400> 198
 tatgtaagta ttggtgtctg ctttaaaaaa ggagacccag acttcacctg tccttttttaa 60
 acatttgaga acagtgttac tctgagcagt tgggccacct tcaccttatc cgacagctga 120
 ctgttgatg tgtccattgt cgccagtttg gctgttgccc ggacaggaca ggacctccat 180
 tgggcgcagc agcaggtggc aggggtgtgg cttgaggtgg gtggcagcgt ctggtcctcc 240
 tctctggtgc tttctgagag ggtctctaaa gcagagtgtg gttggcctgg gggaaggcag 300
 agcacgtatt tctcccctct agtacctctg catttgtgag tgttccctct ggctttctga 360
 agggcagcag actcttgagt atactgcaga ggacatgctt tatcagtagg tcctgagggc 420
 tccaggggct caactgacca agtaacacag aagttggggg atgtggccta tttgggtcgg 480
 aaac 484

<210> 199
 <211> 429
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (77)
 <223> n=A,T,C or G
 <221> unsure
 <222> (88)
 <223> n=A,T,C or G
 <221> unsure
 <222> (134)
 <223> n=A,T,C or G
 <221> unsure
 <222> (151)

<223> n=A,T,C or G
 <221> unsure
 <222> (189)
 <223> n=A,T,C or G
 <221> unsure
 <222> (227)
 <223> n=A,T,C or G
 <221> unsure
 <222> (274)
 <223> n=A,T,C or G
 <221> unsure
 <222> (319)
 <223> n=A,T,C or G

<400> 199

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gcttatgttt tttgttttaa cttttgtttt ttaacattta gaatattaca ttttgtatta 60
tacagtacct ttctcanaca ttttgtanaa ttcatttcgg cagctcacta ggatttttgct 120
gaacattaaa aagngtgata gcgatattag ngccaatcaa atggaaaaaa ggtagtctta 180
ataaacaana cacaacgttt ttatacaaca tactttaaaa tattaanaaa actccttaat 240
attgtttcct attaatgatt attccttggg caanattttc tgatgctttt gatttttctct 300
caatttagca tttgctttng gtttttttct ctatttagca ttctgttaag gcacaaaaac 360
tatgtactgt atgggaaatg ttgtaaatat taccttttcc acatttttaa cagacaactt 420
tgaatccaa                                         429
  
```

<210> 200

<211> 279

<212> DNA

<213> Homo sapiens

<400> 200

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gcttttttga ggaattacag ggaagctcct ggaattgtac atggatatct ttatccctag 60
ggggaaatca aggagctggg caccctaat tctttatgga agtgttttaa actatttttaa 120
ttttattaca agtattacta gagtagtggt tctactctaa gatttcaaaa gtgcatttaa 180
aatcatacat gttcccgcct gcaaataatat tgttattttg gtggagaaaa aaatagtata 240
ttctacataa aaaattaaag atattaacta agaaaaaaaa 279
  
```

<210> 201

<211> 569

<212> DNA

<213> Homo sapiens

<400> 201

```

taggtcagta ttttttagaaa ctcttaatag ctcatactct tgataccaaa agcagccctg 60
attgttaaag cacacacctg cacaagaagc agtgatgggt gcattttacat ttcctgggtg 120
cacaaaaaaa aattctcaaa aagcaaggac ttacgctttt tgcaaagcct ttgagaagtt 180
actggatcat aggaagctta taacaagaat ggaagattct taaataactc actttctttg 240
gtatccagta acagtagatg ttcaaaatat gtagctgatt aataccagca ttgtgaacgc 300
tgtacaacct tgtgggttatt actaagcaag ttactactag cttctgaaaa gtagcttcat 360
aattaatggt atttatacac tgccttccat gacttttact ttgccctaag ctaatctcca 420
aaatctgaaa tgctactcca atatcagaaa aaaaggggga ggtggaatta tatttcctgt 480
gattttaaga gtacagagaa tcatgcacat ctctgattag ttcatatatg tctagtgtgt 540
aataaaagtc aaagatgaac tctcaaaaa                                         569
  
```

<210> 202

<211> 501

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<212> DNA

<213> Homo sapiens

<400> 202

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attaataggc ttaataattg ttggcaagga tccttttgct ttctttggca tgcaagctcc 60
tagcatctgg cagtggggcc aagaaaataa ggtttatgca tgtatgatgg ttttcttctt 120
gagcaacatg attgagaacc agtgtatgtc aacagggtgca tttgagataa ctttaaataa 180
tgtacctgtg tggcttaagc tggaatctgg tcaccttcca tccatgcaac aacttggtca 240
aattcttgac aatgaaatga agctcaatgt gcatatggat tcaatccac accatcgatc 300
atagcaccac ctatcagcac tgaaaactct tttgcattaa gggatcattg caagagcagc 360
gtgactgaca ttatgaaggc ctgtactgaa gacagcaagc tgtagtagca gaccagatgc 420
tttcttggca ggctcgttgt acctcttggg aaacctcaat gcaagatagt gtttcagtgc 480
tgccatattt tggaattctg c 501

```

<210> 203

<211> 261

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (36)

<223> n=A,T,C or G

<221> unsure

<222> (96)

<223> n=A,T,C or G

<400> 203

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gacaagctcc tggctctgag atgtcttctc gttaangaga tgggcctttt ggaggtaaag 60
gataaaatga atgagttctg tcatgattca ctattntata acttgcatga cctttactgt 120
gttagctctt tgaatgttct tgaaatttta gactttcttt gtaaacaaat gatatgtcct 180
tatcattgta taaaagctgt tatgtgcaac agtgtggaga ttccttgtct gatttaataa 240
aataacttaa cactgaaaaa a 261

```

<210> 204

<211> 421

<212> DNA

<213> Homo sapiens

<400> 204

```

agcatctttt ctacaacggt aaaattgcag aagtagctta tcattaataa acaacaacaa 60
caacaataac aataaatcct aagtgtaaat cagttattct acccctacc aaggatatca 120
gcctgttttt tccctttttt ctctgggaa taattgtggg cttcttccca aatttctaca 180
gcctctttcc tcttctcatg cttgagcttc cctgtttgca cgcattcgtg tgcaggactg 240
gcttgtgtgc ttggactcgg ctccagggtg aagcatgctt tcccttggtt ctgttggaga 300
aactcaaacc ttcaagccct aggtgtagcc attttgtcaa gtcattcaact gtatttttgt 360
actggcatta acaaaaaaag aagataaaat attgtaccat taaactttaa taaaacttta 420
a 421

```

<210> 205

<211> 460

<212> DNA

<213> Homo sapiens

<400> 205

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105

```

tactctcaca atgaaggacc tggaatgaaa aatctgtgtc taaacaagtc ctcttttagat 60
tttagtgcaa atccagagacc agcgtcgggt gcctcgagta attctttcat gggtagccttt 120
ggaaaagctc tcaggagacc tcacctagat gcctattcaa gctttggaca gccatcagat 180
tgtcagccaa gagcctttta tttgaaagct cattcttccc cagacttgga ctctgggtca 240
gaggaagatg ggaaagaaag gacagatttt caggaagaaa atcacatttg tacctttaaa 300
cagacttttag aaaactacag gactccaaat tttcagtctt atgacttgga cacatagact 360
gaatgagacc aaaggaaaag cttaacatac tacctcaagg tgaactttta tttaaaagag 420
agagaatctt atgtttttta aatggagtta tgaattttaa 460

```

<210> 206

<211> 481

<212> DNA

<213> Homo sapiens

<400> 206

```

tgtggtggaa ttcgggacgc ccccagaccc tgactttttc ctgcgtgggc cgtctcctcc 60
tgcggaagca gtgacctctg acccctggtg accttcgctt tgagtgcctt ttgaacgctg 120
gtcccgcggg acttggtttt ctcaagctct gtctgtccaa agacgctccg gtcgaggtcc 180
cgctgcctt ggggtggatac ttgaacccca gacgcccctc tgtgctgctg tgtccggagg 240
cggccttccc atctgcctgc ccaccggag ctctttccgc cggcgcaggg tcccaagccc 300
acctcccgcc ctcagtcctg cgggtgtgct ctgggcacgt cctgcacaca caatgcaagt 360
cctggcctcc gcgcccgcgc gccacgcga gccgtaccgc ccgccaactc tgttatttat 420
ggtgtgaccc cctggagggtg ccctcggcgc accggggcta tttattgttt aatttatttg 480
t 481

```

<210> 207

<211> 605

<212> DNA

<213> Homo sapiens

<400> 207

```

accctttttg gattcagggc tcctcacaat taaaatgagt gtaatgaaac aaggtgaaaa 60
tatagaagca tccctttgta tactgttttg ctacttacag tgtacttggc attgctttat 120
ctcactggat tctcacggta ggatttctga gatcttaatc taagctccaa agttgtctac 180
ttttttgatc ctagggtgct cctttttgtt tacagagcag ggtcacttga tttgctagct 240
ggtggcagaa ttggcaccat taccaggtc tgactgacca ccagtcagag gcactttatt 300
tgtatcatga aatgatttga aatcattgta aagcagcgaa gtctgataat gaatgccagc 360
tttccttgct ctttgataac aaagactcca aatattctgg agaacctgga taaaagtttg 420
aagggctaga ttgggatttg aagacaaaat ttaggaaat cttacatttt tgcaataaca 480
aacattaatg aaagcaaaac attataaaag taattttaat tcaccacata cttatcaatt 540
tcttgatgct tccaaatgac atctaccaga tatggttttg tggacatctt tttctgttta 600
cataa 605

```

<210> 208

<211> 655

<212> DNA

<213> Homo sapiens

<400> 208

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ggcgttggtc tggattcccc tcgtaactta aagggaaact ttcacaatgt ccggagccct 60
tgatgtcctg caaatgaagg aggaggatgt ctttaagtcc cttgcagcag gaaccacttt 120
aggtggcacc aatcttgact tccagatgga acagtacatc tataaaagga aaagtgatgg 180
catctatatc ataaatctca agaggacctg ggagaagctt ctgctggcag ctctgtgcaat 240
tgttgccatt gaaaaccctg ctgatgtcag tgttatatcc tccaggaata ctggccagag 300
ggctgtgctg aagtttgctg ctgccactgg agccactcca attgctggcc gcttcaactcc 360

```

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106

```

tggaaccttc actaaccaga tccaggcagc cttccgggag ccacggcttc ttgtggttac 420
tgaccccagg gctgaccacc agcctctcac ggaggcatct tatgttaacc tacctaccat 480
tgcgctgtgt aacacagatt ctctctgcg ctatgtggac attgccatcc catgcaacaa 540
caagggagct cactcagtgg gtttgatgtg gtggatgctg gctcgggaag ttctgcgcat 600
gcgtggcacc atttcccgtg aacacccatg ggaggtcatg cctgatctgt acttc      655

```

<210> 209

<211> 621

<212> DNA

<213> Homo sapiens

<400> 209

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catttagaac atggttatca tccaagacta ctctaccctg caacattgaa ctcccaagag 60
caaatccaca ttctcttga gttctgcagc ttctgtgtaa atagggcagc tgcgtctat 120
gccgtagaat cacatgatct gaggaccatt catggaagct gctaaatagc ctagtctggg 180
gagtcttcca taaagttttg catggagcaa acaaacagga ttaaactagg tttggttcct 240
tcagccctct aaaagcatag ggcttagcct gcaggcttcc ttgggctttc tctgtgtgtg 300
tagttttgta aacactatag catctgttaa gatccagtgt ccatggaaac cttcccacat 360
gccgtgactc tggactatat cagtttttgg aaagcagggt tcctctgcct gctaacaagc 420
ccacgtggac cagtctgaat gtctttcctt tacacctatg tttttaataa gtcaaacttc 480
aagaaacaat ctaaacaagt ttctgttgca tatgtgtttg tgaacttgta tttgtattta 540
gtaggcttct atattgcatt taacttgttt ttgtaactcc tgattcttcc ttttcggata 600
ctattgatga ataaagaaat t                                621

