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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
5 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
10 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
15 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
20 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)
25 *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.

30 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 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.

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 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 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 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 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 hydrophobic 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 hydrophobic 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
5 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
10 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.
15 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
20 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
25 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.
30 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 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 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 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.

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 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 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 , ^{125}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.

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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

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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 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, 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 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 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), 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; 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 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), 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).

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 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 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-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. 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 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 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 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 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 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.

- 10 As noted above, to improve sensitivity, multiple lung tumor protein 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
10 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
15 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
20 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
25 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
30 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

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).

25

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 µg 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 µl 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
5 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
10 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
15 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
20 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
25 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
30 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 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: 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 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 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 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 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

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

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.

25 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.

30 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.

20

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.

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,

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,

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;
- 5 (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.

10 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.

15

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.

20 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
25 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.

30

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

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.

30

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.

5

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,
10 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,
15 162-164, 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
20 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.

25 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.

30

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.

20

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.

20

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.

25

SEQUENCE LISTING

<110> Corixa Corporation et al.

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

<130> 210121.45501PC

<140> PCT

<141> 2000-04-03

<160> 350

<170> FastSEQ for Windows Version 3.0

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<213> Homo sapien

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ttcatctcca gcagagacaa cggaggaggc tcccaccagg acggttctca ttatttatat	180
gttaatatgt ttgtaaactc atgtacagtt ttttttgggg gggaagcaat gggaanggta	240
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aaaaaaaaaaaa	315

<210> 2

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<212> DNA

<213> Homo sapien

<400> 2

athtaggtt aagatthttt ttacccttgt tactaaggag caaattagta ttaaagtata	60
atatatataa acaaatacaa aaagttttga gtggttcagc ttttttattt tttttaatgg	120
cataactttt aacaacactg ctctgtaatg ggttgaactg tggtagctag actgagataa	180
ctgaaatgag tggatgtata gtgttattgc ataattatcc cactatgaag caaagggact	240
ggataaattc ccagtctaga ttattagcct ttgttaacca tcaagcacct agaagaagaa	300
ttattggaaa ttttgtcctc tgtaactggc actttggggg gtgacttatc ttttgccttt	360
gtaaaaaaaaaaaa	380

<210> 3

<211> 346

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<220>
 <221> misc_feature
 <222> (1)... (346)
 <223> n = A,T,C or G

<400> 3
 ttgtaagtat acaatttttag aaaggattaa atgttattga tcatttttact gaatactgca 60
 catcctcacc atacaccatc cacttttccaa taacatttaa tccttttctaa aattgtaagt 120
 atacaattgt acttttctttg gatttttcata acaaataac catagactgt taattttatt 180
 gaagtttctc taatggaatg agtcattttt gtcttgtgct tttgaggta cctttgcttt 240
 gacttccaac aatttgatca tatagtgttg agctgtggaa atctttaagt ttattctata 300
 gcaataattt ctattnnnag annccnggn naaaannann annaaa 346

<210> 4
 <211> 372
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (372)
 <223> n = A,T,C or G

<400> 4
 actagtctca ttactccaga attatgctct tgtacctgtg tggctgggtt tcttagtcgt 60
 tggtttggtt tggttttttg aactggtatg taggggtggtt cacagttcta atgtaagcac 120
 tctcttctcc aagttgtgct ttgtggggac aatcattctt tgaacattag agaggaaggc 180
 agttcaagct gttgaaaaga ctattgctta tttttgtttt taaagacctt cttgacgtca 240
 tgtggacagt gcaogtgcct tacgctacat cttgttttct aggaagaagg ggatgcnggg 300
 aaggantggg tgctttgtga tggataaaac gnctaaataa cacacctta cattttgaaa 360
 aaaacaaaac aa 372

<210> 5
 <211> 698
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (698)
 <223> n = A,T,C or G

<400> 5
 actagtanga tagaaacact gtgtcccag agtaaggaga gaagctacta ttgattagag 60
 cctaaccag gttaactgca agaagaggcg ggatactttc agctttccat gtaactgtat 120
 gcataaagcc aatgtagtcc agtttctaag atcatgttcc aagctaactg aatcccactt 180
 caatacacac tcatgaactc ctgatggaac aataacaggc ccaagcctgt ggtatgatgt 240
 gcacacttgc tagactcaga aaaaatacta ctctcataaa tgggtgggag tattttgggt 300
 gacaacctac tttgottggc tgagtgaagg aatgatattc atatnttcat ttattccatg 360
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata 420
 tntccaaatn ttngtnngt cgctgcacat atctgaaatc ctatattaag antttcccaa 480
 natgangtcc ctggtttttc cagccactt gatcngtcaa ngatctcacc tctgtntgtc 540
 ctaaaaccnt ctncnnang gttagaacng acctctcttc tcccttcccg aanaatnaag 600
 tgtgngaaga nancnncn cccctctnnc tncnncctng ccngctnnnc cncntgtngg 660

ggngngccgcc cccgcggggg gacccccccn ttttcccc

698

<210> 6
 <211> 740
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(740)
 <223> n = A,T,C or G

<400> 6
 actagtcaaa aatgctaaaa taatttgga gaaaatattt ttttaagtagt gttatagttt 60
 catgtttatc ttttattatg tnttgtgaag ttgtgtcttt tcactaatta cctatactat 120
 gccaatattt ccttatatct atccataaca tttatactac atttgtaaga gaatatgcac 180
 gtgaaactta acactttata aggtaaaaat gaggtttcca agatttaata atctgatcaa 240
 gttcttggtt tttccaaata gaatggactt ggtctgttaa ggggctaagg gagaagaaga 300
 agataagggt aaaagttggt aatgaccaa cattctaaaa gaaatgcaa aaaaaattta 360
 ttttcaagcc ttcgaactat ttaaggaaag caaaatcatt tcttanatgc atatcatttg 420
 tgagantttc tcantaatat cctgaatcat tcatttcagc tnaggcttca tgttgactcg 480
 atatgtcatc tagggaaagt ctatttcag gtccaaacct gttgccatag ttggttaggc 540
 tttcctttta ntgtgaanta ttnacangaa attttctct tnanagttct tnatagggtt 600
 aggggtgtgg gaaaagcttc taacaatctg tagtgttncg tggtatctgt ncagaaccan 660
 aatnacggat cgnangaagg actgggtcta tttacangaa cgaatnatct ngttnnntgt 720
 gttnncaact ccngggagcc 740

<210> 7
 <211> 670
 <212> DNA
 <213> Homo sapien

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

<400> 7
 gctggggagc tgggcatggc ggtcccgct gcagccatgg ggcctcggc gttgggcccag 60
 agcggccccg gctcgatggc cccgtggtgc tcagtgaagc ggggccccgc gcgctacgtg 120
 cttgggatgc aggagctgtt ccggggccac agcaagaccg cgagttcctg gcgcacagcg 180
 ccaaggtgca ctcggtggcc tggagttgcg acgggcgctc cctacctcgg ggtcttcgac 240
 aagacgccac gtcttcttgc tgganaanga ccgttggtca aagaaaacaa ttatcgggga 300
 catggggata gtgtggacca ctttgttggc atccaagtaa tcttgacctt tttgttacgg 360
 cgtctggaga taaaaccatt cgcctctggg atgtgaggac tacaaaatgc attgccactg 420
 tgaacactaa aggggagaaac attaatatct gctggantcc tgatgggcan accattgctg 480
 tagcnacaag gatgatgtgg tgactttatt gatgccaaga aaccccggtc caaagcaaaa 540
 aaacanttcc aanttcgaag tcacnnaaat ctctggaac aatgaacatn aatatnttct 600
 tctgacaat ggnccctggg tgnctcacat cctcagctnc cccaaaactg aancctgtnc 660
 natccacccc 670

<210> 8
 <211> 689
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(689)
 <223> n = A,T,C or G

<400> 8
 actagtatct aggaatgaac agtaaaagag gagcagttgg ctacttgatt acaacagagt 60
 aaatgaagta ctggatttgg gaaaacctgg ttttattaga acatatggaa tgaaagccta 120
 cacctagcat tgcctactta gccccctgaa ttaacagagc ccaattgaga caaacccttg 180
 gcaacaggaa attcaaggga gaaaaagtaa gcaacttggg ctaggatgag ctgactccct 240
 tagagcaaag ganagacagc cccattacc aaataccatt tttgcctggg gcttgtgcag 300
 ctggcagtgt tccctgcccc gcatggcacc ttatngtttt gatagcaact tcggtgaatt 360
 ttcaccaact tattacttga aattataata tagcctgtcc gtttgctgtn tccaggctgt 420
 gatatatntt cctagtgggt tgacttttnaa aataaatnag gtttantttt cccccccnn 480
 cnntnctncc nntcnctcnn cnntcccccc cnctcngtcc tccnnnnntn gggggggccn 540
 cccccnccgn ggacccccct ttgggtccctt agtggaggtt natggcccct ggnnttatcc 600
 nggcctann tttccccgtn nnaaatgntt cccccccca ntccnccac ctcaanccgg 660
 aagcctaagt ttntaccctg ggggtcccc 689

<210> 9
 <211> 674
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(674)
 <223> n = A,T,C or G

<400> 9
 gtccactctc ttttgagtgt actgtcttac tgtgcactct gtttttcaac tttctagata 60
 taaaaaatgc ttgttctata gtggagtaag agctcacaca cccaaggcag caagataact 120
 gaaaaaagcg aggctttttt gccaccttgg taaaggccag ttcactgcta tagaactgct 180
 ataagcctga agggaagtag ctatgagact ttccattttt cttagtcttc ccaataggct 240
 ccttcattga aaaaggcttc ctgtaataat tttcaacctaa tgaattagca gtgtgattat 300
 ttctgaaata agagacaaat tgggcccgcag agtcttctct tgatttataa taaacaaccc 360
 aaagttttgt ttggtcttca ccaaaggaca tactctaggg ggtatgttgt tgaagacatt 420
 caaaaacatt agctgttctg tctttcaatt tcaagttatt ttggagactg cctccatgtg 480
 agttaattac tttgctctgg aactagcatt attgtcatta tcatcacatt ctgtcatcat 540
 catctgaata atattgtgga tttccccctc tgcttgcata ttcttttgac tcctctggga 600
 anaaatgtca aaaaaaaagg tcgatctact cngcaaggnc catctaata caatgcgtgga 660
 aggacccnct gcc 674

<210> 10
 <211> 346
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(346)
 <223> n = A,T,C or G

<400> 10

```

actagtctgc tgatagaaag cactatacat cctattgttt ctttctttcc aaaatcagcc      60
ttctgtctgt aacaaaaatg tactttatag agatggagga aaaggtctaa tactacatag      120
ccttaagtgt ttctgtcatt gttcaagtgt attttctgta acagaaacat atttggaatg      180
ttttctttt ccccttataa attgtaattc ctgaaatact gctgctttaa aaagtccac      240
tgtcagatta tattatctaa caattgaata ttgtaaatat acttgtctta cctctcaata      300
aaaggtact tttctattan nnagnngnnn gnnnnataaa anaaaa      346