```

<210> 210

<211> 533

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (20)

<223> n=A,T,C or G

<221> unsure

<222> (21)

<223> n=A,T,C or G

<221> unsure

<222> (61)

<223> n=A,T,C or G

<400> 210

```

cgccttgggg agccggcggn ngagtccggg acgtggagac ccgggggtccc ggcagccggg 60
nggcccgcgg gccaggggtg gggatgcacc gccgcggggt gggagctggc gccatcgcca 120
agaagaaact tgcagaggcc aagtataagg agcgagggac ggtcttggct gaggaccagc 180
tagcccagat gtcaaagcag ttggacatgt tcaagaccaa cctggaggaa tttgccagca 240
aacacaagca ggagatccgg aagaatcctg agttccgtgt gcagttccag gacatgtgtg 300
caaccattgg cgtggatccg ctggcctctg gaaaaggatt ttgggtctgag atgctgggcg 360
tggggggactt ctattacgaa ctagggtgtcc aaattatcga agtgtgcctg gcgctgaagc 420
atcggaatgg aggtctgata actttggagg aactacatca acaggtgttg aagggaaggg 480
gcaagttcgc ccaggatgtc agtcaagatg acctgatcag agccatcaag aaa      533

```

<210> 211

<211> 451

<212> DNA

<213> Homo sapiens

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<400> 211

```

ttagcttgag ccgagaacga ggcgagaaag ctggagaccg aggagaccgc ctagagcgga 60
gtgaacgggg aggggaccgt ggggaccggc ttgatcgtgc gcggacacct gctaccaagc 120
ggagcttcag caaggaagtg gaggagcgga gtagagaacg gccctcccag cctgaggggc 180
tgcgcaaggc agctagcctc acggaggatc gggaccgtgg gcgggatgcc gtgaagcgag 240
aagctgccct acccccagtg agccccctga aggcggctct ctctgaggag gagttagaga 300
agaaatccaa ggctatcatt gaggaatatc tccatctcaa tgacatgaaa gaggcagtcc 360
agtgcgtgca ggagctggcc tcaccctcct tgctcttcat ctttgtacgg catggtgtcg 420
agtctacgct ggagcgcagt gccattgctc g                                     451

```

<210> 212

<211> 471

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (54)

<223> n=A,T,C or G

<400> 212

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gtgattattc ttgatcaggg agaagatcat ttagatttgt tttgcattcc ttanaatgga 60
gggcaacatt ccacagctgc cctggctgtg atgagtgtcc ttgcaggggc cggagtagga 120
gcactggggg gggggcggaa ttgggggttac tcgatgtaag ggattccttg ttgttgtgtt 180
gagatccagt gcagttgtga tttctgtgga tcccagcttg gttccaggaa ttttgtgtga 240
ttggcttaaa tccagttttc aatcttcgac agctgggctg gaacgtgaac tcagtagctg 300
aacctgtctg acccggtcac gttcttggat cctcagaact ctttgctctt gtcgggggtgg 360
gggtgggaac tcacgtgggg agcgggtggc gagaaaatgt aaggattctg gaatacatat 420
tccatgggac tttccttccc tctcctgctt cctcttttcc tgctccctaa c                                     471

```

<210> 213

<211> 511

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (27)

<223> n=A,T,C or G

<221> unsure

<222> (63)

<223> n=A,T,C or G

<221> unsure

<222> (337)

<223> n=A,T,C or G

<221> unsure

<222> (442)

<223> n=A,T,C or G

<400> 213

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ctaattagaa acttgctgta ctttttnttt tcttttaggg gtcaaggacc ctctttatag 60
ctnccatttg cctacaataa attattgcag cagtttgcaa tactaaaata ttttttatag 120
actttatatt tttccttttg ataaagggat gctgcatagt agagttgggt taattaaact 180
atctcagccg tttccctgct ttcccttctg ctccatatgc ctcatgtcc ttccaggag 240

```

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```

ctctttttaat cttaaagttc tacatttcat gctcttagtc aaattctggt accttttttaa 300
taactcttcc cactgcatat ttccatcttg aattggnggt tctaaattct gaaactgtag 360
ttgagataca gctattttaat atttctggga gatgtgcac cctcttcttt gtggttgccc 420
aaggttgttt tgcgtaactg anactccttg atatgcttca gagaatttag gcaaactg 480
gccatggccg tgggagtact gggagtaaaa t 511

```

<210> 214

<211> 521

<212> DNA

<213> Homo sapiens

<400> 214

```

agcattgccca aataatccct aattttccac taaaaatata atgaaatgat gttaagcttt 60
ttgaaaagtt taggttaaac ctactgttgt tagattaatg tatttgttgc ttccctttat 120
ctggaatgtg gcattagctt ttttatttta accctcttta attcttattc aattccatga 180
cttaagggtg gagagctaaa cactgggatt tttggataac agactgacag ttttgcataa 240
ttataatcgg cattgtacat agaaaggata tggctacctt ttgttaaate tgcactttct 300
aaatatcaaa aaagggaaat gaagtataaa tcaatttttg tataatctgt ttgaaacatg 360
agttttatatt gcttaatat agggtcttgc cccttttctg taagtctctt gggatcctgt 420
gtagaagctg ttctcattaa acaccaaaca gttaagtcca ttctctggta ctagctacaa 480
attcgggttct atattctact taacaattta aataaactga a 521

```

<210> 215

<211> 381

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (17)

<223> n=A,T,C or G

<221> unsure

<222> (20)

<223> n=A,T,C or G

<221> unsure

<222> (60)

<223> n=A,T,C or G

<221> unsure

<222> (61)

<223> n=A,T,C or G

<221> unsure

<222> (365)

<223> n=A,T,C or G

<400> 215

```

gagcggagag cggaccngtn agagccctga gcagccccac cgccgcccgc ggcctagttn 60
ncatcacacc ccgggaggag ccgcagctgc cgcagccggc ccagtcacc atcacgcaa 120
ccatgagcag cgaggccgag acccagcagc cgcccgcgc ccccccgcc gcccccgc 180
tcagcgccgc cgacaccaag cccggcacta cgggcagcgg cgcagggagc ggtggcccgg 240
gcggcctcac atcggcgggc cctgccggcg gggacaagaa ggtcatcgca acgaaggttt 300
tggaacagt aaaatgggtc aatgtaagga acggatatgg tttcatcaac aggaatgaca 360
ccaangaaga tgtatttcta c 381

```

<210> 216

<211> 425

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109

<212> DNA

<213> Homo sapiens

<400> 216

```

ttactaacta ggtcattcaa ggaagtcaag ttaacttaaa catgtcacct aaatgcactt 60
gatggtgttg aaatgtccac cttcttaaat ttttaagatg aacttagttc taaagaagat 120
aacaggccaa tcctgaaggt actccctggt tgctgcagaa tgtcagatat tttggatggt 180
gcataagagt cctatattgcc ccagttaatt caacttttgt ctgcctgttt tgtggactgg 240
ctggctctgt tagaactctg tccaaaaagt gcatggaata taacttgtaa agcttcccac 300
aattgacaat atatatgcat gtgttttaaac caaatccaga aagcttaaac aatagagctg 360
cataatagta tttattaaag aatcacaact gtaaacaatga gaataactta aggattctag 420
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<210> 217

<211> 181

<212> DNA

<213> Homo sapiens

<400> 217

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<210> 218

<211> 405

<212> DNA

<213> Homo sapiens

<400> 218

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gcgctgggct gtttttagtgc caggctgcgg tgggcagcca tgagaacaaa acctcttctg 180
tatttttttt ttccattagt aaaacacaag acttcagatt cagccgaatt gtggtgtcct 240
acaaggcagg cttttcctac aggggggtgga gagaccagcc tttcttcctt tggtaggaat 300
ggcctgagtt ggcgttggtg gcaggctact ggtttgtatg atgtattagt agagcaaccc 360
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<210> 219

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (207)

<223> n=A,T,C or G

<221> unsure

<222> (210)

<223> n=A,T,C or G

<400> 219

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tcaattgtaa acttcttggt aagactgtta cgtttctatt gcttttgtat gggatattgc 180

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110

aaaaataaaa aggaaagaac cctcttnaan aaaaaa

216

<210> 220

<211> 380

<212> DNA

<213> Homo sapiens

<400> 220

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atttcacatt tgagggaac tgattagatg gggtgtgttt gtgttctgat ggagaaaaca 180
gcacccaag gactcagaag atgattttta cagttcagaa cagatgtgtg caatattggt 240
gcatgtaata atgttgagtg gcagtcaaaa gtcattgatt ttatcttagt tcttcattac 300
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gtaagtcttt gacaaaaaaa                                     380

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<210> 221

<211> 398

<212> DNA

<213> Homo sapiens

<400> 221

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gtgagtctgc aagtgaattt cactgatgtt gatattcatt gtgtgtagtt ttatttcggt 180
cccagccccg tttcctttta ttttgaggct aatgccagct gcgtgtctag ttttgagtgc 240
agtaaaatag aatcagcaaa tcaactcttat ttttcattct tttccggtat tttttgggtt 300
gtttctgtgg gagcagtgtt caccaactct tcctgtatat tgcctttttg ctggaaaatg 360
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<210> 222

<211> 301

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (49)

<223> n=A,T,C or G

<221> unsure

<222> (64)

<223> n=A,T,C or G

<400> 222

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gatgacttta ggatttgcat ttttcctttt attgcctcat ttcttgtagc gccttggttg 240
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a                                                                 301

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<210> 223

<211> 200

<212> DNA

<213> Homo sapiens

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111

<400> 223

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 attccttcac actgtaattt aatgtgtttt atattctttt gtagtaaaac aacataactc 120
 agatttctac aggagacagt ggttttattt ggattgtctt ctgtaatagg tttcaataaa 180
 gctggatgaa cttaaaaaaa 200

<210> 224

<211> 385

<212> DNA

<213> Homo sapiens

<400> 224

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 tctccaacac cagcaagccc taaccagggc cctcctccac aagttccagt atctcctgga 180
 ccaccaaaagg acagttctgc ccttggtgga cccccagaaa ggactgttac tccagcccta 240
 tcatcaaagt tgttaccaag acatcttgga tcccctgcta cttcagtgcc tggaatgggt 300
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<210> 225

<211> 560

<212> PRT

<213> Homo sapien

<400> 225

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

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112

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

<210> 226

<211> 9

<212> PRT

<213> Homo sapien

<400> 226

Ile Leu Ile Pro Ala Thr Trp Lys Ala

1

5

<210> 227

<211> 9

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113

<212> PRT

<213> Homo sapien

<400> 227

Phe Leu Leu Asn Asp Asn Leu Thr Ala
1 5

<210> 228

<211> 9

<212> PRT

<213> Homo sapien

<400> 228

Leu Leu Gly Asn Cys Leu Pro Thr Val
1 5

<210> 229

<211> 10

<212> PRT

<213> Homo sapien

<400> 229

Lys Leu Leu Gly Asn Cys Leu Pro Thr Val
1 5 10

<210> 230

<211> 10

<212> PRT

<213> Homo sapien

<400> 230

Arg Leu Thr Gly Gly Leu Lys Phe Phe Val
1 5 10

<210> 231

<211> 9

<212> PRT

<213> Homo sapien

<400> 231

Ser Leu Gln Ala Leu Lys Val Thr Val
1 5

<210> 232

<211> 20

<212> PRT

<213> Homo sapiens

<400> 232

Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr Ser Arg Tyr Phe
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Phe Ser Phe Ala

20

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114

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<213> Homo sapiens

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Asn His Ser Pro Ser
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<210> 234
<211> 20
<212> PRT
<213> Homo sapiens

<400> 234
Phe Leu Val Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe
5 10 15

Asp Pro Asp Gly
20

<210> 235
<211> 20
<212> PRT
<213> Homo sapiens

<400> 235
Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu Phe Ile Pro
5 10 15

Pro Asn Ser Asp
20

<210> 236
<211> 20
<212> PRT
<213> Homo sapiens

<400> 236
Ile Gln Asp Asp Phe Asn Asn Ala Ile Leu Val Asn Thr Ser Lys Arg
5 10 15

Asn Pro Gln Gln
20

<210> 237

WO 00/61612

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115

<211> 21
<212> PRT
<213> Homo sapiens

<400> 237
Arg Asn Ser Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu
5 10 15

Phe Ile Pro Pro Asn
20

<210> 238
<211> 20
<212> PRT
<213> Homo sapiens

<400> 238
Thr His Glu Ser His Arg Ile Tyr Val Ala Ile Arg Ala Met Asp Arg
5 10 15

Asn Ser Leu Gln
20

<210> 239
<211> 20
<212> PRT
<213> Homo sapiens

<400> 239
Arg Asn Pro Gln Gln Ala Gly Ile Arg Glu Ile Phe Thr Phe Ser Pro
5 10 15

Gln Ile Ser Thr
20

<210> 240
<211> 21
<212> PRT
<213> Homo sapiens

<400> 240
Gly Gln Ala Thr Ser Tyr Glu Ile Arg Met Ser Lys Ser Leu Gln Asn
5 10 15

Ile Gln Asp Asp Phe
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<210> 241
<211> 20
<212> PRT
<213> Homo sapiens

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116

<400> 241

Glu Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser
5 10 15

Val Leu Gly Val
20

<210> 242

<211> 20

<212> PRT

<213> Homo sapiens

<400> 242

Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn Ile
5 10 15

Gln Met Asn Ala
20

<210> 243

<211> 20

<212> PRT

<213> Homo sapiens

<400> 243

Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile Pro Gly
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Ser His Ala Met
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<210> 244

<211> 20

<212> PRT

<213> Homo sapiens

<400> 244

Ala Val Pro Pro Ala Thr Val Glu Ala Phe Val Glu Arg Asp Ser Leu
5 10 15

His Phe Pro His
20

<210> 245

<211> 20

<212> PRT

<213> Homo sapiens

<400> 245

Lys Pro Gly His Trp Thr Tyr Thr Leu Asn Asn Thr His His Ser Leu

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117

5

10

15

Gln Ala Leu Lys
20

<210> 246
<211> 20
<212> PRT
<213> Homo sapiens

<400> 246
Asn Leu Thr Phe Arg Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys
5 10 15

Pro Gly His Trp
20

<210> 247
<211> 20
<212> PRT
<213> Homo sapiens

<400> 247
Leu His Phe Pro His Pro Val Met Ile Tyr Ala Asn Val Lys Gln Gly
5 10 15

Phe Tyr Pro Ile
20

<210> 248
<211> 20
<212> PRT
<213> Homo sapiens

<400> 248
Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu Leu Asp Asp Gly Ala
5 10 15

Gly Ala Asp Val
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<210> 249
<211> 20
<212> PRT
<213> Homo sapiens

<400> 249
Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val Thr Ala Thr Val Glu Pro
5 10 15

Glu Thr Gly Asp

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118

20

<210> 250
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 250
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Leu Thr Phe Arg
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<210> 251
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 <212> PRT
 <213> Homo sapiens

<400> 251
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 5 10 15

Val Pro Pro Ala
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<210> 252
 <211> 153
 <212> PRT
 <213> Homo sapien

<400> 252
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 20 25 30
 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly
 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr
 85 90 95
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala
 100 105 110
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu
 115 120 125
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser
 130 135 140
 Glu Asn Gln Gly Ala Phe Lys Gly Met
 145 150

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119

<210> 253
 <211> 462
 <212> DNA
 <213> Homo sapien

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 cagtttatct cagagaacca gggagccttc aagggcattg ag 462

<210> 254
 <211> 8031
 <212> DNA
 <213> Homo sapien

<400> 254
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<210> 255

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

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<222> (1)...(401)

<223> n = A,T,C or G

<400> 255

gtggccagng	actagaaggc	gaggcgccgc	gggacccatgg	cggcgggcggc	ggacgagcgg	60
agtccanagg	acggagaaga	cgaggaagag	gaggagcagt	tggttctggt	ggaattatca	120
ggaattattg	attcagactt	cctctcaaaa	tgtgaaaata	aatgcaaggt	tttgggcatt	180
gacactgaga	ggcccattct	gcaagtggac	agctgtgtct	ttgctgggga	gtatgaagac	240
actctangga	cctgtgttat	atttgaagaa	aatgntnaac	atgctgatac	agaaggcaat	300
aataaaacag	tgctaaaata	taaatgccat	acaatgaaga	agctcagcat	gacaagaact	360
ctcctgacag	agaagaagga	aggagaagaa	aacatangtg	g		401

<210> 256

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 256

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gggcccgggt	cgcggccgng	gacggggccg	gggccnangc	cgngganctc	gcggangcaa	120
ggccgaggat	aaggagtgga	tgcccgtcac	caacttgggc	cgcttgncca	aggacatgaa	180
nancaagccc	ctgnaggaga	tctatntctt	cttccctgcc	ccattaagga	atcaagagat	240
catttgatth	cttccctggg	gcctctctca	aggatnaggt	ttttgaagat	tatgccagtg	300
canaaannan	accccgttgc	ccngtccatc	tncacccaac	ncttccaagg	gcnatthttg	360
tttaggcctc	attncngggg	ggaaccttaa	cccaatthtg	g		401

<210> 257

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 257

atgtatgtaa	aacacttcat	aaaatgtaaa	gggctataac	aaatatgtta	taaagtgatt	60
ctctcagccc	tgaggtatac	agaatcattt	gcctcagact	gctgttggtt	tttaaaattt	120
ttaaaatatc	tgctaagtaa	tttgctatgt	cttctcccac	actatcaata	tgcttgcttc	180
taacaggctc	cccactttct	tttaatgtgc	tgttatgagc	tttggacatg	agataaccgt	240
gcctgttcag	agtgtctaca	gtaagagctg	gacaaactct	ggagggacac	agtctttgag	300
acagctcttt	tggttgcttt	ccacttttct	gaaaggttca	cagtaacctt	ctagataata	360
gaaactccca	gttaaagcct	angctancaa	tttttttttag	t		401

<210> 258

<211> 401

<212> DNA

<213> Homo sapien

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<400> 258

ggagcgctag	gtcgggtgtac	gaccgagatt	aggggtgcgtg	ccagctccgg	gaggccgcgg	60
tgagggggccg	ggcccaagct	gccgacccga	gccgatcgtc	agggtcgcca	gcgcctcagc	120
tctgtggagg	agcagcagta	gtcggagggt	gcaggatatt	agaaatggct	actccccagt	180
caattttcat	ctttgcaatc	tgcattttaa	tgataacaga	attaattctg	gcctcaaaaa	240
gctactatga	tatcttaggt	gtgccaaaat	cggcatcaga	gcgccaaatc	aagaaggcct	300
ttcacaagtt	ggccatgaag	taccaccctg	acaaaaataa	gacccagatg	ctgaagcaaa	360
attcagagag	attgcagaag	catatgaaac	actctcagat	g		401

<210> 259

<211> 401

<212> DNA

<213> Homo sapien

<400> 259

attggggttg	gagggaggat	gatgacagag	gaatgccctt	tggccatcac	ggttttgatt	60
ctccagaata	ttgtgggttt	gatcatcaat	gcagtcattg	taggctgcat	tttcatgaaa	120
acagctcagg	ctcacagaag	ggcagaaact	ttgattttca	gccgccatgc	tgtgattgcc	180
gtccgaaatg	gcaagctgtg	cttcatgttc	cgagtgggtg	acctgaggaa	aagcatgatc	240
attagtgcct	ctgtgcgcat	ccagggtggc	aagaaaacaa	ctacacctga	aggggagggtg	300
gttcctattc	accaactgga	cattcctgtt	gataacccaa	tcgagagcaa	taacattttt	360
ctggtggccc	ctttgatcat	ctgccacgtg	attgacaagc	g		401

<210> 260

<211> 363

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(363)

<223> n = A,T,C or G

<400> 260

aggaganang	gagggggana	tgaataggga	tggagaggga	natagtggat	gagcagggca	60
canggagagg	aancagaaag	gagaggcaag	acagggagac	acacancaca	nangangana	120
caggtggggg	ctgggggtggg	gcatggagag	cctttnangt	cncccaggcc	acctgctct	180
cgctggntctg	ttgaaaccca	ctccatggct	tcttgccact	gcagttgggc	ccagggctgg	240
cttattnctg	gaatgcaagt	ggctgtggct	tggagcctcc	cctctggnnn	anggaaannn	300
attgctccct	tatctgcttg	gaatatctga	gtttttccan	cccggaaata	aaacacacac	360
aca						363

<210> 261

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 261

cggtctccg	ccgtctccc	ggggtttcgg	ggcacttggg	tcccacagtc	tggtcctgct	60
tcaccttccc	ctgacctgag	tagtcgccat	ggcacagggt	ctcagaggca	ctgngactga	120

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cttccctgga	tttgatgagc	gggctgatgc	anaaactctt	cggaaggcta	tgaaaggctt	180
gggcacagat	gaggagagca	tcctgactct	gttgacatcc	cgaagtaatg	ctcagcgcca	240
ggaaatctct	gcagctttta	agactctggt	tggcagggat	cttctggatg	acctgaaatc	300
agaactaact	ggaaaatttg	aaaaattaat	tgtggctctg	atgaaaccct	ctcggcttta	360
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<210> 262

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (401)

<223> n = A,T,C or G

<400> 262

agtctanaac	atttctaata	ttttgngctt	tcatatatca	aaggagatta	tgtgaaacta	60
tttttaaata	ctgtaaagtg	acatatagtt	ataagatata	tttctgtaca	gtagagaaag	120
agtttataac	atgaagaata	ttgtaccatt	atacatcttc	attctcgatc	tcataagaaa	180
ttcaaaagaa	taatgataga	ggtgaaaata	tgtttacttt	ctctaaatca	agcctagtgtg	240
tcaactcaaa	aattatgntg	catagtttta	ttttgaattt	aggttttggg	actacttttt	300
tccancttca	atgagaaaat	aaaatctaca	actcaggagt	tactacagaa	gttctaanta	360
tttttttgct	aannagcnaa	aatataaac	atatgaaaat	g		401

<210> 263

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (401)

<223> n = A,T,C or G

<400> 263

ctgtccgacc	aagagaggcc	ggccgagccc	gaggcttggg	cttttgcttt	ctggcggagg	60
gatctgcggc	ggtttaggag	gcggcgctga	tcctgggagg	aagaggcagc	tacggcggcg	120
gcggcgggtg	cggctagggc	ggcggcgaat	aaaggggccc	cgcgcgggtg	atgcggtgac	180
cactgcggca	ggcccaggag	ctgagtgggc	cccggccctc	agcccgtccc	gncggaccgc	240
ctttcctcaa	ctctccatct	tctcctgccg	accgagatcg	ccgaggcggn	ctcaggctcc	300
ctanccctt	ccccgtccct	tcccncccc	cgcccccgcc	ccgggggccc	ccgccaccgc	360
cctcccacca	tggtcttgaa	ganaatccac	aaggaattga	a		401