```

```

<210> 11
<211> 602
<212> DNA
<213> Homo sapien

```

```

<400> 11
actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataatgaaat      60
gatgttaaac 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 tctaaatata aaaaaaggga aatgaagtta taaatcaatt tttgtataat      360
ctgtttgaaa catgagtttt atttgcttaa tattagggct ttgccccttt tctgtaagtc      420
tcttgggata ctgtgtagaa ctgttctcat taaacaccaa acagttaagt ccattctctg      480
gtactagcta caaattcggt ttcataattc acttaacaat ttaaataaac tgaaatattt      540
ctagatggtc tacttctgtt catataaaaa caaaacttga tttccaaaaa aaaaaaaaaa      600
aa                                                    602

```

```

<210> 12
<211> 685
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(685)
<223> n = A,T,C or G

```

```

<400> 12
actagtcctg tgaaagtaca actgaaggca gaaagtgtta ggattttgca tctaattgttc      60
attatcatgg tattgatgga cctaagaaaa taaaaattag actaagcccc caaataagct      120
gcatgcattt gtaacatgat tagtagattt gaatatatag atgtagtatn ttgggtatct      180
agggtgttta tcattatgta aaggaattaa agtaaaggac tttgtagttg tttttattaa      240
atatgcataat agtagagtgc aaaaatatag caaaaatana aactaaagggt agaaaagcat      300
tttagatatg cottaatnta nnaactgtgc caggtggccc tcggaataga tgccaggcag      360
agaccagtgc ctgggtgggtg cctccccttg tctgcccccc tgaagaactt ccctcacgtg      420
angtagtgc ctcgtagggtg tcacgtggan tantggganc aggccgnnn gtnanaagaa      480
ancanngtga nagtttcncc gtngangcng aactgtccct gngccnnnac gctccanana      540
cntntccaat ngacaatoga gtttcennnc tcngnaaacc tngccgnnnn cnngccennc      600
cantntgnta accccgcgcc cggatcgctc tcnnntcggt ctcnncnnaa ngggnnttcn      660
cnnccgcggt cncnncccg cnncc                                                    685

```

```

<210> 13
<211> 694
<212> DNA
<213> Homo sapien

```

```

<220>

```

<221> misc_feature
 <222> (1)...(694)
 <223> n = A,T,C or G

<400> 13
 cactagtcac tcattagcgt tttcaatagg gctcttaagt ccagtagatt acgggtagtc 60
 agttgacgaa gatctgggtt acaagaacta attaaatgtt tcattgcatt tttgtaagaa 120
 cagaataatt ttataaaatg tttgtagttt ataattgccg aaaataatth aaagacactt 180
 tttctctgtg tgtgcaaatg tgtgtttgtg atccattttt tttttttttt taggacacct 240
 gtttactagc tagctttaca atatgccaaa aaaggatttc tccctgacct catccgtggg 300
 tcacctctt tcccccccat gctttttgcc ctagtattata acaaaggaat gatgatgatt 360
 taaaaagtag ttctgtatct tcagtatctt ggtcttcag aacctcttg ttgggaaggg 420
 gatcattttt tactggtcac ttccctttgg agtgtactac tttaacagat ggaaagaact 480
 cattggccat ggaaacagcc gangtggtgg gagccagcag tgcattggc acgtccggcat 540
 ctggcntgat tggctctggc gccgtcattg tcagcacagt gccatgggac atggggaana 600
 ctgactgcac ngccaatggg tttcatgaag aatacnagc ncnngtgat cactnanc 660
 angacgtat gggggncana gggccanttg ctte 694

<210> 14
 <211> 679
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(679)
 <223> n = A,T,C or G

<400> 14
 cagccgctg catctgtatc cagcccgang tcccgccagt cccagctgcg cgcgcccccc 60
 agtcccgnc cgttcggcc cangctnagt tagncctcac catnccggc aaaggangca 120
 ccaagtgcac caaatacctg cngtncggat ntaaattcat cttctggctt gccgggattg 180
 ctgtccntgc cattggacta nggtccgat ncgactctca gaccanganc atcttcganc 240
 naganactaa tnatnatnt tccagcttct acacaggagt ctatattctg atcgatccg 300
 gncctctnt gatgctggg ggcttctga gctgctgcg ggctgtgcaa gagtccant 360
 gcatgctggg actgttcttc ggcttctct tggatgatn cgcattgaa atacctgcg 420
 ccatctggg atattccact ncgatnatgt gattaaggaa ntccacggag tttacaagg 480
 acacgtacaa cnacctgaaa accnnggatg anccccaccg ggaanncctg aangccatcc 540
 actatgcgtt gaactgcaat ggtttgctg gggnccttga acaatttaat cncatacatc 600
 tggccccann aaaggacntn ctcgannct tncctgtna attengttct gatnccatca 660
 cagaagtctc gaacaatcc 679

<210> 15
 <211> 695
 <212> DNA
 <213> Homo sapien

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

<400> 15
 actagtggat aaaggccagg gatgctgctc aacctctac catgtacagg gacgtctccc 60
 cattacaact acccaatccg aagtgtcaac tgtgtcagga ctaanaaacc ctggttttga 120

ttaaaaaagg	gcctgaaaaa	aggggagcca	caaattctgtc	tgttctctca	cnttantcnt	180
tggcaaatna	gcattctgtc	tenttggtg	cngcctcanc	ncaaaaaanc	ngaactcnat	240
cngggccagg	aatacatctc	ncaatnaacn	aaattganca	aggcnntggg	aaatgccnga	300
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tctncanaaa	cttctgggcc	acnattcnaa	ttnanggnca	cgnacanatn	ccttccatna	480
anencacccc	acntttgana	gccangacaa	tgactgcntn	aantgaaggc	ntgaagggaan	540
aactttgaaa	ggaaaaaaa	ctttgtttcc	ggcccttccc	aacncttctg	tgtnnancac	600
tgcttctctg	naaccctgga	agcccnngga	cagtgttaca	tggtgttcta	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	gcagcgagg	ttgtccccgt	ttccccctcc	ccttcccttc	tcgggttgcc	60
ttccccggcc	ccttactctc	cacagtcctc	gtccccccat	gtcccagaaa	caagaagaag	120
agaaccctgc	ggaggagacc	ggcgaggaga	agcaggacac	gcaggagaaa	gaaggtattc	180
tgcttgagag	agctgaagag	gcaaagctaa	aggccaaata	cccaagccta	ggacaaaagc	240
ctggaggctc	cgacttcctc	atgaagagac	tccagaaaag	gcaaaaagta	tttgactcng	300
gagactacaa	catggccaaa	gccaacatga	agaataagca	gctgcccaag	gcangaccag	360
acaagaacct	ggtgactggt	gatcacatcc	ccaccccaca	ggatctgccc	agagaaaagtc	420
ctcgctcgtc	accagcaagc	ttgcgggttg	ccaagttgaa	tgatgctgcc	ggggctctgc	480
canatctgag	acgcttcctc	ccctgcccc	cccgggtcct	gtgctggctc	ctgcccttcc	540
tgcttttgca	gccangggtc	aggaagtggc	ncnggtngtg	gctggaaaag	aaaacccttt	600
cctgttggtg	tcccacccat	ggagccccct	gggcgagccc	angaacttga	ncctttttgt	660
tntcttnc						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	ctcngggcnn	60
gacgcgctga	ggagannnac	gctggcccan	ctgccggcca	cacacgggga	tentggtnat	120
gcctgcccac	gggancccca	ncnctcggan	cccatntcac	acccgnncn	tncccccacn	180
ncctggctcn	cnengccng	nccagctenc	gnccccctcc	gcnnnctcn	ttnnentctc	240
cnncnccctc	ncnncncc	cctaccnccg	gtctccctcc	cagccccccc	ccgcaancct	300
ccacnacncc	ntcnncncca	ancnccnctc	genctengcc	ccngccccct	gccccccgcc	360
cnncnacncc	cgntcccccg	cgncngngc	ctnccccctc	cccacnacag	ncncaaccgc	420
agncaagcnc	tcggcccnct	gaagcccnnc	cccgcgcgcg	tcaccttcat	ggncnncncc	480
ccccgctcnc	ncnctgcncc	gcccgnnngg	cgcgccgcgc	cnnccngntn	ccnncngnng	540

```

ccccngcngn angcngtgcg cnncaangncc gngccggnncn ncaccctccg nccnccgccc      600
cgccccgtgg gggctccccg cncgcggncc antcccccnc cntncgcccc ctntccgntc      660
cnnctctcnc gctcngcgcn cgcccccnc ccccccc      697

```

```

<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 gcacccccctt      60
ctgacctcca gtgcgcgcgg cctcaagatc agacatggcc cagaacttga acgacttggc      120
gggacggctg cccgcggggc cccggggcat gggcacggcc ctgaagctgt tgctgggggc      180
cggcgcctg gctacgggtg tgcgcgaatc tgtgttcacc gtggaaggcg ggcnacagagc      240
catcttcttc aatcggatcg gtggagtgc caggacacta tcctggggccg anggccttca      300
cttcaggatc cttggttcca gtaccccanc atctatgaca ttccggggccag acctcgaaaa      360
aatctcctcc ctacaggctc caaagacctc cagatgggtga atatctccct gcgagtgttg      420
tctcgaccaa tgctcangaa cttoctaaca tggtccancg cctaagggtc ggactacnaa      480
gaacgantgt tgccgtccat tgtaacgaag tgctcaagaa tttnggtggc caagttcaat      540
gncctcacnn ctgactnccc agcggggcca agttanccct ggttgatccc cgggganctg      600
acnnaaaagg gccaaaggact tccctcctac ctggataatg tggcctcac aaagctcaac      660
tttanccacc      670

```

```

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

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

```

```

<400> 19
actagtgcc aacctcagctc ccaggccagt tctctgaatg tcgaggagtt ccaggatctc      60
tggcctcagt tgtccttggg tattgatggg ggacaaattg gggatggcca gagccccgag      120
tgtgccttg gctcaactgt ggttgatttg tctgtgcccg gaaagtttgg catcattcgt      180
ccaggctgtg ccctggaaag tactacagcc atcctccaac agaagtaagg actgctcccc      240
tcacatgcgt cctacctgtg aaactctggg aagcaggaag gccaagacc tgggtgctgga      300
tactatgtgt ctgtccactg acgactgtca aggcctcatt tgcagaggcc accggagcta      360
gggcactagc ctgactttta aggcagtgtg tctttctgag cactgtagac caagcccttg      420
gagctgctgg tttagccttg cacctgggga aaggatgtat ttatttgtat tttcataatat      480
cagccaaaag ctgaatggaa aagtttagaa cattcctagg tggccttatt ctaataagtt      540
tcttctgtct gttttgtttt tcaattgaaa agttattaaa taacagattt agaactctagt      600
gagacc      606