<210> 264

<211> 401

<212> DNA

<213> Homo sapien

<400> 264

aacaccagcc	actccaggac	ccctgaaggc	ctctaccagg	tcaccagtgt	tctgcgccta	60
aagccacccc	ctggcagaaa	cttcagctgt	gtgttctgga	atactcacgt	gagggaaactt	120
actttggcca	gcattgacct	tcaaagtcag	atggaacca	ggacccatcc	aacttggtgtg	180
cttcacattt	tcacccctc	ctgcatcatt	gctttcattt	tcatagccac	agtgatagcc	240
ctaagaaaac	aactctgtca	aaagctgtat	tcttcaaaag	acacaacaaa	aagacctgtc	300

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accacaacaa agaggggaagt gaacagtgct gtgaatctga acctgtggtc ttgggagcca 360
 ggggtgacctg atatgacatc taaagaagct tctggactct g 401

<210> 265
 <211> 271
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(271)
 <223> n = A,T,C or G

<400> 265
 gccacttcct gtggacatgg gcagagcgct gctgccagtt cctggtagcc ttgaccacna 60
 cgctggggggg tctttgtgat ggtcatgggt ctcatttgca cttgggggtg tgggattcaa 120
 gttagaagtt tctagatctg gccgggcgca gtggctcaca cctgtaatcc cagcacttta 180
 ggaggctgag gcaggcggat catgaggtca ggagatcgag accgtcctgg ctaacacagt 240
 gaaaccccgct ctctactaaa aatacaaaaa a 271

<210> 266
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 266
 attcataaat ttagctgaaa gatactgatt caatttgtat acagnngaata taaatgagac 60
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 tctatttttaa atgactttct ggatttttaa aaatttcttt aaatacaatc atttttgtaa 180
 tattttatttt atgcttatga tctagataat tgcagaatat cattttatct gactctgtct 240
 tcataagaga gctgtggccg aattttgaac atctgttata gggagtgatc aaattagaag 300
 gcaatgtgga aaaacaattc tgggaaagat ttctttatat gaagtccttg ccactagcca 360
 gccatcctaa ttgatgaaag ttatctgttc acaggcctgc a 401

<210> 267
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 267
 gaagaggcat cacctgatcc cggagacctt tggagttaag aggcggcgga agcgagggcc 60
 tgtggagtcg gatcctcttc ggggtgagcc agggtcggcg cgcgcggtg tctcanaact 120
 catgcagctg ttcccgcgag gcctgtttga ggacgcgctg ccgcccacg tgctgaggag 180
 ccaggtgtac agccttgtgc ctgacaggac cgtggccgac cggcagctga aggagcttca 240
 agagcanggg gagacaaaat cgtccagctg ggcttcnact tggatgcca tggaanttta 300

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tctttcnctt ganggactta cnngggaccc aagaancct tncaaggggc ccttngtgga 360
 tgggncccgga aaccccnnta tttgcccttg ggggggncca a 401

<210> 268
 <211> 223
 <212> DNA
 <213> Homo sapien

<400> 268
 tcgccatgtt ggccaggctg gtcttgaact cctgacttta agtgatccac ccgcctcaac 60
 ctcccaaagt gctgggatta caggtgtgag ccaccgcgcc tggcctgata catactttta 120
 gaatcaagta gtcacgcact ttttctgttc atttttctaa aaagtaaata tacaaatgtt 180
 ttgttttttg ttttttttgt ttgtttgttt ctgttttttt ttt 223

<210> 269
 <211> 401
 <212> DNA
 <213> Homo sapien

<400> 269
 actatgtaaa ccacattgta cttttttttta ctttggcaac aaatatattat acatacaaga 60
 tgctagttca tttgaatatt tctcccaact tatccaagga tctccagctc taacaaaatg 120
 gtttatTTTT atttaaatgt caatagttgt tttttaaaat ccaaatcaga ggtgcaggcc 180
 accagttaaa tgccgtctat caggttttgt gccttaagag actacagagt caaagctcat 240
 ttttaaagga gtaggacaaa gttgtcacag gtttttgttg ttgtttttat tgcccccaaa 300
 attacatgtt aatttccatt tatatcaggg attctattta cttgaagact gtgaagttgc 360
 cattttgtct cattgttttc tttgacataa ctaggatcca t 401

<210> 270
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 270
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 ccttgtcaac tgaaaaatgc acctgacttc gagcaagact ctttccttag gttctggatc 120
 tgtttgagcc ccatggcact gagctggaat ctgaggggtct tgttccaagg atgtgatgat 180
 gtgggagaat gttctttgaa agagcagaaa tccagtctgc atggaaacag cctgtagagn 240
 agaagtttcc agtgataagt gttcactgtt ctaaggaggt acaccacagc tacctgaatt 300
 ttcccaaaat gagtgcttct gtgcgttaca actggccttt gtacttgact gtgatgactt 360
 tgttttttct tttcaattct anatgaacat gggaaaaaat g 401

<210> 271
 <211> 329
 <212> DNA
 <213> Homo sapien

<400> 271
 ccacagcctc caagtcaggt ggggtggagt cccagagctg cacagggttt ggcccaagtt 60
 tctaagggag gcacttcctc cctcgcacca tcagtgccag cccctgctgg ctggtgcctg 120

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agccccctcag	acagccccct	gccccgcagg	cctgccttct	cagggacttc	tgcggggcct	180
gaggcaagcc	atggagtgag	acccaggagc	cggacacttc	tcaggaaatg	gctttttcca	240
acccccagcc	cccacccggt	ggttcttcct	gttctgtgac	tgtgtatagt	gccaccacag	300
cttatggcat	ctcattgagg	acaaaaaaaa				329

<210> 272
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 272						
nggctgntaa	cntcggaggt	nacttcctgg	actatcctgg	agacccccctc	cgcttccacg	60
nncatnatat	cnctcatngc	tggggccentn	angacacnat	cccactccaa	cacctgngng	120
atgctggnen	cctnggaacc	ancntcagaa	ngaccctgnt	cntntgtnt	ccgcaanctg	180
aagnnaangc	gggntacacc	tncntgcant	ggnccacnct	gcnggggaact	ntacacacac	240
acgggatgtg	gctgcgccan	gagccaagag	cntttctgga	tgattcccca	gcctcttggn	300
agggantcta	caacattgct	nnntaccttt	ntccnnncngc	nnntnntgga	ntacaggngn	360
tnntaacact	acatcttttt	tactgcncen	tncttggtgg	g		401

<210> 273
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 273						
cagcaccatg	aagatcaaga	tcatcgcacc	cccagagcgc	aagtactcgg	tgtggatcgg	60
tggctccatc	ctggcctcac	tgtccacctt	ccagcagatg	tggattagca	agcaggagta	120
cgacgagtcg	ggccccctca	tcgtccaccg	caaattgctt	taaaccggact	cagcagatgc	180
gtagcatttg	ctgcatgggt	taattgagaa	tagaaatttg	cccctggcaa	atgcacacac	240
ctcatgctag	cctcacgaaa	ctggaataag	ccttcgaaaa	gaaattgtcc	ttgaagcttg	300
tatctgatat	cagcactgga	ttgtagaact	tgttgctgat	tttgaccttg	tattgaagtt	360
aactgttccc	cttgggtatta	acgtgtcagg	gctgagtgn	c		401

<210> 274
 <211> 401
 <212> DNA
 <213> Homo sapien

<400> 274						
ccaccacac	ccaccgcgcc	ctcgttcgcc	tcttctccgg	gagccagtcc	gcgccaccgc	60
cgccgccag	gccatcgcca	ccctccgcag	ccatgtccac	caggtccgtg	tcctcgtcct	120
cctaccgcag	gatgttcggc	ggccccggga	ccgcgagccg	gccgagctcc	agccggagct	180
acgtgactac	gtccaccgcg	acctacagcc	tgggcagcgc	gctgcgcccc	agcaccagcc	240
gcagcctcta	cgctcgtcc	ccgggcggcg	tgtatgccac	gcgctcctct	gccgtgcgcc	300
tgcggagcag	cgtgccccgg	gtgcggctcc	tgcaggactc	ggtggacttc	tcgctggccg	360

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acgccatcaa caccgagttc aagaacaccc gcaccaacga g 401

<210> 275
 <211> 401
 <212> DNA
 <213> Homo sapien

<400> 275
 ccactttccac cacttttgtgg agcagtgctt tcagcgcaac ccggatgccca ggtatccctg 60
 ctggcctggg cctgggcttc gggagagcag aggggtgctca ggagggtaag gccaggggtg 120
 gaagggactt acctcccaaa ggttctgcag gggaatctgg agctacacac aggagggatc 180
 agctcctggg tgtgtcagag gccagcctgg ggagctctgg ccactgcttc ccatgagctg 240
 agggagaggg agaggggacc cgaggctgag gcataagtgg caggatttcg ggaagctggg 300
 gacacggcag tgatgctgcg gtctctcttc ccttttccct ccaggcccag tgccagcacc 360
 ctctgaacc actctttctt caagcagatc aagcgacgtg c 401

<210> 276
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 276
 tctgatattg ntacccttga gccacctaag ttagaagaaa ttggaaatca agaagttgtc 60
 attgttgaag aagcacagag ttcagaagac tttaacatgg gctcttcctc tagcagccag 120
 tatactttct gtcagccaga aactgtattt tcatctcagc ctagtgatga tgaatcaagt 180
 agtgatgaaa ccagtaatca gccagtcct gcctttagac gacgccgtgc taggaagaag 240
 accgtttctg cttcagaatc tgaagaccgg ctagttgggtg aacaagaaac tgaaccttct 300
 aaggagttga gtaaacgtca gttcagtagt ggtctcaata agtggttat acttgctttg 360
 gtgattgcaa tcagcatggg atttggccat ttctatggca c 401

<210> 277
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 277
 aactttggca acatatctca gcaaaaacta cagctatggt attcatgccca aaataaaagc 60
 tgtgcagagg agtggctgca atgaggtcac aacgggtggg gatgtaaaag agatcttcaa 120
 gtcctcatca cccatccctc gaactcaagt cccgctcatt acaaattctt cttgccagtg 180
 tccacacatc ctgccccatc aagatgttct catcatgtgt tacgagnggc gctcaaggat 240
 gatgcttctt gaaaattgct tagttgaaaa atggagagat cagcttagta aaagatccat 300
 acagtgggaa gagaggctgc aggaacagcg ganaacagtt caggacaaga agaaaacagc 360
 cgggcgcacc agtcgtagta atccccccaa accaaaggga a 401

<210> 278

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<211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 278

aatgagtgtg	agaccacaaa	tgaatgccgg	gaggatgaaa	tgtgttggaa	ttatcatggc	60
ggcttccgtt	gttatccacg	aaatccttgt	caagatccct	acattctaac	accagagAAC	120
cgatgtgttt	gcccagtctc	aaatgccatg	tgccgagAAC	tgccccagtc	aatagtctac	180
aaatacatga	gcatccgata	tgataggtct	gtgccatcag	acatcttcca	gatacaggcc	240
acaactattt	atgccAACac	catcaatact	tttcggatta	aatctggaaa	tgaaaatgga	300
gagtctacct	acgacaacaa	anccctgtaa	gtgcaatgct	tgtgctcgtg	aagncattat	360
caggaccaag	agaacatatc	gtggacctgg	agatgctgac	a		401

<210> 279
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 279

aaattattgc	ctctgataca	tacctaagtn	aacanaacat	taatacctaa	gtaaACataa	60
cattacttgg	agggttgcag	nttctaantg	aaactgtatt	tgaaactttt	aagtataactt	120
taggaaacaa	gcatgaacgg	cagtctagaa	taccagAAC	atctacttgg	gtagcttggN	180
gccattatcc	tgtggaatct	gatatgtctg	gnagcatgtc	attgatggga	catgaagaca	240
tctttggaaa	tgatgagatt	atttcctgtg	ttaaaaaaaa	aaaaaatctt	aaattcctac	300
aatgtgAAC	tgaaactaat	aattttgatc	ctgatgtatg	ggacagcgta	tctgtaccag	360
gctctaaata	acaaaagnta	ggngacaag	nacatgttcc	t		401

<210> 280
 <211> 326
 <212> DNA
 <213> Homo sapien

<400> 280

gaagtggAat	tgtataattc	aattcgataa	ttgatctcat	gggctttccc	tggaggAaag	60
gttttttttg	ttgttttttt	tttaagaact	tgaaacttgt	aaactgagat	gtctgtagct	120
tttttgccca	tctgtagtgt	atgtgaagat	ttcaAACct	gagagcactt	tttctttgtt	180
tagaattatg	agaaaggcac	tagatgactt	taggatttgc	atttttccct	ttattgcctc	240
atttcttgtg	acgccttgtt	ggggagggaa	atctgtttat	tttttcctac	aaataaaaag	300
ctaagattct	atatcgcaaa	aaaaaa				326

<210> 281
 <211> 374
 <212> DNA
 <213> Homo sapien

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<400> 281

caacgcgttt	gcaaatatte	ccctggtagc	ctacttcctt	acccccgaat	attggtaaga	60
tcgagcaatg	gcttcaggac	atgggttctc	ttctcctgtg	atcattcaag	tgctcactgc	120
atgaagactg	gcttgtctca	gtgtttcaac	ctcaccaggg	ctgtctcttg	gtccacacct	180
cgctccctgt	tagtgccgta	tgacagcccc	catcaaata	ccttggccaa	gtcacgggtt	240
ctctgtggtc	aagggttggt	ggctgattgg	tggaaagtag	ggtggaccaa	aggaggccac	300
gtgagcagtc	agcaccagtt	ctgcaccagc	agcgctccg	tcctagtggg	tgttcctggt	360
tctcctggcc	ctgg					374

<210> 282

<211> 404

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(404)

<223> n = A,T,C or G

<400> 282

agtgtggtgg	aattcccgc	tcctanncg	cgactcacac	aaggcagagt	ngccatggag	60
aaaattccag	tgtcagcatt	cttgctcctt	gtggccctct	cctacactct	ggccagagat	120
accacagtca	aacctgnagc	caaaaaggac	acaaaggact	ctcgacccaa	actgccccan	180
accctctcca	gaggttgggg	tgaccaactc	atctggactc	anacatatga	agaagctcta	240
tataaatcca	agacaagcaa	caaacccttg	atgattattc	atcacttgga	tgagtgccca	300
cacagtcaag	ctttaaagaa	agtgtttgct	gaaaataaag	aatccagaa	attggcagag	360
cagtttgtcc	tcctcaatct	ggtttatgaa	acaactgaca	aaca		404

<210> 283

<211> 184

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(184)

<223> n = A,T,C or G

<400> 283

agtgtggtgg	aattcacttg	cttaanttgt	gggcaaaaga	gaaaaagaag	gattgatcag	60
agcattgtgc	aatacagttt	cattaactcc	ttccctcgct	cccccaaaaa	tttgaatttt	120
tttttcaaca	ctcttacacc	tgttatggaa	aatgtcaacc	tttgtaagaa	aaccaaata	180
aaaa						184

<210> 284

<211> 421

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(421)

<223> n = A,T,C or G

<400> 284

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```

ctattaatcc tgccacaata tttttaatta cgtacaaaga tctgacatgt caccagggga      60
cccatthtcac ccactgctct gtttgggccgc cagtcttttg tctctctctt cagcaatggg      120
gaggcggata ccctttcctc ggggaanana aatccatggg ttgttgccct tgccaataac      180
aaaaatgttg gaaagtcgag tggcaaagct gttgccattg gcatctttca cgtgaaccac      240
gtcaaaagat ccagggtgcc tctctctgtt ggtgatcaca ccaattcttc ctaggttagc      300
acctccagtc accatacaca ggttaccagt gtcgaacttg atgaaatcag taatcttgcc      360
agtctctaaa tcaatctgaa tggatatcatt caccttgatg aggggatcgg ggtagcggat      420
g                                                                    421

```

<210> 285
 <211> 361
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(361)
 <223> n = A,T,C or G

```

<400> 285
ctgggtggta actctttatt tcattgtccg gaanaaagat gggagtggga acaggggtgga      60
cactgtgcag gcttcagctt ccactccggg caggattcag gctatctggg accgcagggga      120
ctgccaggtg cacagccctg gctcccaggg caggcaggca aggtgacggg actggaagcc      180
cttttcanag ccttgaggga gctggtccgt ccacaagcaa tgagtggcac tctgcagttt      240
gcaggggatg gataaacagg gaaacactgt gcattcctca cagccaacag tgtaggtctt      300
ggtgaagccc cggcgctgag ctaagctcag gctgttccag ggagccacga aactgcaggt      360
a                                                                    361

```

<210> 286
 <211> 336
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(336)
 <223> n = A,T,C or G