```

```

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

```



```

<400> 20
actagtaa ac aacagcagca gaaacatcag tatcagcagc gtcgccagca ggagaatatg      60
cagcgccaga gccgaggaga acccccgctc cctgaggagg acctgtccaa actcttcaaa      120
ccaccacagc cgctgccag gatggactcg ctgctcattg caggccagat aaacacttac      180
tgccagaaca tcaaggagtt cactgccc aaacttaggca agctcttcat ggcccaggct      240
cttcaagaat acaacaacta agaaaaggaa gtttccagaa aagaagttaa catgaactct      300
tgaagtcaca ccagggcaac tcttggaaga aatatatttg catattgaaa agcacagagg      360
atctctttag tgtcattgcc gattttggct ataacagtgt ctttctagcc ataataaaat      420
aaaacaaaat cttgactgct tgc tcaaaa      449

```

```

<210> 21
<211> 409
<212> DNA
<213> Homo sapien

```

```

<400> 21
tatcaatcaa ctggtgaata attaaacaat gtgtggtgtg atcatacaaa gggtaccact      60
caatgataaa aggaacaagc tgcctatatg tggaacaaca tggatgcatt tcagaaactt      120
tatgttgagt gaaagaacaa acacggagaa catactatgt gggtctcttt atgtaacatt      180
acagaaataa aaacagaggc aaccaccttt gaggcagtat ggagtgagat agactggaaa      240
aaggaaggaa ggaaactcta cgctgatgga aatgtctgtg tcttcattgg gtggtagtta      300
tgtggggata tacatttgtc aaaatttatt gaactatata ctaaagaact ctgcatttta      360
ttgggatgta aataatacct caattaaaaa gacaaaaaaa aaaaaaaaaa      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
acaattttca ttatcttaag cacattgtac atttctacag aacctgtgat tattctcgca      60
tgataaggat ggtacttgca tatggtgaat tactactgtt gacagtttcc gcagaaatcc      120
tatttcagtg gaccaacatt gtggcatggc agcaaatgcc aacattttgt ggaatagcag      180
caaactctaca agagacctg gttgggtttt cgttttgttt tctttgtttt tcccccttc      240
tcctgaatca gcaggggatg aangagggtg gggaaagtta gaattactcc tccagtagt      300
agctctgaag tgtcacattt aatatcagtt ttttttaa ac atgattctag ttnaatgtag      360
aagagagaag aaagaggaag tgttcacttt ttaatacac tgatttagaa atttgatgtc      420
ttatatcagt agttctgagg tattgatagc ttgctttatt tctgccttta cgttgacagt      480
gttgaagcag ggtgaataac taggggcata tataattttt ttttttgtaa gctgtttcat      540
gatgttttct ttggaatttc cggataagtt caggaaaaca tctgcatgtt gttatctagt      600
ctgaagtctn tatccatctc attacaacaa aaacnccag aacggnntg      649

```

```

<210> 23
<211> 669
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```

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

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

<400> 23

actagtgcog	tactggctga	aatccctgca	ggaccaggaa	gagaaccagt	tcagactttg	60
tactctcagt	caccagctct	ggaattagat	aaattccttg	aagatgtcag	gaatgggac	120
tatcctctga	cagcctttgg	gctgcctcgg	ccccagcagc	cacagcagga	ggaggtgaca	180
tcacctgtcg	tgccccctc	tgtcaagact	ccgacacctg	aaccagctga	ggtggagact	240
cgcaagggtg	tgtctgatgca	gtgcaacatt	gagtcggtgg	aggagggagt	caaacaaccac	300
ctgacacttc	tgtctgaagtt	ggaggacaaa	ctgaaccggc	acctgagctg	tgacctgatg	360
ccaaatgaga	atatccccga	gttggcggct	gagctggtgc	agctgggctt	cattagttag	420
gctgaccaga	gcccgtttgac	ttctctgcta	gaagagactt	gaacaagttc	aattttgcca	480
ggaacagtac	cctcaactca	gcccgtgtca	ccgtctcctc	ttagagctca	ctcggggccag	540
gccttgatct	gcctgtggc	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	tccccaaacg	tttgttacca	cacttaaaaa	60
tcactgccat	cattaagcat	cagtttcaaa	attatagcca	ttcatgattt	actttttcca	120
gatgactatc	attattctag	tcctttgaat	ttgtaagggg	aaaaaaaaa	aaaacaaaaa	180
cttacgatgc	actttttctc	agcacatcag	atttcaaatt	gaaaattaaa	gacatgctat	240
ggtaatgcac	ttgctagtac	tacacacttt	ggtacaacaa	aaaacagagg	caagaaacaa	300
cggaaagaga	aaagccttcc	tttgttgggc	cttaaaactga	gtcaagatct	gaaatgtaga	360
gatgatctct	gacgatacct	gtatgttctt	attgtgtaaa	taaaattgct	ggtatgaaat	420
gacctaaaaa	aaaaaaaaa	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	cccagtggtg	acatgaccac	tccttttggg	180
aggcctgagg	tagaggggag	tggtatgtgt	tttctcagtg	gaagcagcac	atgagtgggt	240
gacaggatgt	tagataaaag	ctctagttag	ggtgtcattg	tcatttgaga	gactgacaca	300
ctcctagcag	ctggtaaaag	ggtgctggan	gccatggagg	anctctagaa	acattagcat	360
gggctgatct	gattacttcc	tggcatcccg	ctcactttta	tgggaagtct	tattagangg	420
atgggacagt	tttccatate	cttgcgttgg	agctctggaa	cactctctaa	atttccctct	480
attaaaaatc	actgccctaa	ctacacttcc	tccttggaagg	aatagaaatg	gaactttctc	540
tgacatannt	cttggcatgg	ggagccagcc	acaaatgana	atctgaacgt	gtccagggtt	600
ctcctganac	tcactacat	agaattggtt	aaaccctccc	ttggaataag	gaaaaa	656

<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
 ctagggtgttt ccatctatgt ttcaatctgt ccatctacca ggctctcgca taaaaacaaa 120
 acaaaaaaac gctgccaggt tttagaagca gttctggctc caaaaccatc aggatcctgc 180
 caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcattc 240
 aataactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttgagg 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
 tttatactgc atcctttaca ttagccacta aatacgttat tgcttgatga agacctttca 180
 cagaatoccta tggattgcag catttcactt ggctacttca taccatgcc ttaaagaggg 240
 gcagtttctc aaaagcagaa acatgcgcc agttctcaag ttttctctc aactccattt 300
 gaatgtaagg gcagctggcc cccaatgtgg ggaggtcga acattttctg aattccattt 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 ccanaanga 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 ctgcacgggc acagccctta cggattgcc 60

```

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

```

<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

```

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

```

<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

```

actagttcta tctggaaaaa gcccggttg 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 ttctggaaga gtcttcttat aaagtaattg tcatgccgac tacgaaagaa 360
aaatgcccccc gttgttgga gatacacagc ggagtcttca gatacactgt gtctctgatg 420
tgcagaagtt gtcagtggga aaatagtatt aacagctcac tcgagcaaga accctcctga 480
cagtactggg ctagaagttt ggatggatta tttacaatat aggaaagaaa gccaaagaatt 540
aggtnatgag tggatgagta aatggtggan gatggggaat tcaaatcaga attatggaag 600

```

```

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 gttgtaaag gttacatgat      300
tcatgatcag ggaaagcaaa tcagangttc agattcetta cctctgttca 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 ctcatctggt 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
ttaagacca cacaaggaag caaaatcttt ctgaaagaag taaatgatac acttctgggtg      180
aatgaattga aatcaaaaga atctgacatc atgacaacaa atgggtgtaat tcatgttgta      240
gataaactcc tctatccagc agacacacct gttggaaatg atcaactgct ggaaataactt      300
aataaattaa tcaaatacat ccaaattaag tttgttcgtg gtagcacctt caaagaaatc      360
cccgtagctg 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

```

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

<400> 33
 actagttatt tactttcctc cgettcagaa ggtttttcag actgagagcc taagcatact 60
 ggatctgttg tttcttttgg gtctcacctc atcagtggtc atagtggcag aaattataaa 120
 gaagggtgaa aggagcaggg aaaagatcca gaagcatgtt agttcgacat catcatcttt 180
 tcttgaagta tgatgcatat tgcattattt tatttgcaaa ctaggaattg cagtctgagg 240
 atcattttaga 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 gaaccacct 480
 ctgcacttaa agaagtctaa cagtacaaat acctatctat cttagatgga tntatttntt 540
 tntattttta aatattgtac tatttatggg 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 gaggggcagg 60
 tgatcagggc tgggtgtagca tccggttcct ttagtgagc taactgcatt tgtcactgat 120
 gaccaaggag gaaatcacta agacatttga gaagcagtgga tatgaacgtt cttggacaag 180
 ccacagttct gagccttaac cctgtagttt gcacacaaga acgagctcca cctccccctc 240
 ttcaggagga atctgtgagg atagattggc tggacttttc aatgggtctg ggttgcaagt 300
 gggcactggt atggctgggt atggagcgga cagccccagg aatcagagcc tcagcccggc 360
 tgcttggttg gaaggtagag gtgttcagca ccttcggaaa aagggcataa agtngtgggg 420
 gacaattctc agtccaagaa gaatgcattg accattgctg gctatttgct tncctagtan 480
 gaattggatn catttttgac cangatnntt ctncatgct tntttgcaat gaaatcaaat 540
 cccgcattat ctacaagtgg tatgaagtcc tgcnnccccc agagaggctg ttcaggcnat 600
 gtcttccaag ggcagggtgg gttacacat 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 cttcettacc cccgaatatt 60