```

<400> 286
tttgagtggc agcgccttta tttgtggggg ccttcaaggg agggtcgtgg ggggcagcgg      60
ggaggaanag ccganaaact gtgtgaccgg ggcctcaggt ggtgggcatt gggggctcct      120
cttgcanatg ccatttgcca tcaccggtgc agccattggg ggcagcgggt accggtcctt      180
tcttgttcaa catagggtag gtggcagcca cgggtccaac tcgcttgagg ctgggccctg      240
ggcgctccat tttgtgttcc angagcatgt ggttctgtgg cgggagcccc acgcaggccc      300
tgaggatggt ctcgatgcag ctgcgctggc ggaaaaa                        336

```

<210> 287
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

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<400> 287

tgggtaccaa	atttntttat	ttgaaggaat	ggnacaaatc	aaanaactta	agnggatggt	60
ttggtacaac	ttatanaaaa	ggnaaaggaa	accccaacat	gcatgcnctg	ccttgngac	120
cagggaagtc	acccacggc	tatggggaaa	ttancccgag	gcttancttt	cattatcact	180
gtctcccagg	gngngcttgt	caaaaanata	ttcncccaag	ccaaattcgg	gcgctcccat	240
nttgcncaa	gtggtcacgt	ggtcacccaa	ttctttgatg	gctttcacct	gctcattcag	300
g						301

<210> 288

<211> 358

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (358)

<223> n = A,T,C or G

<400> 288

aagtttttaa	acttttttatt	tgcatattaa	aaaaattgng	cattccaata	attaaaatca	60
tttgaacaaa	aaaaaaaaatg	gcactctgat	taaactgcat	tacagcctgc	aggacacctt	120
gggccagctt	ggttttactc	tanatttcac	tgctgtccca	ccccacttct	tccacccccc	180
ttcttccttc	accaacatgc	aagttctttc	cttccctgcc	agccanata	atagacagat	240
gggaaaggca	ggcgcggcct	tcgttgtcag	tagttctttg	atgtgaaagg	ggcagcacag	300
tcattttaac	ttgatccaac	ctctttgcat	cttacaaagt	taaacagcta	aaagaagt	358

<210> 289

<211> 462

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (462)

<223> n = A,T,C or G

<400> 289

ggcatcagaa	atgctgttta	tttctctgct	gctcccaagc	tggctggcct	ttgcagagga	60
gcagacaaca	gatgcatagt	tgggganaaa	gggaggacag	gttccaggat	agagggtgca	120
ggctgaggga	ggaagggtaa	naggaaggaa	ggccatcctg	gatccccaca	tttcagtctc	180
anatgaggac	aaagggactc	ccaagcccc	aaatcatcan	aaaacaccaa	ggagcaggag	240
gagcttgagc	aggccccagg	gagcctcana	gccataccag	ccactgtcta	cttcccatcc	300
tcctctccca	ttccctgtct	gcttcanacc	acctcccagc	taagccccag	ctccattccc	360
ccaatcctgg	cccttgccag	cttgacagtc	acagtgcctg	gaattccacc	actgaggctt	420
ctcccagttg	gattaggacg	tcgccctggt	agcatgctgc	cc		462

<210> 290

<211> 481

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (481)

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<223> n = A,T,C or G

<400> 290

tactttccta	aactttatta	aagaaaaaag	caataagcaa	tggnggtaaa	tctctanaac	60
atacccaatt	ttctgggctt	cctcccccca	gaatgtgaca	ttttgatttc	caaacatgcc	120
anaagtgtat	ggttcccaac	tgtactaaag	taggtganaa	gctgaagtcc	tcaagtgttc	180
atcttccaac	ttttcccagt	ctgtggtctg	tctttggatc	agcaataatt	gcctgaacag	240
ctactatggc	ttcgttgatt	tttgtctgta	gctctctgag	ctcctctatg	tgcagcaatc	300
gcanaatttg	agcagcttca	ttaanaactg	catctcctgt	gtcaaaacca	anaatatgtt	360
tgtctaaagc	aacaggtaag	ccctcttttg	tttgatttgc	cttancaact	gcctcctgtg	420
tcaggcgctc	ctgaacaaaa	atccgaattg	ccttaagcat	taccaggtaa	tcctcatgac	480
g						481

<210> 291

<211> 381

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(381)

<223> n = A,T,C or G

<400> 291

tcataagtaat	gtaaaaccat	ttgtttaatt	ctaaatcaaa	tcactttcac	aacagtgaag	60
attagtgtact	gggttaaggng	tgccactgta	catatcatca	ttttctgact	ggggtcagga	120
cctgggtccta	gtccacaagg	gtggcaggag	gaggggtggag	gctaanaaca	cagaaaacac	180
acaaaanaaa	ggaaagctgc	cttggcanaa	ggatgaggng	gtgagcttgc	cgaaggatgg	240
tgggaagggg	gctccctgtt	ggggccgagc	caggagtccc	aagtcagctc	tcctgcctta	300
cttagctcct	ggcanagggt	gagtggggac	ctacgagggt	caaaatcaaa	tggcatttgg	360
ccagcctggc	tttactaaca	g				381

<210> 292

<211> 371

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(371)

<223> n = A,T,C or G

<400> 292

gaaaaaataa	tccgtttaat	tgaaaaacct	gnaggatact	attccactcc	cccanatgag	60
gaggctgagg	anaccaaacc	cctacatcac	ctcgtagcca	cttctgatac	tcttcacgag	120
gcagcaggca	aagacaattc	ccaaaacctc	nacaaaagca	attccaaggg	ctgctgcagc	180
taccaccanc	acatttttcc	tcagccagcc	cccaatcttc	tccacacagc	cctccttatg	240
gatcgcttcc	tcgttgaaat	taatcccaca	gccacagta	acattaatgc	ancaggagtc	300
ggggactcgg	ttcttcgaca	tggaagggat	tttctcccaa	tctgtgtagt	tagcagcccc	360
acagcactta	a					371

<210> 293

<211> 361

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(361)
 <223> n = A,T,C or G

<400> 293
 gattttaaag aaaacacttt attgttcagc aattaaaagt tagccaaata tgtatttttc 60
 tccataattt attgngatgt tatcaacatc aagtaaaatg ctcattttca tcatttgctt 120
 ctgttcatgt tttcttgaac acgtcttcaa ttttccttcc aaaatgctgc atgccacact 180
 tgaggtaacg aagcanaagt attttttaaac atgacagcta anaacattca tctacagcaa 240
 cctatatgct caatacatgc cgcgtgatcc tagtagtttt ttcacaacct tctacaagtt 300
 tttggaaaac atctgttatg atgactttca tacaccttca cctcaaaggc tttcttgcac 360
 c 361

<210> 294
 <211> 391
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(391)
 <223> n = A,T,C or G

<400> 294
 tatttttaaag tttaattatg attcanaaaa aatcgagcga ataactttct ctgaaaaaat 60
 atattgactc tgtatanacc acagttattg gggganaagg gctggtaggt taaattatcc 120
 tatttttttat tctgaaaatg atattaatan aaagtcccgt ttcagtcctg attataaaga 180
 tacatatgcc caaaatggct ganaataaat acaacaggaa atgcaaaagc tgtaaagcta 240
 agggcatgca ananaaaatc tcanaatacc caaagnggca acaaggaacg tttggctgga 300
 atttgaagtt atttcagtc tctttgtctt tggctccatg tttcaggatg cgtgtgaact 360
 cgatgtaatt gaaattcccc tttttatcaa t 391

<210> 295
 <211> 343
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(343)
 <223> n = A,T,C or G

<400> 295
 ttcttttgtt ttattgataa cagaaactgt gcataattac agatttgatg aggaatctgc 60
 aaataataaa gaatgtgtct actgccagca aaatacaatt attccatgcc ctctcaacat 120
 acaaatatag agttcttcac accanatggc tctgggtgtaa caaagccatt ttanatgttt 180
 aattgtgctt ctacaaaacc ttcanagcat gaggtagttt cttttaccta cnatattttc 240
 cacatttcca ttattacact tttagtgagc taaaatcctt ttaacatagc ctgcggatga 300
 tctttcacaa aagccaagcc tcatttacia agggttttatt tct 343

<210> 296
 <211> 241
 <212> DNA

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<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(241)

<223> n = A,T,C or G

<400> 296

ttcttgata	ttggttgtt	ttgtgaaaa	gtttttgtt	ttcttctcag	tcaactgaat	60
tatttctcta	ctttgccctc	ctgatgcca	catgananaa	cttaanataa	tttctaacag	120
cttccacttt	ggaaaaaaaa	aaaacctgtt	ttcctcatgg	aaccccagga	gttgaaagtg	180
gatanatcgc	tctcaaaatc	taaggctctg	ttcagcttta	cattatgtta	cctgacgttt	240
t						241

<210> 297

<211> 391

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(391)

<223> n = A,T,C or G

<400> 297

gttgtggctg	anaatgctgg	agatgctcag	ttctctccct	cacaaggtag	gccacaaatt	60
cttggtgggtg	ccctcacatc	tggggtcttc	aggcaccagc	catgcctgcc	gaggagtgtt	120
gtcaggacan	accatgtccg	tgctaggccc	aggcacagcc	caaccactcc	tcatccaagt	180
ctctcccagg	tttctgggtc	cgatgggcaa	ggatgacccc	tccagtgggt	ggtacccac	240
catcccacta	cccctcacat	gctctcactc	tccatcaggt	ccccaatcct	ggcttccctc	300
ttcacgaact	ctcaaagaaa	aggaaggata	aaacctaata	aaaccagaca	gaagcagctc	360
tggaaaagta	caaaaagaca	gccagaggtg	t			391

<210> 298

<211> 321

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(321)

<223> n = A,T,C or G

<400> 298

caagccaaac	tgtntccagc	tttattaaan	atactttcca	taaacaatca	tggtattttca	60
ggcaggacat	gggcanacaa	tcgttaacag	tatacaacaa	ctttcaaact	cccttnttca	120
atggactacc	aaaaatcaaa	aagccactat	aaaacccaat	gaagtcttca	tctgatgtctc	180
tgaacaggga	aagttaaag	ngaggggtga	catttcacat	ttagcatgtt	gtttaacaac	240
ttttcacaag	ccgaccctga	ctttcaggaa	gtgaaatgaa	aatggcanaa	tttatctgaa	300
natccacaat	ctaaaaatgg	a				321

<210> 299

<211> 401

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 299
 tatcataaag agtggtgaag tttatattatt atagcaccat tgagacattt tgaaattgga 60
 attggtaaaa aaataaaaaca aaaagcattt gaattgtatt tggnggaaca gcaaaaaaag 120
 agaagtatca tttttctttg tcaaattata ctgtttccaa acattttgga aataaataac 180
 tggaattttg tcggtcactt gcaactggtg acaagattag aacaagagga acacatatgg 240
 agttaaatTT tttttgttgg gatttcanat agagtttggg ttataaaaag caaacagggc 300
 caacgtccac accaaattct tgatcaggac caccaatgtc atagggngca atatctacaa 360
 taggtagtct cacagccttg cgtgttcgat attcaaagac t 401

<210> 300
 <211> 188
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(188)
 <223> n = A,T,C or G

<400> 300
 tgaatgcttt gtcataattaa gaaagttaaa gtgcaataat gtttgaanac aataagtggg 60
 ggtgtatctt gtttctaata agataaactt ttttgtcttt gctttatctt attagggagt 120
 tgtatgtcag tgtataaaaac atactgtgtg gtataacagg cttaataaat tctttaaaag 180
 gaaaaaaa 188

<210> 301
 <211> 291
 <212> DNA
 <213> Homo sapien

<400> 301
 aagattttgt tttatatttat tatggctaga aagacactgt tatagccaaa atcggcaatg 60
 aactaaaga aatcctctgt gcttttcaat atgcaaatat atttcttcca agagttgccc 120
 tgggtgtgact tcaagagttc atgttaactt cttttctgga aacttccttt tcttagttgt 180
 tgtattcttg aagagcctgg gccatgaaga gcttgccata gttttgggca gtgaactcct 240
 tgatgttctg gcagtaagtg tttatctggc ctgcaatgag cagcgagtcc a 291

<210> 302
 <211> 341
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(341)
 <223> n = A,T,C or G

<400> 302
 tgatttttca taattttatt aaatnatcac tgggaaaact aatgggtcgc gtatcacaca 60

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attacactac	aatctgatag	gagtggtaaa	accagccaat	ggaatccagg	taaagtacaa	120
aaacgccacc	ttttattgtc	ctgtcttatt	tctcgggaag	gagggttcta	ctttacacat	180
ttcatgagcc	agcagtggac	ttgagttaca	atgtgtaggt	tccttgtggt	tatagctgca	240
gaagaagcca	tcaaattctt	gaggacttga	catctctcgg	aaagaagcaa	actagtggat	300
cccccgggct	gcaggaattc	gatatcaagc	ttatcgatac	c		341

<210> 303

<211> 361

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(361)

<223> n = A,T,C or G

<400> 303

tgcagacagt	aatnaattt	tatttgngtt	cacagaacat	actaggcgat	ctcgacagtc	60
gctccgtgac	agcccaccaa	cccccaacc	tntacctcgc	agccacccta	aaggcgactt	120
caanaanatg	gaaggatctc	acggatctca	ttcctaattg	tccgccgaag	tctcacacag	180
tanacagacg	gagttganat	gctggaggat	gcagtcacct	cctaaactta	cgaccaccca	240
ccanacttca	tcccagccgg	gacgtcctcc	cccacccgag	tcctcccat	ttcttctcct	300
actttgccgc	agttccaggn	gtcctgcttc	caccagtccc	acaaagctca	ataaatacca	360
a						361

<210> 304

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 304

ctctttacaa	cagcctttat	ttncggccct	tgatcctgct	cggatgctgg	tggaggccct	60
tagctccgcc	cgccaggctc	tgtgccgcct	ccccgcaggc	gcanattcat	gaacacggtg	120
ctcaggggct	tgaggccgta	ctccccagc	gggagctggt	cctccagggg	cttccccctc	180
aaggtcagcc	anaacaggtc	gtcctgcaca	ccctccagcc	cgctcacttg	ctgcttcagg	240
tggggccacg	tctgcgtcag	ccgcacctcg	taggtgctgc	tgcggccctt	gttattcctc	300
a						301

<210> 305

<211> 331

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(331)

<223> n = A,T,C or G

<400> 305

ganaggctag	taacatcagt	tttattgggt	tggggnggca	accatagcct	ggctgggggn	60
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ggggctggcc	ctcacagggt	gttgagttcc	agcaggggtct	ggccaaggt	ctggtgaatc	120
tcgacgttct	cctccttggc	actggccaag	gtctcttcta	ggcatcgat	ggttttctcc	180
aactttgcca	canacctctc	ggcaaactct	gctcggggtct	cancctcctt	cagcttctcc	240
tccaacagtt	tgatctcctc	ttcatattta	tcttctttgg	gggaatactc	ctcctctgag	300
gccatcaggg	acttgagggc	ctggtccatg	g			331

<210> 306

<211> 457

<212> DNA

<213> Homo sapien

<400> 306

aatatgtaaa	ggtaataact	tttattatat	taaagacaat	gcaaacgaaa	aacagaattg	60
agcagtgcaa	aattttaaagg	actgttttgt	tctcaaagtt	gcaagtttca	aagccaaaag	120
aattatatgt	atcaaataata	taagtaaaaa	aaagttagac	tttcaagcct	gtaatcccag	180
cactttggga	ggctgaggca	ggtggatcac	taacattaaa	aagacaacat	tagattttgt	240
cgatttatag	caattttata	aatatataac	tttgtcactt	ggatcctgaa	gcaaaataat	300
aaagtgaatt	tgggattttt	gtacttggtg	aaaagtttaa	caccctaaat	tcacaactag	360
tggatcccc	gggctgcagg	aattcgatat	caagcttata	gataccgtcg	acctcgaggg	420
ggggcccgg	acccaattcg	ccctatagtg	agtcgta			457

<210> 307

<211> 491

<212> DNA

<213> Homo sapien

<400> 307

gtgcttggac	ggaacccggc	gctcgttccc	caccccggcc	ggccgcccac	agccagccct	60
ccgtcacctc	ttcacgcac	cctcggactg	ccccaggcc	cccgcgcgcg	ctccagcgcc	120
gcgcagccac	cgccgcccgc	gccgcctctc	cttagtcgcc	gccatgaaga	ccgcgtccac	180
ctcgcagggt	cgccagaact	accaccagga	ctcagaggcc	gccatcaacc	gccagatcaa	240
cctggagctc	tacgcctcct	acgtttacct	gtccatgtct	tactactttg	accgcgatga	300
tgtggctttg	aagaactttg	ccaaataactt	tcttcaccaa	tctcatgagg	agagggaaca	360
tgctgagaaa	ctgatgaagc	tgacagaacca	acgaggtggc	cgaatcttcc	ttcaggatat	420
caagaaacca	gactgtgatg	actgggagag	cgggctgaat	gcaatggagt	gtgcattaca	480
tttggaaaaa	a					491

<210> 308

<211> 421

<212> DNA

<213> Homo sapien

<400> 308

ctcagcgctt	cttctttctt	ggtttgatcc	tgactgctgt	catggcgtgc	cctctggaga	60
aggccctgga	tgtgatgggt	tccaccttcc	acaagtactc	gggcaaagag	ggtgacaagt	120
tcaagctcaa	caagtcagaa	ctaaaggagc	tgctgacctg	ggagctgccc	agcttcttgg	180
ggaaaaggac	agatgaagct	gctttccaga	agctgatgag	caacttggac	agcaacaggg	240
acaacgaggt	ggacttccaa	gagtactgtg	tcttcctgtc	ctgcatcgcc	atgatgtgta	300
acgaattctt	tgaaggcttc	ccagataagc	agcccaggaa	gaaatgaaaa	ctcctctgat	360
gtgggtgggg	ggtctgccag	ctggggccct	ccctgtcgcc	agtgggcact	tttttttttc	420
c						421

<210> 309

<211> 321

<212> DNA

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<213> Homo sapien

<400> 309

accaaattggc	ggatgacgcc	ggtgcagcgg	gggggcccgg	gggccctggg	ggccctggga	60
tggggaaccg	cggtggcttc	cgcggagggt	tcggcagtgg	catccggggc	cggggtcgcg	120
gccgtggacg	gggccggggc	cgaggccgcg	gagctcgcg	aggcaaggcc	gaggataagg	180
agtggatgcc	cgtcaccaag	ttgggcccgt	tggccaagga	catgaagatc	aagtccttgg	240
aggagatcta	tctcttctcc	ctgcccatta	aggaatcaga	gatcattgat	ttcttcttgg	300
gggcctctct	caaggatgag	g				321

<210> 310

<211> 381

<212> DNA

<213> Homo sapien

<400> 310

ttaaccagcc	atattggctc	aataaatagc	ttcggtaagg	agttaatttc	cttctagaaa	60
tcagtgccta	tttttcttgg	aaactcaatt	ttaaatagtc	caattccatc	tgaagccaag	120
ctgttgatcat	tttcattcgg	tgacattctc	tcccatgaca	cccagaaggg	gcagaagaac	180
cacatttttc	atttatagat	gtttgcatcc	tttgtattaa	aattattttg	aaggggttgc	240
ctcattggat	ggcttttttt	tttttctctc	agggagaagg	ggagaaatgt	acttggaaat	300
taatgtatgt	ttacatctct	ttgcaaattc	ctgtacatag	agatatatct	tttaagtgtg	360
aatgtaacaa	catactgtga	a				381

<210> 311

<211> 538

<212> DNA

<213> Homo sapien

<400> 311

tttgaattta	caccaagaac	ttctcaataa	aagaaaatca	tgaatgctcc	acaatttcaa	60
cataccacaa	gagaagttaa	tttcttaaca	ttgtgttcta	tgattatttg	taagaccttc	120
accaagtctt	gatatctttt	aaagacatag	ttcaaaattg	cttttgaaaa	tctgtattct	180
tgaaaatata	cttgttggtg	attaggtttt	taaataaccag	ctaaaggatt	acctcactga	240
gtcatcagta	ccctcctatt	cagctcccca	agatgatgtg	tttttgctta	ccctaagaga	300
ggttttcttc	ttatttttag	ataattcaag	tgcttagata	aattatgttt	tctttaagtg	360
tttatggtaa	actcttttaa	agaaaattta	atatgttata	gctgaatctt	tttggtaact	420