```

ggtaagatcg agcaatggct tcaggacatg ggttctcttc tcctgtgacg attcaagtgc 120
tcaactgcag aagactggct tgtctcagtg tntcaacctc accagggctg tctcttggtc 180
cacacctcgc tccctgttag tgccgtatga cagcccccat canatgacct tggccaagtc 240
acggtttctc tgtgggtcaat gttggtnggc tgattgggtg aaagtanggt ggaccaaagg 300
aagnncgctg agcagncanc nccagttctg caccagcagc gcctccgtcc tactnggggtg 360
ttcngtttcc tcctggccct gngtgggcta nggcctgatt cgggaanatg cctttgcang 420
gaaggganga taantgggat ctaccaattg attctggcaa aacnatntct aagattnttn 480
tgctttatgt ggganacana tctanctctc atttnttgct gnanatnaca cctactcgt 540
gntcgancnc gtcttcgatt ttcgganaca cnccantnaa tactggcggt ctgttggtta 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 cggttctcgc cttctcccca tcccctactt tcctccctcc ctccctttcc 60
ctccctcgtc gactgttget tgctggctgc agactccctg accctccct caccctcccc 120
taacctcggg gccaccggat tgcccttctt ttccctgttg ccagcccagc cctagtgtca 180
gggcgggggc ctggagcagc ccgaggcact gcagcagaag ananaaaaga cagcacnaac 240
ctcagctcgc cagtcgggtc gctncttcc cgcgcagtg caatnagaca gacgcgctc 300
acctgctctg ggcacacgcg acccgtggtt gatttggcct tcagtggcat cacccttatg 360
ggtatttctt aatcagcget tgcaaagatg gttaacctat gctacgccag ggagatacag 420
gagactggat tggaacattt ttggggctca aaggtctgtt tggggtgcaa cactgaataa 480
ggatgccacc aaagcagcta cagcagctgc agatttcaca gcccagtggt gggatgctgt 540
ctcagganat naattgataa cctggctcat aacacattgt caagaatgtg gatttcccca 600
ggatattatt attgtttac cggggganag gataactgtt tcnctattt taattgaaca 660
aactnaaaca aaanctaagg aaatcc 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 naagtcang agaanaaaag angcatggaa cacaanccag gncgatggc 60
caccttccca ccagcancca gcgcccccca gcngccccc ngnccggang accangactc 120
cancctgnat caatctganc tctattcctg gcccatnctt acctcggagg tggangccgn 180
aaaggtcgca cnnncagaga agctgctgcc ancaccancc gcccnnccc tgnccggctn 240
nataggaac tggtgaccnn gctgcanaat tcatacagga gcacgcgang ggacnnnct 300
cacactgagt tnnngatgan geetnaccan ggacctnccc cagcnnattg annacnggac 360
tgccggaggaa ggaagacccc gnaacggatc ctggccggcn tgccacccc ccaccctag 420
gattatnccc cttgactgag tctctgagg gctaccgaa ccgcctcca ttccctacca 480
natnntgctc natcgggact gacangctgg ggatnggagg ggctatcccc cancatcccc 540

```

```

tnanaccaac agcnacngan natngggggt ccccnnggggtc ggngcaacnc tctncaccc 600
cggcgcnggc cttcggtgnt gtccctccntc aacnaattcc naaangggcg 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
canaaaaaaaaa aaaacatggc cgaaaccagn aagctgcgcg atggcgccac ggccccctctt 60
ctccccggcct gtgtccggaa ggtttccctc cgaggcgccc cggctcccgc aagcggagga 120
gagggcgggga cntgccgggg ccggagctca nagggccctgg ggccgctctg ctctcccgcc 180
atcgcaaggg cggcgctaac ctnaggcctc ccgcgaaagg tcccnange ggnggcggcg 240
gggggctgtg anaaccgcaa aaanaacgct gggcgcgeng cgaacccgct ccccccgcg 300
aaggananac ttccacagan gcagcgtttc cacagccan agccacnttt ctaggggtgat 360
gcaccccgagt aagttcctgn cggggaagct caccgctgtc aaaaaanctc ttcgctccac 420
cggcgcacna aggggangan ggcangangc tgccgcccgc acaggtcac tgatcacgtc 480
gcccgcccta ntctgctttt gtgaatctcc actttgttca accccaccgc cgtttctctc 540
ctccttgccg cttcctctna ccttaanaac cagcttccctc taccnatng tanttntctc 600
genenngtng 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 ttatcatcaat tcaaaacccc 60
tagaaaaacg tatacagatt atataagtag ggataagatt tctaacattt ctgggctctc 120
tgacccctgc gctagactgt ggaaagggag tattattata gtatacaaca ctgctgttgc 180
cttattagtt ataacatgat aggtgctgaa ttgtgattca caatttaaaa acactgtaat 240
ccaaactttt ttttttaact gtagatcatg catgtgaatg ttaatgttaa ttgtttcaan 300
gttgttatgg gtagaaaaaa ccacatgcct taaaatttta aaaagcaggg cccaaactta 360
ttagtttaaa attaggggta tgtttccagt ttgttattaa ntggttatag ctctgttttag 420
aanaaatcna ngaacangat ttngaaantt aagntgacat tatttncag tgacttgtaa 480
atltgaaatc anacacggca ccttccgttt tggtnctatt ggnntttgaa tccaancngg 540
ntccaaatct tnttgaaac ngtcnctta acttttttac nanatcttat ttttttattt 600
tggaatggcc ctatttaang ttaaaagggg ggggnccac naccattcnt gaataaaact 660
naatatatat ccttggtccc ccaaaattta aggnng 695

```

```

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

```


<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	tgcgctcgaa	gtgctaata	240
ggtgtaacaa	tagcacaat	cgaacttagg	atgtgtttct	tctcttctgt	gtttcgattt	300
tgatcaattc	tttaattttg	ggaacctata	atacagtttt	cctattcttg	gagataaaaa	360
ctaaatggat	cactgatatt	taagtcattc	tgcttctcat	ctnaatattc	catattctgt	420
attagganaa	antacctccc	agcacagccc	cctctcaaac	cccacccaaa	accaagcatt	480
tggaatgagt	ctcctttatt	tccgaantgt	ggatgggtata	acccataten	ctccaatttc	540
tgnttgggtt	gggtattaat	ttgaactgtg	catgaaaagn	ggnaatcttt	nctttgggtc	600
aaantttnc	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	tgccctctaa	aggctgacat	120
accttgggac	cctaattggg	cagagagtat	agccctagcc	cagtgggtgac	atgaccactc	180
cctttggggag	gctgaagtta	aaggggaatg	tatgtgtttt	ctcatggaag	cagcacatga	240
atnggtnaca	ngatgttaaa	ntaaggntct	antttgggtg	tcttgtcatt	tgaaaaantg	300
acacactcct	ancanctggg	aaaggggtgc	tggaagccat	ggaagaactc	taaaaacatt	360
agcatgggct	gatctgatta	cttcttgcca	tcccgetcac	ttttatggga	agtcttatta	420
naaggatggg	ananttttcc	atatecttgc	tgttggaact	ctggaacact	ctctaaattt	480
ccctctatta	aaaatcactg	nccttactac	acttcctcct	tganggaata	gaaatggacc	540
tttctctgac	ttagttcttg	gcatgggganc	cagcccaaat	taaaatctga	cttntccggt	600
ttctcngaa	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

```

actagtgtctg aggaatgtaa acaagtttgc tgggccttgc gagacttcac caggttgttt      60
cgatagctca cactcctgca ctgtgcctgt caccagga tgtctttttt aattagaaga      120
caggaagaaa acaaaaacca gactgtgtcc cacaatcaga aacctccgtt gtggcagang      180
ggccttcacc gccaccaggg tgtcccgcca gacagggaga gactccagcc ttctgaggcc      240
atcctgaaga attcctgttt ggggggttgg aaggaaaatc acccggtatt aaaaagatgc      300
tgttgcttgc ccgcgtngtn gggaagggaac tggtttctct gtgaatttct taaaagaaaa      360
atattttaag ttaagaaaaa aaaaaaaaaa      389

```

```

<210> 43
<211> 279
<212> DNA
<213> Homo sapien

```

```

<400> 43
actagtgaca agctcctggg cttgagatgt cttctcgtta aggagatggg ctttttgagg      60
gtaaaggata aaatgaatga gttctgtcat gattcactat tctagaactt gcatgacctt      120
tactgtgtta gtcctttgaa tgttcttgaa attttagact ttctttgtaa acaaataata      180
tgtccttatac attgtataaa agctgttatg tgcaacagtg tggagatcct tgtctgattt      240
aataaaatac ttaaacactg 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 taaaaaacaa      60
caacaacaac aataacaata aatcctaagt gtaaatcagt tattctaccc cctaccaagg      120
atatcagcct gttttttccc ttttttctcc tgggaataat tgtgggcttc tcccaaatt      180
tctacagcct ctttccctctt ctcattgctt agcttccctg tttgcacgca tgcgttgtgc      240
aagantgggc tgtttngctt ggantnccgt ccnagtggaa ncatgctttc ccttgttact      300
gttggaagaa actcaaacct tcnancccta 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 gggaaatcac 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

```

```

ggtgaagctc ttggaaaaaa ttnactagaa tactttttgt gttaagttaa ttacataagt      300
tgtatittgt taactttatc tttctacact acaattatgc ttttgtatat atattttgta      360
tgatggatat ctataattgt agattttgtt tttacaagct aatactgaag actcgactga      420
aatattatgt atctagccca tagtattgta ctttaactttt acaggggtgaa aaaaaaattc      480
tgtgtttgca ttgattatga tattctgaat aaatatggga atatatttta atgtgggtaa      540
aaaaaaaaaa aaaaaggaa

```

```

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

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

```

```

<400> 46
actagttcta gtaccatggc tgtcatagat gcaaccatta tattccattt agtttcttcc      60
tcaggttccc taacaattgt ttgaaactga atatatatgt ttatgtatgt gtgtgtgttc      120
actgtcatgt atatgggtgta 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 ctttaacttta      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 gacctgannt aatananact tgaataatga atagttaatt      720
taggnntggg c

```

```

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

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

```

```

<400> 47
tgcgngccgg tttggccctt ctttgtanga cactttcate cgccctgaaa tcttcccgat      60
cgtaataaac tcctcaggtc cctgcctgca cagggttttt tcttantttg ttgcctaaca      120
gtacacccaa tgtgacatcc tttcaccaat atngattnet tcataccaca tctcnatgg      180
anaegactnc aacaattttt tgatnaccen aaanactggg ggctnnaana agtacantct      240
ggagcagcat ggacctgten gcnactaang gaacaanagt nntgaacatt tacacaacct      300
ttggatatgt ttactgaaag anagaaacat gcttctnncc ctgaccacg aggncaaccg      360
caganattgc caatgccaaag tccgagcggg tagatcaggg aatacattcc atggatgcat      420
tacatacntt gtccccgaaa nanaagatgc cctaanggct tcttcnactt ggtccngaaa      480
acantacac ctggtgcttg ganaacanat tctttggaag atcatctggc acaagttccc      540
cccagtgggg tttnccttgg cacctanctt accanactna ttccggaancc attctttgcc      600
ntggcnttnt nttgggacca ntcttctcac aactgnaccc

```

<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 tgttcttgaa aaagtgattt gtattagttt tacatttggt ttttggaaga 180
 ttatatttgt atatgtatca tcataaaata tttaaataaa aagtatctt 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 atgagtggtt gctgaagggg ccccttctgc attttcatta taacccaatt 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
 ttctttaaag cagctatatc ccaacccatg actttggaga tataacctatn aaaccaatat 420
 aacagcangg ttattgaagc agctttctca aatgttgctt cagatgtgca agttgcaaat 480
 tttattgtat 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 ggcttgtgce ctgtttcact tatagggtct agaatgcttg 60
 tgttgagtaa aaaggagatg cccaatatte aaagctgcta aatgttctct ttgccataaa 120
 gactccgtgt aactgtgtga acacttgga tttttctct ctgtcccgag gtctgtctct 180
 gcttttcttt ttgggttctt tctagaagat tgagaaatgc atatgacagg ctgagancac 240
 ctccccaaac acacaagctc tcagccacan gcagcttctc cacagcccca gcttcgcaca 300
 ggctcctgga nggctgcctg ggggaggcag acatgggagt gccaaaggtg ccagatgggt 360
 ccaggactac aatgtcttta tttttaactg tttgccactg ctgccctcac cctgcccgg 420
 ctctggagta ccgtctgccc canacaagtg ggantgaaat ggggggtggg gggaaactg 480
 attcccantt agggggtgcc taactgaaca gtagggatan aaggtgtgaa cctgngaant 540

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gcttttataa attatnttcc ttgttanatt tatttttttaa tttaatctct gttnaactgc      600
ccngggaaaa ggggaaaaaa aaaaaaaaaat tctnttttaa 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 ccagggttagc tgaagtttgg gtctgggact ggagattggc cattaggcct      60
cctganattc cagctccctt ccaccaagcc cagtcttget acgtggcaca gggcaaacct      120
gactcccttt gggcctcagt tccccctccc ctccatgana tgaaaagaat actacttttt      180
cttgtttggt taaconttget ggacncaaag tgtngtcatt attgttgtat tgggtgatgt      240
gtncaaaact gcagaagctc actgcctatg agaggaanta agagagatag tggatganag      300
ggacanaagg agtcattatt tggatatagat ccaccntcc caacctttct ctccctcagtc      360
cctgcnctc atgtntctgg tntggtgagt cctttgtgcc accanccatc atgcttttga      420
ttgctgccat cctgggaagg ggggtgnatcg 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 gaacttttgc gctttttgtgc ctctcacagg cgcctaaagt cattgcatg      60
ggaggaagac gatttggggg gggagggggg gggggcangg tccgtggggc tttccctant      120
ntatctccat ntccantggn cnntgtcgcc tcttccctcg tencattnga anttantccc      180
tggnccccnn nccctctccn nccnncncc ccccccctcg ncnccctcnn cttttnttan      240
nettccccat ctccntcccc cctnanngtc ccaacnccgn cagcaatnnc ncacttnctc      300
netcenenec tccnnccggt cttctnttct cnacntntnc ncnntnccn tgcenntnaa      360
annctctccc cnetgcaanc gattctctcc ctccnccnnc ctnccactc cntncttctc      420
nncgctcct nttctcnnc ccacctctcn ccttcgnccc cantacnctc nccncccttn      480
cgnntcnttn nnntcctenn accnccncc tcccttccc cctcttctcc cgggtntntc      540
tetctccncc nncnccncc cncnccncc nngcgnccnt ttccgccccn cncnccntt      600
ccttctctc cantccatcn cntntnccat nctnccncc nctcacnccc gctncccccn      660
ntctctttca cacngtcc      678

```

```

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

<220>

```

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

<400> 53
 tgaagatcct ggtgtcgcca tggggcgcgcg ccccgcccgt tgttaccggt attgtaagaa 60
 caagccgtac ccaaagtctc gcttctgcgcg aggtgtccct gatgccaaaa ttgcgatttt 120
 tgacctgggg cggaaaaang caaaantgga tgagtctccg ctttgtggcc acatggtgtc 180
 agatcaatat gagcagctgt cctctgaagc cctgnangct gcccgaattt gtgccataaa 240
 gtacatggta aaaagtngtg gcnaagatgc ttccatatcc ggggtgcggnt ccaccccttc 300
 cacgtcatcc gcatcaacaa gatgttgtec tgtgctgggg ctgacaggct cccaacaggc 360
 atgcgaagtg cctttggaaa acccanggca ctgtggccag gggtcacatt gggccaattn 420
 atcatgttca tccgcaccaa ctgcagaaca angaactgt 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 ctttghatat gttaacctgt 60
 tttaatgccaa aaagtgtgtc ttgtccacaa ttcccttaag acctcttcag aaagggattt 120
 gtttgcccta atgaatactg ttgggaaaaa acacagtata atgagtgaag agggcagaag 180
 caagaaattt ctacatctta gogactccaa gaagaatgag tatccacatt tagatggcac 240
 attatgagga ctttaattctt tccttaaaaca caataatgtt ttcttttttc ttttattcac 300
 atgatttcta agtatatttt tcatgcagga cagtttttca accttgatgt acagtgactg 360
 tgttaaatTT ttctttcagt ggcaacctct ataactttta 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 ataatgaaat 60
 gatgttaagc tttttgaaaa gtttaggtta aacctactgt tgttagatta 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 tgttagtctc 420
 ttgggatcct gtgtaaaact gttctcatta aacaccaaac agttaagtcc attctctggt 480

```

actagctaca aattccgttt catattctac ntaacaattt aaattaactg aaatatttct 540
anatggtcta cttctgtcnt ataaaaacna aacttgantt nccaaaaaaa aaaaaaaaaa 600
aaaaaa 606

```

```

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

```

```

<400> 56
actagtatat ttaaacttac aggettattt 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 cacctgcccc ctgagttggg gaaagaggat 120
aatcagtgag cactgttctg ctcagagctc ctgatctacc ccaccacctt ggatccagga 180
ctgggtcaaa gctgcatgaa accaggccct ggcagcaacc tgggaatggc tggaggtggg 240
agagaacctg acttctcttt cccctcctcc cctccaacat tactggaact ctatcctgtt 300
agggatcttc tgagcttggt tccctgctgg gtgggacaga agacaaaagga gaaggggangg 360
tctacaanaa gcagcccttc tttgtcctct ggggttaatg agcttgacct ananttcacg 420
gaganaccan aagcctctga tttttaattt centnaaatg tttgaagtnt atatntacat 480
atatatatat cttttaatnt ttgagtcttt gatatgtctt aaaatccant cccctctgcn 540
gaaacctgaa ttaaaaccat gaanaaaaat gtttncctta aagatgttan taattaattg 600
aaacttgaaa aaaaaaaaaa aa 622

```

```

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

```

```

<400> 58
gaacaaattc tgattggtta 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 ttatttgttt tgacttgaat 360
ttatccacca aagacttcatt ttgtgtatca tcaataaagt tgtatgttcc aactgaaaaa 420
aaaaaaaaa aaa 433

```

```

<210> 59
<211> 649

```

<212> DNA
<213> Homo sapien

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

<400> 59

actagttatt	atctgacttt	cngggtataa	tcatttetaat	gagtggtgaag	tagcctctgg	60
tgtcatttgg	atttgcattt	ctctgatgag	tgatgctatc	aagcaccttt	gctgggtgctg	120
ttggccatat	gtgtatgttc	cctggagaag	tgctctgtgct	gagccttgge	ccacttttta	180
attaggcgtn	tgtcttttta	ttactgagtt	gtaaganttc	tttatatatt	ctggattcta	240
gacccttate	agatacatgg	tttgcaaata	ttttctccca	ttctgtgggt	tgtgttttca	300
ctttatcgat	aatgtcctta	gacatataat	aaatttgtat	tttaaaagtg	acttgatttg	360
ggctgtgcaa	ggtggggtca	cgcttgtaat	cccagcactt	tgggagactg	aggtgggtgg	420
atcatatgan	gangctagga	gttcgaggtc	agcctggcca	gcatagcgaa	aacttgtctc	480
tacnaaaaaa	acaaaaatta	gtcaggcatg	gtgggtgcacg	tctgtaatac	cagcttctca	540
ggangctgan	gcacaaggat	cacttgaacc	ccagaangaa	gangttgcag	tgantcgaag	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	tcactgacaa	acatggggaa	gtgtgcccag	ctggctggaa	60
acctggcagt	gataccatca	agcctgatgt	ccaaaagagc	aaagaatatt	tctccaagca	120
gaagtgagcg	ctgggctgtt	ttagtgccag	gctgcggtgg	gcagccatga	gaacaaaaacc	180
tcttctgtat	tttttttttc	cattagtana	acacaagact	cngattcagc	cgaattgtgg	240
tgtcttacia	ggcagggctt	tcctacaggg	ggtgganaaa	acagcctttc	ttcctttggg	300
aggaatggcc	tgagttggcg	ttgtgggcag	gctactgggt	tgtatgatgt	attagtagag	360
caaccatta	atcttttgta	gtttgtatna	aacttgantc	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

egggactgga	atgtaaagtg	aagttcggag	ctctgagcac	gggtctttcc	cgccgggtcc	60
tcctctccca	gacccagag	ggagaggccc	accccgccca	gccccgccc	agccctgct	120
caggtctgag	tatggctggg	agtcgggggc	cacaggcctc	tagctgtgct	getcaagaag	180


```

actggatcag ggtanctaca agtggccggg ccttgccctt gggattctac cctgttccta      240
atttggtgtt ggggtgcggg gtccctggcc cccctttcca cactnccctc ctcngacag      300
caacctccct tggggcaatt gggcctggnt ctcncccgnt tgttgcnaac ctttgttggg      360
ttaaggncct taaaaatgtt annttttccc ntgcnggggt 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 ggaaagtga agacgcttag      120
gctgtcaaca cttaaaggaa gtccccttga agcccagagt ggacagacta gaccattga      180
tggggccact ggccatggtc cgtggacaag acattccngt gggccatggc acaccggggg      240
ggatcaaaat gtgtacttgt ggggtctcgc ccttgccaa aaccaaacca ntccactcc      300
tgtenttgga ctttcttccc attccctcct ccccaaagt ccttccctc ctcctctgc      360
ccctcctgtg tttttggaat tetgtttccc tcaaaattgt taatttttta ntttngacc      420
atgaacttat gtttggggtc nangttcccc ttnccaatgc atactaatat attaatgggt      480
atztattttt gaaatatttt ttaatgaact tggaaaaaat tnntggaatt tccttncttc      540
cntttntttt ggggggggtg gggggntggg ttaaaatttt tttggaance cnatnggaaa      600
ttnttacttg gggccccctt naaaaaantn anttccaatt cttnnatngc cctnttccn      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 gegtcttctga cgtggcggtc ttggcgccac tgctgcgaga      60
cccggccctg gacctcaagg tcatccactt ggtgcgtgat cccgcgcggg tggcgagttc      120
acggatccgc tgcgcgccag gctcctccg tgagagccta cagggtgggt gcagccgaga      180
ccgcgagctc accgcctgcc cttcttggag gccgcggggc acaagcttgg cgccananaa      240
gaaggcgtng gggggccgca aantaccacg ctctgggcgc tatggaangt cctcttgcaa      300
taatattggt tnaaaanctg canaanagcc cctgcancec cctgaactgg gntgcagggc      360
cncttacctn gtttggntgc ggttaciaag aacctgtttn ggaaaaccct nccnaaaacc      420
ttccgggaaa attntncaaa ttttnttgg ggaattnttg ggtaaaaccct ccnaaaatgg      480
gaaacntttt tgccctnnaa antaaaccat tnggttccgg gggccccccc ncaaaaccct      540
ttttnttttt tttntgeccc cantnncccc cggggggccc ttttttngg ggaaaanccc      600
ccccctncc nanantttta aaaggngggg anaatttttn nttnecccc gggncccccn      660
ggngntaaaa nggtttcncc ccccgagggg gnggggnnnc ctcnnaaacc cntntcnnaa      720
ccnctttttn n                                              731