ttaaatcttt	atcatagact	ctgtacatat	gttcaaatta	gctgcttgcc	tgatgtgtgt	480
atcatcgggtg	ggatgacaga	acaaacatat	ttatgatcat	gaataatgtg	ctttgtaa	538

<210> 312

<211> 176

<212> DNA

<213> Homo sapien

<400> 312

ggaggagcag	ctgagagata	gggtcagtga	atgcggttca	gcctgctacc	tctcctgtct	60
tcatagaacc	attgccttag	aattattgta	tgacacgttt	tttggttggtt	aagctgtaag	120
gttttgttct	ttgtgaacat	gggtattttg	aggggagggt	ggaggagata	gggaag	176

<210> 313

<211> 396

<212> DNA

<213> Homo sapien

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<400> 313

ccagcacc	ccccc	caggcc	ctgg	gggac	ctggg	ttctc	agact	gccaa	agaag	ccttg	ccatc	60
tggcgc	tccc	atggc	tcttg	caaca	tctcc	ccttc	gtttt	tgagg	gggtc	atgcc	ggggg	120
agccac	cagc	ccctc	actgg	gttcg	gagga	gagtc	caggaa	gggca	aagca	cgaca	aagca	180
gaaaca	tcgg	atttg	gggaa	cgcgt	gtcaa	tccct	tgtgc	cgcag	ggctg	ggcgg	gagag	240
actgtt	ctgt	tcctt	gtgta	actgt	gttgc	tgaaa	gacta	cctcg	ttcct	gtctt	gatgt	300
gtcac	cggg	caact	gcctg	ggggc	gggga	tgggg	gcagg	gtgga	agcgg	ctccc	atctt	360
tatacc	aaag	gtgct	acatc	tatgt	gatgg	gtggg						396

<210> 314

<211> 311

<212> DNA

<213> Homo sapien

<400> 314

cctcaac	atc	ctcag	agagg	actgg	aagcc	agtcct	tacg	ataaa	actcca	taattt	atagg	60
cctgcag	tat	ctctt	cttgg	agccca	accc	cgagg	accca	ctgaac	aagg	aggcc	gcaga	120
ggctct	gcag	aacaac	cggc	ggctg	tttga	gcaga	acgtg	cagcg	ctcca	tgcg	gggtg	180
ctacat	cggc	tccac	ctact	ttgag	cgctg	cctga	aatag	ggttg	ggcgca	taccc	acccc	240
cgccac	ggcc	acaag	ccctg	gcatc	ccctg	caaata	tatta	ttggg	gggcca	tgggt	tagggg	300
tttggg	ggggc	g										311

<210> 315

<211> 336

<212> DNA

<213> Homo sapien

<400> 315

tttaga	aacat	ggttat	catc	caagac	tact	ctacc	ctgca	acatt	gaact	cccaag	agagca	60
aatccac	att	cctctt	gagt	tctgc	agctt	ctgtg	ttaa	agggc	agctg	tcgtc	tatgc	120
cgtaga	aatca	catgat	ctga	ggacc	attca	tggaa	gctgc	taaat	agcct	agtc	tgggga	180
gtcttc	cata	aagttt	tgc	tggag	caaac	aaacag	gatt	aaact	aggtt	tggtt	ccttc	240
agccct	ctaa	aagcat	aggg	cttag	cctgc	aggct	tcctt	gggct	ttctc	tgtgt	gtgta	300
gttttg	tataa	cactat	agca	tctgt	ttaaga	tccagt						336

<210> 316

<211> 436

<212> DNA

<213> Homo sapien

<400> 316

aacatg	gtct	gcgtgc	cctta	agagag	acgc	ttcctg	caga	acagg	acctg	actaca	aaaga	60
atgttt	ccat	tggaatt	gtt	ggtaa	agact	tggagt	tttac	aatct	atgat	gatgat	gatg	120
tgtctc	catt	cctgga	aggt	cttga	agaaa	gaccac	agag	aaagg	cacag	cctgct	caac	180
ctgctg	atga	acctgc	agaa	aaggct	gatg	aacca	atgga	acatta	agtg	ataag	ccagt	240
ctatat	atgt	attatc	aaat	atgta	agaat	acagg	cacca	catact	gatg	acaata	aatct	300
atactt	tga	ccaaa	agttg	cagagt	gggtg	gaatg	ctatg	ttttag	gaat	cagtcc	agat	360
gtgagt	tttt	tccaag	caac	ctcact	gaaa	cctata	tataat	ggaata	acatt	tttctt	tga	420
agggtc	tgta	taatca										436

<210> 317

<211> 196

<212> DNA

<213> Homo sapien

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<400> 317

tattccttgt	gaagatgata	tactatTTTT	gttaagcgtg	tctgtattta	tgtgtgagga	60
gctgctggct	tgcagtgcgc	gtgcacgtgg	agagctgggtg	cccggagatt	ggacggcctg	120
atgctccctc	ccctgccctg	gtccagggaa	gctggccgag	ggctcctggct	cctgaggggc	180
atctgcccct	ccccca					196

<210> 318

<211> 381

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(381)

<223> n = A,T,C or G

<400> 318

gacgcttnng	ccgtaacgat	gacggagac	atcctgctgt	tcgggacggt	gctgatgaat	60
gccggggcgg	tgctgaactt	taagctgaaa	aagaaggaca	cncagggtt	tggggaggag	120
tncagggagc	ccaacacagg	tgacaacatc	cggaattct	tgctgancct	cagatacttt	180
cnaatcttca	tcnccctgtg	gaacatcttc	atgatgttct	gcatgattgt	gctgntcggc	240
tcttgaatcc	cancgatgaa	accannaact	cactttcccg	ggatgccgan	tctccattcc	300
tccattcctg	atgacttcaa	naatgttttt	gaccaaaaaa	ccgacaacct	tcccagaaag	360
tccaagctcg	tggtggngg	a				381

<210> 319

<211> 506

<212> DNA

<213> Homo sapien

<400> 319

ctaagcttta	cgaatggggt	gacaacttat	gataaaaact	agagctagtg	aattagccta	60
tttgtaaata	cctttgttat	aattgatagg	atacatcttg	gacatggaat	tgtaagcca	120
cctctgagca	gtgtatgtca	ggacttggtc	attagggttg	cagcagaggg	gcagaaggaa	180
ttatacagg	agagatgtat	gcagatgtgt	ccatatatgt	ccatatttac	atthttgatag	240
ccattgatgt	atgcatctct	tggtgtact	ataagaacac	attaattcaa	tggaaataca	300
ctttgcta	atthtaattg	tatagatctg	ctaataga	ctcttaaaaa	catactgtat	360
tctgttgctg	tgtgtttcat	tttaaattga	gcattaagg	aatgcagcat	ttaaatcaga	420
actctgccaa	tgcttttatc	tagaggcgtg	ttgccatttt	tgtcttatat	gaaatttctg	480
tccaagaaa	ggcaggatta	catctt				506

<210> 320

<211> 351

<212> DNA

<213> Homo sapien

<400> 320

ctgacctgca	ggacgaaacc	atgaagagcc	tgatccttct	tgccatcctg	gccgccttag	60
cggtagtaac	tttgtgttat	gaatcacatg	aaagcatgga	atcttatgaa	cttaatccct	120
tcattaacag	gagaaatgca	aataccttca	tatccccctca	gcagagatgg	agagctaaag	180
tccaagagag	gatccgagaa	cgctctaagc	ctgtccacga	gctcaatagg	gaagcctgtg	240
atgactacag	actttgcgaa	cgctacgcca	tggttttatg	atacaatgct	gcctataatc	300
gctacttcag	gaagcgccga	gggaccaa	gagactgagg	gaagaaaaaa	a	351

<210> 321

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<211> 421
 <212> DNA
 <213> Homo sapien

<400> 321
 ctccggaggcg ttcagctgct tcaagatgaa gctgaacatc tccttcccag ccactggctg 60
 ccagaaactc attgaagtgg acgatgaacg caaacttcgt actttctatg agaagcgtat 120
 ggccacagaa gttgctgctg acgctctggg tgaagaatgg aagggttatg tgggccgaat 180
 cagtgggtggg aacgacaaac aagggttccc catgaagcag ggtgtcttga cccatggccg 240
 tgtccgcctg ctactgagta aggggcattc ctgttacaga ccaaggagaa ctggagaaaag 300
 aaagagaaaa tcagttcgtg gttgcattgt ggatgcaaat ctgagcgttc tcaacttggt 360
 tattgtaaaa aaaggagaga aggatattcc tggactgact gatactacag tgcctcgccg 420
 c 421

<210> 322
 <211> 521
 <212> DNA
 <213> Homo sapien

<400> 322
 agcagctctc ctgccacagc tcttcacccc ctgaaaatgt tcgcctgctc caagtttgtc 60
 tccactccct ccttgggtcaa gagcacctca cagctgctga gccgtccgct atctgcagtg 120
 gtgctgaaac gaccggagat actgacagat gagagcctca gcagcttggc agtctcatgt 180
 ccccttacct cacttgtctc tagccgcagc ttccaaacca gcgccatttc aagggacatc 240
 gacacagcag ccaagttcat tggagctggg gctgccacag ttgggggtggc tggttctggg 300
 gctgggattg gaactgtgtt tgggagcctc atcattgggt atgccaggaa cccttctctg 360
 aagcaacagc tcttctccta cgccattctg ggctttgccc tctcggaggc catggggctc 420
 ttttgtctga tggtagcctt tctcatcctc ttgccatgt gaaggagccg tctccacctc 480
 ccatagttct cccgcgtctg gttggccccg tgtgttcctt t 521

<210> 323
 <211> 435
 <212> DNA
 <213> Homo sapien

<400> 323
 ccgaggtcgc acgcgtgaga cttctccgcc gcagacgccg ccgcgatgcg ctacgtcgcc 60
 tcttacctgc tggctgccct aggggggcaac tcctcccccga gcgccaagga catcaagaag 120
 atcttggaac gcgtgggtat cgaggcggac gacgaccggc tcaacaaggt tatcagtga 180
 ctgaatggaa aaaacattga agacgtcatt gccagggta ttggcaagct tgccagtgt 240
 cctgctgggtg gggctgtagc cgtctctgct gcccaggct ctgcagcccc tgctgctgg 300
 tctgcccctg ctgcagcaga ggagaagaaa gatgagaaga aggaggagtc tgaagagtca 360
 gatgatgaca tgggatttgg cctttttgat taaattcctg ctcccctgca aataaagcct 420
 ttttacacat ctcaa 435

<210> 324
 <211> 521
 <212> DNA
 <213> Homo sapien

<400> 324
 aggagatcga ctttcggtgc ccgcaagacc agggctggaa cgccgagatc acgctgcaga 60
 tgggtgcagta caagaatcgt caggccatcc tggcgggtcaa atccacgcgg cagaagcagc 120
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<210> 325

<211> 451

<212> DNA

<213> Homo sapien

<400> 325

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<210> 326

<211> 421

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(421)

<223> n = A,T,C or G

<400> 326

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tacaagaaaa	actccttggtg	gtgaaggttc	taagacgtgg	gatcgtttcc	agatgagaat	360
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<210> 327

<211> 456

<212> DNA

<213> Homo sapien

<400> 327

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<210> 328
 <211> 471
 <212> DNA
 <213> Homo sapien

<400> 328
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 tgattatccg aaatgtttca ttgtgggagc agacaatgtg ggctccaagc agatgcagca 180
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<210> 329
 <211> 278
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(278)
 <223> n = A,T,C or G

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 <211> 338
 <212> DNA
 <213> Homo sapien

<400> 330
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<210> 331
 <211> 2820
 <212> DNA
 <213> Homo sapiens

<400> 331
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<210> 332

<211> 2270

<212> DNA

<213> Homo sapiens

<400> 332

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<210> 333

<211> 2816

<212> DNA

<213> Homo sapiens

<400> 333

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<210> 334

<211> 2082

<212> DNA

<213> Homo sapiens

<400> 334

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<210> 335

<211> 4849

<212> DNA

<213> Homo sapiens

<400> 335

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150

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<210> 336

<211> 1386

<212> DNA

<213> Homo sapiens

<400> 336

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<210> 337

<211> 1551

<212> DNA

<213> Homo sapiens

<400> 337

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151

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<210> 338

<211> 586

<212> PRT

<213> Homo sapiens

<400> 338

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Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
      35                                40                        45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Pro Thr Phe Asp Ala
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Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
      65                                70                        75                        80

His Ser Ser Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
      85                                90                        95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
      100                               105                        110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
      115                               120                        125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
      130                               135                        140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
      145                               150                        155                        160

Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
      165                               170                        175

Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val

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	210					215					220				
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val
225					230					235					240
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg
				245					250					255	
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp
			260					265					270		
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr
		275					280					285			
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp
	290					295					300				
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu
305					310					315					320
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His
				325					330					335	
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		340					345						350		
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		355					360					365			
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		370				375					380				
Ser	Gln	Leu	Ile	Asn	Pro	Gln	Gln	Arg	Asn	Ala	Leu	Thr	Pro	Thr	Thr
385				390						395					400
Ile	Pro	Asp	Gly	Met	Gly	Ala	Asn	Ile	Pro	Met	Met	Gly	Thr	His	Met
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Pro	Met	Ala	Gly	Asp	Met	Asn	Gly	Leu	Ser	Pro	Thr	Gln	Ala	Leu	Pro
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Pro	Pro	Leu	Ser	Met	Pro	Ser	Thr	Ser	His	Cys	Thr	Pro	Pro	Pro	Pro
		435					440					445			
Tyr	Pro	Thr	Asp	Cys	Ser	Ile	Val	Ser	Phe	Leu	Ala	Arg	Leu	Gly	Cys
	450					455					460				
Ser	Ser	Cys	Leu	Asp	Tyr	Phe	Thr	Thr	Gln	Gly	Leu	Thr	Thr	Ile	Tyr
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153

Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro
485 490 495

Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
500 505 510

Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
515 520 525

Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val
530 535 540

Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
545 550 555 560

Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn
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Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
580 585

<210> 339

<211> 641

<212> PRT

<213> Homo sapiens

<400> 339

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Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
35 40 45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
50 55 60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
65 70 75 80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
85 90 95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
100 105 110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
115 120 125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln-Gln
130 135 140

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				165					170					175	
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr
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Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His
		195					200					205			
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His
	210					215					220				
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro
225					230					235					240
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val
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Gly	Thr	Glu	Phe	Thr	Thr	Val	Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser
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Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu
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Glu	Thr	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg
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Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile
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Lys	Arg	Arg	Ser	Pro	Asp	Asp	Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly
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	370					375					380				