```

<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 atgttggttc tgtagagaaa catcttgagg agcagattgc 120
 taaagttgat agagaatatg aagaatgcat gtcagaagat ctctcggaag atattaaaga 180
 gattagagat aagtatgaga agaaagctac tctaattaag tcttctgaag aatgaagatn 240
 aaatgttgat catgtatata tatccatagt gaataaaaatt 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 gggtctccaa ctgaggcagt gcatgtgtgg cagagagagg 60
 caggaagctg gcagtggcag cttctgtgtc tagggagggg tgtggctccc tccctccctg 120
 tctgggaggt tggagggaag aatctaggcc ttagcttgcc ctccctgccac ccttcccctt 180
 gtagatactg ccttaacact ccctcctctc tcagctgtgg ctgccacca agccagggtt 240
 ctccgtgctc actaatttat ttccaggaaa ggtgtgtgga agacatgagc cgtgtataat 300
 atttgtttta acattttcat tgcaagtatt gaccatcacc 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
 actagttccc tatgatcatt aaactcattc tcagggttaa gaaaggaatg taaattttctg 60
 cctcaatttg tacttcatca ataagttttt gaagagtgca gatttttagt caggctcttaa 120
 aaataaaact acaaactctg atgcatttct aaattctgca aatgtttcct ggggtgactt 180
 aacaaggaat aatcccacaa tatacctagc tacctaatac atggagctgg ggctcaaccc 240
 actgttttta aggatttgcg cttacttgtg gctgaggaaa aataagtagt tccgagggaa 300
 gtagttttta aatgtgagct tatagatngg aaacagaata tcaacttaat tatggaaaatt 360
 gttagaaacc tgttctcttg ttatctgaat cttgattgca attactattg tactggatag 420

```

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

```

```

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

```

```

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

```

```

<400> 67
caccattaaa gctgcttacc aagaacttcc ccagcatttt gacttccttg tttgatagct      60
gaattgtgag caggtgatag aagagccttt ctagttgaac atacagataa tttgctgaat      120
acattccatt taatgaaggg gttacatctg ttacgaagct actaagaagg agcaagagca      180
taggggaaaa aaatctgata agaacgcata aaactcacat gtgccccctc tactacaaac      240
agattgtagt gctgtggttg tttattccgt tgtgcagaac ttgcaagctg agtcactaaa      300
cccaaagaga ggaaattata ggtaggttaa acattgtaat ccaggaact aagtttaatt      360
cacttttgaa gtgttttggt ttttattttt ggttgtcttg atttactttg ggggaaaang      420
ctaaaaaaaa agggatatca atctctaatt cagtgcccac taaaagtgtt ccctaaaaag      480
tctttactgg aanttatggg actttttaag ctccaggtnb tttggctctc caaattaacc      540
ttgcatgggc cccttaaaat tgttgaangg cattcctgcc tctaagtttg gggaaaattc      600
ccccnttttn aaaatttgga                                     620

```

```

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

```

```

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

```

```

<400> 68
actagtagct ggtacataat cactgaggag ctatttctta acatgctttt atagaccatg      60
ctaagtctag accagtattt aagggtctaat ctcacacctc cttagctgta agagtctggc      120
ttagaacaga cctctctgtg caataacttg tgccactgg aaatccctgg gccggcattt      180
gtattggggg tgcaatgact cccaagggcc aaaagagtta aaggcacgac tgggatttct      240
tctgagactg tggtgaaact ccttccaagg ctgagggggg cagtangtgc tctgggaggg      300
actcggcacc actttgatata tcaacaagcc acttgaagcc caattataaa attgttattt      360
tacagctgat ggaactcaat ttgaaccttc aaaactttgt tagtttatcc tattatattg      420
ttaaaccctaa ttacatttgt ctagcattgg atttgggtcc tgtngcatat gtttttttcn      480
cctatgtgct cccctccccc nnatcttaat ttaaacncea attttgcnat tcnccnnnnn      540
nanannanna a                                     551

```

```

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

```

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

<400> 69
 cagaaatgga aagcagagtt ttcattttctg tttataaaacg tctccaaaca aaaatggaaa 60
 gcagagtttt cattaaatcc ttttaccttt tttttttctt ggtaatcccc tcaaataaca 120
 gtatgtggga tattgaatgt taaagggata tttttttcta ttatttttat aattgtacaa 180
 aattaagcaa atgttaaaag ttttatatgc tttattaatg ttttcaaag gtatnatata 240
 tgtgatacat tttttaagct tcagttgctt gtcttctggt 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 aaggcggtcc tcacggttagc tgaagatata 60
 cttcgaaaga cccctgtaaa agagcccaac agtgaaaatg tagatatcag cagtggagga 120
 ggcgtgacag gctggaagag caaatgctgc tgagcattct cctgttccat cagttgccat 180
 ccactacccc gttttctctt cttgctgcaa aataaaccac tctgtccatt ttttaactcta 240
 aacagatatt tttgtttctc atcttaacta tccaagccac ctattttatt tgttctttca 300
 tctgtgactg cttgtgact ttatcataat tttcttcaaa caaaaaaatg tatagaaaaa 360
 tcatgtctgt gacttcattt ttaaatgnta cttgtcagc 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
 gacaaaagcgt taggagaaga anagaggcag ggaanaactnc ccaggcacga tggccnccctt 60
 cccaccagca accagcgccc cccaccagcc cccaggcccg gacgacgaag actccatcct 120
 ggattaatct nacctctntc gcctgnccca ttctacctc ggaggtggag gccggaaagg 180
 tcncaccaag aganaactg ctgccaacac caaccgcccc agccctggcg ggcacganag 240
 gaaaactggtg accaatctgc agaattctna gaggaanaag cnaggggccc cgcgctnaga 300
 cagagctgga tatgangcca gaccatggac nctacncccn ncaatncana cgggactgcy 360
 gaagatggan gaccnccgac nngatcagcg cngctnncca nccccacc cctatgaatt 420
 attcccgctg aangaatctc tgannggett ccannaaagc gcctcccnc cnaacgnaan 480

```

tncaacatng ggattanang ctgggaactg naaggggcaa ancctnnaat atccccagaa      540
acaanctctc ccnaanaaac tggggcncct catnggtggn accaactatt aactaaaccg      600
cacgccagn  aantataaaa ggggggcccc tcnccggnng accccctttt gtcccttaat      660
ganggttatc cnccttgctg accatggtnc ccnnttctgt ntgnatgttt ccnctcccct      720
ccnctatnt  cnagccgaac tcnnatttnc cggggggtgc natchantng tncnctttt      780
ttngttgncc cngccctttc cgnoggaacn cgtttccccg ttantaacgg caccgggggn      840
aagggtgntt ggccccctcc ctecc                                           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 gaccggcgga cggcgacgtc tcttttgact      60
aaaagacagt gtccagtgtc ccngcctagg agtctacggg gaccgcctcc cgcgccgcca      120
ccatgcccaa cttctctggc aactggaaaa tcatccgacg ggaaaacttc gangaatgac      180
tcnaantgct gggggtgaat gtgatgctna ngaanattgc tgtggctgca gcgtccaagc      240
cagcagtgga gatcnaacag gagggagaca ctttctacat caaaacctcc accaccgtgc      300
gcaccacaaa gattaacttc nnngttgggg aggantttga ggancaaaact gtggatngga      360
ngcctgtnaa aacctggtga aatgggagaa tganaataaa atggtctgtg ancanaaaact      420
cctgaaagga gaagggcccc anaactcctg gaccngaaaa actgaccenc cnatngggga      480
actgatnctt gaacctgaa  cgggggggat ganccttttt tnttgcncnc naanggggtc      540
tttcnntttc ccaaaaaaaa                                           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
ctggggancc ggcggttnngc nccatntcnn gncggaagg tggcaataaa aancnctga      60
aacgcncnaa naaacatgcc naagatatgg acgaggaaga tngnctttc nngnacaanc      120
gnannagga  acanaacaaa ctcnangagc tctcaagcta atgccgcggg gaaggggccc      180
ttggccacnn gtggaattaa gaaatctggc aaanngtann tgttccttgt gcctnangag      240
ataangnacc ctttatttca tctgtattta aacctctctn ttccctgnca taacttcttt      300
tnccacgtan agntggaant anttgttgtc ttggactgtt gtncatttta gannaaactt      360
ttgttcaaaa aaaaaataa                                           379

```

```

<210> 74
<211> 437
<212> DNA
<213> Homo sapien

```

```

<220>

```

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

<400> 74
 actagtccag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60
 ctaggtgttt ccactatgt ttcaatctgt ccactacca ggctcgcga taaaaacaaa 120
 acaaaaaaac gctgccaggt ttanaagca gttctggtct caaaaccatc aggatcctgc 180
 caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcatct 240
 aatcactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttggtg 300
 gaataagtta taatcagtat tcactctctt gttttttgtc actcttttct ctctnattgt 360
 gtcatttgta ctgtttgaaa aatatttctt 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
 ctccgtcgc gccaaagatga tgtgcggggc gccctcgcgc acgcagccgg ccaccgccga 60
 gaccagcac atgcgcgacc aggtgaggtc ccagcttgaa gagaaagaaa acaagaagtt 120
 ccctgtgttt aaggccgtgt cattcaagag ccagggtggtc gcggggacaa actacttcat 180
 caagggtcac gtgcggcagc aggacttcgt acacctgcga gtgttccaat ctctccctca 240
 tgaaaaacaag cccttgacct tatctaacta ccagaccaac aaagccaagc atgatgagct 300
 gacctatttc tgatcctgac ttgggacaag gcccttcagc cagaagactg acaaagtcac 360
 cctccgtcta ccagagcgtg cacttggtgat cctaaaataa gcttcatctc cgggctgtgc 420
 ccttggggtg gaaggggcan gatctgcact gcttttgcat ttctcttctt aaatttcatt 480
 gtgttgatct tttccttcca ataggtgatc ttnattactt tcagaatatt ttccaaatna 540
 gatataattt 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
 gtttatccta tctctccaac cagattgtca gctccttgag ggcaagagcc acagtatatt 60
 tccctgtttc ttccacagtg cctaataata ctgtggaact aggttttaata aatttttta 120
 ttgatgttgt tatgggcagg atggcaacca gaccattgtc tcagagcagg tgcgtgctct 180
 ttcttggtta ctocatgttg gctagcctct ggtaacctct tacttattat cttcaggaca 240
 ctactacag ggaccaggga tgatgcaaca tcttgtctt tttatgacag gatgtttgct 300
 cagcttctcc aacaataaaa agcacgtggt aaaacaactg cggatattct ggactgtttt 360
 taaaaatat acagtttacc gaaaatcata ttatcttaca atgaaaagga ntttatagat 420
 cagccagtga acaacctttt cccaccatac aaaaattcct tttcccgaan gaaaanggct 480

```

ttctcaataa ncctcacttt cttaanatct tacaagatag ccccganac ttatcgaaac      540
tcatttttagg caaatatgan ttttattgtt cgttacttgt ttcaaaattt ggtattgtga      600
atatcaatta ccaccccat 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
ctgcagcccc ggggatccac taatctacca nggttatttg gcagetaatt ctanatttgg      60
atcattgccc aaagttgcac ttgctggtct cttgggattt ggcccttgga aggtatcata      120
catanganta tgccanaata aattccattt ttttgaaaat canctccttg gggctgggtt      180
tggtccacag cataacangc actgctctct tacctgtgag gaatgcaaaa taaagcatgg      240
attaagttag aaggagact ctgagccttc agcttctctaa attctgtgtc tgtgactttc      300
gaagtttttt aaacctctga atttgtacac atttaaaatt tcaagtgtac tttaaaataa      360
aatacttcta atgggaacaa aaaaaaaaaa aaaaaa                                     396

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

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

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<400> 78
gcactctagc cgcgcactca cacaaggcag gtgggtgagg aaatccagag ttgccatgga      60
gaaaattcca gtgtcagcat tcttgtctct tgtggccctc tctacactc tggccagaga      120
taccacagtc aaacctggag ccaaaaagga cacaaggac tctcgacca aactgccccca      180
gacctctctc agaggttggg gtgaccaact catctggact cagacatatg aagaagctct      240
atataaatcc aagacaagca acaaaccctt gatgattatt catcacttgg atgagtgtcc      300
acacagtcna gctttaaaga aagtgtttgc tgaaaataaa gaaatccaga aattggcaga      360
gcagtttgtc ctctcaatc tggtttatga aacaactgac aaacaccttt ctctgatgg      420
ccagtatgtc ccaggattat gtttgttgac ccatctctga cagttgaagc cgatatcttg      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 tntctttttn aaacaatntg tttctacntt gnganctgat ttctaaaaaa      780
aataatnttt ggc                                     793

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<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 ggtgggaggc cccacccttc tcccctaggc gctgttcttg ctccaaaggg 60
 ctccgtggag agggactggc agagctgang ccacctgggg ctggggatcc cactcttctt 120
 gcagctgttg agcgcaccta accactgggc atgccccac cctgctctc cgcacccgct 180
 tcttcccgac cccangacca ggctaactct cccctcctct tgccctccctc ctgccccctg 240
 tgccctctgat cgtangaatt gangantgtc ccgccttggt gctganaatg gacagtggca 300
 ggggctggaa atgggtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt gcnccccccc 360
 tgcaagaccg agattgaggg aaancatgtc tgctgggtgt gacctgttt cctctccata 420
 aantnccct gtgaactca naaaaaaaa 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 gtcattgaaac ttgagtttaa attttatata 60
 taaaactaaa agtaatgtc actttagcaa cacatactaa aattggaacc atactgagaa 120
 gaatagcatg acctccgtgc aaacaggaca agcaaatttg tgatgtgttg attaaaaaga 180
 aataaataaaa tgtgtatatg tgtaacttgt atgtttatgt ggaatacaga ttgggaaata 240
 aaatgtattt cttactgtga aaaaaaaaa aaaaaaaaa 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 cctgggttac ctttgtgcag tagaagctag tgagcatgtg 60
 agcaagcggg gtgcacacgg agactcatcg ttataattta ctatctgcc aagtagaaaa 120
 gaaaggctgg ggatatttgg gttggcttgg ttttgatttt ttgcttgttt gtttgttttg 180
 tactaaaaa gtattatctt ttgaatatcg tagggacata agtatataca tgttatccaa 240
 tcaagatggc tagaatggtg cttttctgag tgtctaaaac ttgacacccc tggtaaactc 300
 ttcaacacac ttccactgcc tgcgtaatga agttttgatt catttttaac cactggaatt 360
 tttcaatgcc gtcattttca gttagatnat ttggcacttt gagattaaaa tgccatgtct 420
 atttgattag tcttattttt ttatttttac aggcattatca gtctcactgt tggctgtcat 480
 tgtgacaaag tcaaataaac cccnaggac aacacacagt atgggatcac atattgtttg 540
 acattaagct ttggccaaaa aatgttgcac gtgttttacc tcgacttgct aaatcaatan 600
 canaaaggct ggctnataat gttggtggtg aaataattaa tnantaacca aaaaaaaaaa 660
 aaaaaaaaa a 671

<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 acctttttgt 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
 gagtgaattt tcttaagatc ctggaggatt tcttaccctc gtcctcttcg agaccccgat 240
 cgtgatgttg aggaagagcc acctgcaaga tggacacgag ccacaagctg cactgtgaac 300
 ctgggcactc cgcgcgatg ccaccggcct gtgggtctct gaagggacct cccccaatcg 360
 gaactgccaaa ttctcgggtt tgccccggga tattatacaa nattatttgt atgaataatg 420
 annataaaac acacctcgtg gcancaanaa 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
 tgggtgatct tggtctctgt gagctgctgg gacgggatct aaaagactat tctggaagct 60
 gtgggtccaan gcatttttget ggcttaacgg gtcccggaac aaaggacacc agctctctaa 120
 aattgaagtt tacccganat aacaatcttt tgggcagaga tgcctatttt aacaaacncc 180
 gtccctgcgc aacaacnaac aatctctggg aaataccggc catgaacntg ctgtctcaat 240
 cnancatctc tctagctgac cgatcatatc gtcccagatt actacanatc ataataattg 300
 atttctgtga 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 taaaaacat gtgctgtacc 60
 aanagtgtgc tcctggctgc tttgatgtca gtgctgtac tccacctctg cggcgaatca 120
 gaagcaagca actttgactg ctgtcttgga tacacagacc gtattcttca tcctaaatctt 180
 attgtgggct tcacacggca gctggccaat gaaggctgtg acatcaatgc tatcatcttt 240
 cacacaaaga aaaagtgtgc tgtgtgcgca aatccaaaac agacttgggt gaaatatatt 300
 gtgctgtctc tcagtaaaaa agtcaagaac atgtaaaaac tgtggctttt ctggaatgga 360
 attggacata gcccagaagc agaaagaact tgctgggggt ggaggtttca cttgcacatc 420
 atgganggtt tagtgcttat cttatttgtg cctcctggac ttgtccaatt natgaagtta 480
 atcatattgc atcatanttt gctttgttta acatcacatt naaattaaac tgtattttat 540
 gttatttata gctntagggt ttctgtgttt aactttttat acnaantttc ctaaactatt 600
 ttggnttant gcaanttaaa aatttatatt ggggggggaa taaatattgg antttctgca 660
 gccacaagct ttttttaaaa aaccantaca nccnngttaa atggtnggtc ccnaatgggt 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 ttttttgtc caagtgttta tcaactaaac 60
 cttgtgttag gtaagaatgg aatttattaa gtgaatcagt gtgaccttc ttgtcataag 120
 attatcttaa agctgaagcc aaaatatgct tcaaaagaaa angactttat tgttcattgt 180
 agttcataca ttcaaagcat ctgaactgta gtttctatag caagccaatt acatccataa 240
 gtggagaang aaatagatta atgtcnaagt atgattgggt gagggagcaa gggtgaagat 300
 aatctggggt tgaaattttc tagttttcat tctgtacatt tttagtnga catcagattt 360
 gaaatattaa tgtttacctt tcaatgtgtg gtatcagctg gactcantaa caccctttc 420
 ttccctnngg gatggggaat ggattattgg aaaatggaaa gaaaaaagta cttaaagcct 480
 tcctttcnca gtttctggct cctaccctac tgatttancc agaataagaa aacattttat 540
 catctctgc tttattccca ttaatnaant tttgatgaat aaatctgctt ttatgcnnac 600
 ccaaggaatt nagtggnttc ntenttgt 628

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

<220>
 <221> misc_feature

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

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

<400> 87

tttttttattt	tttttagaga	gtagttcagc	ttttattttat	aaattttattg	cctgtttttat	60
tataacaaca	ttatactgtt	tatggtttta	tacatatggg	tcaaaatgta	taatacatca	120
agtagtacag	ttttaaaatt	ttatgcttaa	aacaagtttt	gtgtaaaaaa	tgcagataca	180
ttttacatgg	caaatcaatt	tttaagtcac	cctaaaaatt	gatttttttt	tgaaatttaa	240
aaacacattt	aatttcaatt	tctctcttat	ataaccttta	ttactatagc	atggtttcca	300
ctacagttta	acaatgcagc	aaaattccca	tttcacggta	aattggggtt	taagcggcaa	360