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Gln	Gln	Gln	His	Gln	His	Leu	Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser
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Pro	Ser	Ser	Tyr	Gly	Asn	Ser	Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser
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435	440	445
Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile		
450	455	460
Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu		
465	470	475 480
Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser		
	485	490 495
His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly		
	500	505 510
Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr		
	515	520 525
Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp		
	530	535 540
Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys		
545	550	555 560
Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His		
	565	570 575
Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser		
	580	585 590
Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg		
	595	600 605
Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe		
	610	615 620
Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly		
625	630	635 640
Glu		

<210> 340

<211> 448

<212> PRT

<213> Homo sapiens

<400> 340

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe		
	5	10 15
Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro		
	20	25 30
Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn		
	35	40 45

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

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Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350

Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365

Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380

Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400

Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys
 405 410 415

Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser
 420 425 430

Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro
 435 440 445

<210> 341

<211> 356

<212> PRT

<213> Homo sapiens

<400> 341

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
 5 10 15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45

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

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80

His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115 120 125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn

158

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

<210> 342

<211> 680

<212> PRT

<213> Homo sapiens

<400> 342

Met Asn Phe Glu Thr Ser Arg Cys Ala Thr Leu Gln Tyr Cys Pro Asp
5 10 15

Pro Tyr Ile Gln Arg Phe Val Glu Thr Pro Ala His Phe Ser Trp Lys
20 25 30

Glu Ser Tyr Tyr Arg Ser Thr Met Ser Gln Ser Thr Gln Thr Asn Glu
35 40 45

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

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

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625		630		635		640
Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro Arg Asp						
		645		650		655
Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn Lys Gln						
		660		665		670
Gln Arg Ile Lys Glu Glu Gly Glu						
		675		680		
<210> 343						
<211> 461						
<212> PRT						
<213> Homo sapiens						
<400> 343						
Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln						
		5		10		15
Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn						
		20		25		30
Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser						
		35		40		45
Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala						
		50		55		60
Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro						
		65		70		75
						80
His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala						
		85		90		95
Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala						
		100		105		110
Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly						
		115		120		125
Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr						
		130		135		140
Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn						
		145		150		155
						160
Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn						
		165		170		175
Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val						
		180		185		190
Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val						
		195		200		205

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

<210> 344

<211> 516

<212> PRT

<213> Homo sapiens

<400> 344

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

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290	295	300
Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile 305 310 315 320		
Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys 325 330 335		
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys 340 345 350		
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly 355 360 365		
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu 370 375 380		
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln 385 390 395 400		
Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser 405 410 415		
Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser 420 425 430		
Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg 435 440 445		
Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile 450 455 460		
Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu 465 470 475 480		
Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser 485 490 495		
His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Arg 500 505 510		
Ile Trp Gln Val 515		

<210> 345

<211> 1800

<212> DNA

<213> Homo sapiens

<400> 345

gcgcctcatt gccactgcag tgactaaagc tgggaagacg ctggtcagtt cacctgcccc 60
 actggttggt ttttaaaca attctgatac aggcgacatc ctactgacc gagcaaagat 120
 tgacattcgt atcatcactg tgcaccattg gcttctaggc actccagtgg ggtaggagaa 180

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ggaggtctga aaccctcgca gagggatctt gccctcattc tttgggtctg aaacactggc 240
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tttcatcggg ggtgtcaaca aacactccac cagcatcggg aaggtgtgga tcacagtcac 360
ctttattttc cgagtcacga tcctagtggg ggctgcccag gaagtgtggg gtgacgagca 420
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acggaacagt gtggaagcag aaggcttttt taactcatcc gtttgccga tcgttgacga 1740
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<210> 346

<211> 261

<212> PRT

<213> Homo sapiens

<400> 346

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Met Asp Trp Gly Thr Leu His Thr Phe Ile Gly Gly Val Asn Lys His
      5                                10                                15

Ser Thr Ser Ile Gly Lys Val Trp Ile Thr Val Ile Phe Ile Phe Arg
      20                                25                                30

Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln
      35                                40                                45

Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
      50                                55                                60

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

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

Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
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166

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167

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Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val
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Cys	Lys	Ser	Ile	Leu	Glu	Ile	Met	His	Lys	Glu	Ala	Gln	Asp	Ile	Lys
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465					470					475					480

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Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His
50 55 60

Gly Ala Asn Arg Phe
65

CLAIMS

1. An isolated polypeptide, comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) sequences recited in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349;
- (b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 under moderately stringent conditions; and
- (c) complements of sequences of (a) or (b).
2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158,

78

160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences.

5

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 110, 112, 114, 152, 155, 156, 159, 161, 165, 166, 169, 170, 172, 174, 176, 226-252, 346, 348 and 350.

4. An isolated polynucleotide encoding at least 15 amino acid
10 residues of a lung tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29,
15 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a
20 complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO:
25 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317,
30 323, 345, 347 and 349 or a complement of any of the foregoing sequences.

6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.

7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349_ under moderately stringent conditions.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a lung tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84,

80

86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154,
157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207,
209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-
281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and
5 349_or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein, comprising at least one polypeptide according
to claim 1.

10 13. A fusion protein according to claim 12, wherein the fusion
protein comprises an expression enhancer that increases expression of the fusion protein
in a host cell transfected with a polynucleotide encoding the fusion protein.

14. A fusion protein according to claim 12, wherein the fusion
15 protein comprises a T helper epitope that is not present within the polypeptide of claim
1.

15. A fusion protein according to claim 12, wherein the fusion
protein comprises an affinity tag.

20

16. An isolated polynucleotide encoding a fusion protein according
to claim 12.

17. A pharmaceutical composition, comprising a physiologically
25 acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- 30 (e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 18.

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

5 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171,
10 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions;
and

(c) complements of sequences of (i) or (ii);
in combination with an immunostimulant.

15 26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

20

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient,
25 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

30 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and

349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii) encoded by a polynucleotide recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and thereby inhibiting the development of a cancer in the patient.

30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is lung cancer.

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and

(ii) complements of the foregoing polynucleotides; wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

5

35. A method for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

(a) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(iii) complements of sequences of (i) or (ii);

(b) polynucleotides encoding a polypeptide of (a); and

(c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

25

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

30

38. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient
5 with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

10 (1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158,
15 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that expresses a polypeptide of

20 (i);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

25 39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion
30 of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence

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selected from the group consisting of:

(1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

5 (2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

10 (ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that express a polypeptide of (i);
such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells;

and

15 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

20 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the
25 foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

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41. A method according to claim 40, wherein the binding agent is an

antibody.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

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43. A method according to claim 40, wherein the cancer is lung cancer.

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

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47. A method according to claim 44, wherein the cancer is a lung

cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 5 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347
10 and 349 or a complement of any of the foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the
15 presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

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50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

25 51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a
30 polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347

and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained
5 from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

10 52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15 53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 11; and
20 (b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

25 56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

30 57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.

60. A diagnostic kit, comprising:
(a) an oligonucleotide according to claim 59; and
(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.