ggttaaaatg	ctttgaggat	cctnaatacc	ctttgaactt	caaataaagg	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	tgattatttt	60
tatttttattt	tatttttcga	gactccgtct	caaaaaaaaa	aaaaaaaaaa	agaatcacaa	120
ggtattttgct	aaagcathtt	gagctgcttg	gaaaaaggga	agtagttgca	gtagagtttc	180
ttccatcttct	ttgggtgctgg	gaagccatat	atgtgtcttt	tactcaagct	aaggggtata	240
agcttatgtg	ttgaatttgc	tacatctata	tttcacatat	tctcacaata	agagaatttt	300
gaaatagaaa	tatcatagaa	catttaagaa	agtttagtat	aaataatatt	ttgtgtgttt	360
taatcccttt	gaagggatct	atccaaagaa	aatattttac	actgagctcr	ttcctacacg	420
tctcagtaac	agatcctgtg	ttagtctttg	aaaatagctc	atttttttaa	tgtcagttag	480
tagatgtagc	atacatatga	tgtataatga	cgtgtattat	gttaacaatg	tctgcagatt	540
ttgtaggaat	acaaaacatg	gcctttttta	taagcaaaac	gggccaatga	ctagaataac	600
acatagggca	atctgtgaat	atgtattata	agcagcattc	cagaaaagta	gttgggtgaaa	660
taatttttcaa	gtcaaaaagg	gatatggaaa	gggaattatg	agtaacctct	attttttaag	720
ccttgctttt	aaatttaaag	ctacagccat	ttaagccttg	aggataataa	agcttgagag	780
taataatggt	aggttagcaa	aggtttagat	gtatcacttc	atgcatgcta	ccatgtagat	840
aatgcagctc	ttcgagtcac	ttctggtcac	tcaagatatt	cacccttttg	cccatagaaa	900
gcaccctacc	tcacctgctt	actgacattg	tcttagctga	tcacaagatc	attatcagcc	960
tccattattc	cttactgtat	ataaaataca	gagttttata	ttttcctttc	ttcgtttttc	1020
accatattca	aaacctaaat	ttgtttttgc	agatggaatg	caaagtaatc	aagtgttcgt	1080
gctttcacct	agaagggtgt	ggtcctgaag	gaaagaggtc	cctaaatata	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
atltgaagtt	caaagggtga	ttcaggatcc	tcaaagcatt	ttaaccttgc	cgcttaaaac	1500
ccaattttacc	gtgaaatggg	aattttgctg	cattgttaaa	ctgtagtgga	aaccatgcta	1560
tagtaataaa	ggttatataa	gagagaaatt	gaaattaaat	gtgtttttta	atttcaaaaa	1620
aaaatcaatc	tttaggatga	cttaaaaatt	gatttgccat	gtaaaatgta	tctgcatttt	1680
ttacacaaaa	cttggtttta	gcataaaatt	ttaaaactgt	actacttgat	gtattatata	1740
ttttgaacca	tatgtattaa	accataaaca	gtataatgtt	gttataataa	aacaggcaat	1800
aaattttataa	ataaaagctg	aaaaaaaaaa	aaaaaaaaaa	aaaa		1844

<210> 89

<211> 523

<212> DNA

<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	tgactgttag	tcactcacag	taaggaagaa	aactagcaaa	taagacgatt	120
acaatatgat	gtagaaaatg	ctaagccaga	gatatagaaa	ggtcctattg	ggtccttctg	180
tcacctgtgc	tttccacatc	cctacccttc	acaggccttc	cctccagctt	cctgcccccg	240
ctccccactg	cagatccctt	gggattttgc	ctagagctaa	acgagganat	gggccccctg	300
gccctggcat	gacttgaacc	caaccacaga	ctgggaaagg	gagcctttcg	anagtggatc	360
actttgatna	gaaaacacat	agggaattga	agagaaantc	cccaaattggc	caccctgtgc	420
gggtgtcaag	aaaagtgtgc	agaatggata	aatgaaggat	caaggggaatt	aatanatgaa	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

ccagtgtggg	ggaatgcaaa	gattaccccg	gaagcttttcg	agaagctggg	attccctgca	60
gcaaaggaaa	tagccaatat	gtgtcgtttc	tatgaaatga	agccagaccg	agatgtcaat	120
ctcaccaccc	aactaaatcc	caaagtcaaa	agcttcagcc	agtttatctc	agagaaccag	180
gggagccttc	aagggcattg	agaaaaatcag	ctgttcagat	aggcctctgc	accacacagc	240
ctcttttctc	tctgatcctt	ttcctcttta	cggcacaaca	ttcatgtttg	acagaacatg	300
ctggaatgca	attgtttgca	acaccgaagg	atttcctgcg	gtcgcctctt	cagtaggaag	360
cactgcattg	gtgataggac	acggtaattt	gattcacatt	taacttgcta	gttagtgata	420
aggggtggta	cacctgtttg	gtaaaaatgag	aagcctcgga	aacttgggag	cttctctcct	480
accactaatg	gggagggcag	attattactg	ggattttctcc	tgggggtgaat	taattttcaag	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
tggeagagtt	tctgatgctt	aataaacatt	tgttctgate	agataagtgg	aaaaaattgt	120
catttcttta	ttcaagccat	gctttttctgt	gatattctga	tcctagttga	acatacagaa	180

ataaatgtct	aaaacagcac	ctcgattctc	gtctataaca	ggactaagtt	caactgtgatc	240
ttaaataagc	ttggctaaaa	tgggacatga	gtggaggtag	tcacacttca	gcgaagaaag	300
agaatctcct	gtataatctc	accaggagat	tcaacgaatt	ccaccacact	ggactagtgg	360
atcccccg	ctgcaggaat	togatatcaa	gcttatcgat	accgtcgacc	tcgagggggg	420
gcccggtagc	caattcgccc	tatagtga	cgtattacgc	gcgctcactg	gccgtcgttt	480
tacaacgtcg	tgactgggaa	aacctggcg	ttaccaact	taatcgccct	gcagcacatc	540
cccctttcgc	cagctggcgt	aatagcgaan	agcccgacc	gatcgccctt	ncaacagttg	600
cgcagcctga	atggcgaaatg	ggaacgcgcc	tgtagcggcg	cattaaagcg	cggcnggggtg	660
tggnggntcc	cccacgtgac	cgntacactt	ggcagcgcct	tacgcgggtc	nttcgctttc	720
ttcccttcc	ttctcgacc	gttcgcggg	tttccccg	agctnttaat	cgggggngctc	780
cctttanggg	tncnaattaa	nggnttacng	gaccttngan	cccaaaaact	ttgattaggg	840
ggaaggtccc	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	gccaaagctta	tttaagatca	cagtgaactt	agtcctgtta	120
tagacgagaa	tcgaggtgct	gttttagaca	tttatttctg	tatgttcaac	taggatcaga	180
atatcacaga	aaagcatggc	ttgaataagg	aatgacaat	ttttccact	tatctgatca	240
gaacaaatgt	ttattaagca	tcagaaactc	tgccaacact	gaggatgtaa	agatcaataa	300
aaaaaataat	aatcatnann	naaanannan	nngaaggcg	gccgccaccg	cgggtggagct	360
ccagcttttg	ttccctttag	tgagggttaa	ttgcgcgctt	ggcgtaatac	atgggtcatag	420
ctgtttcctg	tgtgaaattg	ttatccggct	cacaattccn	cncaacatac	gagccgggaa	480
gcntnangtg	taaaagcctg	gggggtgccta	attgagtga	ctnactcaca	ttaattgngt	540
tgcgtccac	ttgcccgctt	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	gctgtctg	tgccacctt	ggaatctggc	tgaactggct	gggaggacca	60
agactgcggc	tggggtgggc	anggaaggga	accgggggct	gctgtgaagg	atcttggaac	120
ttccctgtac	ccaccttccc	cttgcttcat	gtttgtanag	gaaccttggtg	ccggccaagc	180
ccagtttct	tgtgtgatac	actaatgtat	ttgctttttt	tgggaaatan	anaaaaatca	240
attaaattgc	tantgtttct	ttgaannnnn	nnnnnnnnnn	nnnnnnnnng	ggggncgccc	300
ccnccgngga	aacnccccct	tttgctccct	ttaattgaaa	ggttaattng	cnncntggc	360
gttaancct	gggccaaaanc	tngttncccg	tgntgaaatt	gttnatcccc	tcccaaattc	420
ccccccncc	ttccaaaacc	ggaaancctn	annntgttna	ancccggggg	gttgccctaan	480
ngnaattnaa	ccnaaccccc	ntttaaatng	nnnttgcncn	ccacnngccc	cnctttccca	540

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 taatttggga gaaaatattt ttttaagtagt 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 agttgttaa tgaccaaaca ttctaaaaga aatgcaaaaa aaaagtattat 360
 tttcaagcct tcgaactatt taaggaaagc aaaatcattt cctaaatgca tatcatttgt 420
 gagaatttct cattaatatc ctgaatcatt catttcacta aggcctcatgt tnactccgat 480
 atgtctctaa gaaagtacta tttcatgggc caaacctggg tgccatantt gggtaaaggc 540
 tttcccttaa gtgtgaaant atttaaaatg aaattttcct ctttttaaaa 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 cctttacccc accacctcag cttcaacagc 180
 agcaggtgaa acaacccatc cagcctccac ctnaggaaat atttgttccc acaaccaagg 240
 agccatgcca ctcaaagggt ccacaacctg naaacacaaa nattccagag ccaggctgta 300
 ccaagggtccc tgagccaggg ctgtaccaan gtccctgagc caggttgtag caangtcctt 360
 gagccaggat gtaccaaggt ccctgancca ggttggtccaa ggtccctgag 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

<400> 96

tttttttttt	tttttttttt	ggaattaaaa	gcaatttaaat	gagggcagag	caggaaacat	60
gcattttcttt	tcattcgaat	cttcagatga	accctgagca	gccgaagacc	agaaaagcca	120
tgaagactttt	ctgcttaatt	caggggctta	caggattctt	cagagtgtgt	gtgaacaaaa	180
gctttatagt	acgtattttt	aggatacaaa	taagagagag	actatggctt	ggggtgagaa	240
tgtactgatt	acaaggtcta	cagacaatta	agacacagaa	acagatggga	agaggggtgnc	300
cagcatctgg	ngggttgctt	ctcaagggct	tgtctgtgca	ccaaattact	tctgcttggg	360
cttctgctga	gctgggcctg	gagtgaccgt	tgaaggacat	ggctctggta	cctttgtgta	420
gcttgnacac	ggaacttttg	tgtatccttg	ctcaggaaact	ttgatggcac	ctggctcagg	480
aaacttgatg	aagccttggt	caagggacct	tgatgcttgc	tggtcagggg	accttggngn	540
ancctgggct	canggacctt	tgncncaacc	ttggcttcaa	gggacccttg	gnacatcctg	600
gcnnagggac	ccttgggncc	aacctggggc	ttnagggacc	ctttggntnc	nancttggc	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	tgcttgagcc	ctgccagccc	aaggttccag	240
agccatgcca	ccccaaagtg	cctgagccct	gccttccaat	agtcaatcca	gcaccagccc	300
agcagaanac	caagcagaag	taatgtggtc	cacagccatg	cccttgagga	gccggccacc	360
agatgctgaa	tcccctatcc	cattctgtgt	atgagtccca	tttgcttgc	aatttagcatt	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	ctgttgccgc	atgagttccc	agcagcagaa	60
gcagccctgc	atcccacccc	ctcagcttca	gcagcagcag	gtgaaacagc	cttgccagcc	120
tccacctcag	gaaccatgca	tccccaaaac	caaggagccc	tgccacccca	aggtgcctga	180
gccctgccac	cccaaagtgc	ctgagccctg	ccagcccaaag	gttccagagc	catgccaccc	240
caaggtgcct	gagccctgcc	cttcaatagt	cactccagca	ccagcccagc	agaanaccaa	300
gcagaagtaa	tgtggtccac	agccatgccc	ttgaggagcc	ggccaccana	tgctgaatcc	360
cctatcccat	tctgtgtatg	agtcccattt	gccttgcaat	tagcattctg	tctcccccaa	420
aaaagaatgt	gcatgaagc	tttcttctct	acacactctg	agtctctgaa	tgaagctgaa	480
ggtcttaant	acagantcag	ttttcagctg	ctcagaattc	tctgaagaaa	agatttaaga	540
tgaagggcaa	atgattcagc	tccttattac	cccattaaat	tcnctttcaa	ttccaaaaaa	600

<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
 accattttaa aaaatcagt aaggatttga gctgctcaat tcaggacaaa gcattcgaac 120
 ggtcctgacg ttttgagatc caaagtggca ggaggctctgt gttgtcatgg tgaactggag 180
 tttctcttgt gagagttccc tcatctgaaa tcatgtatct gtctcacaaa tacaagcata 240
 agtagaagat ttgttgaaga catagaaccc ttataaagaa ttattaacct ttataaacat 300
 ttaaagtctt gtgagcacct gggaattagt ataataacaa tgttnatatt tttgatttac 360
 attttgaag gctataattg tatcttttaa gaaaacatac cttggatttc tatgttgaaa 420
 tggagatttt taagagtttt aaccagctgc tgcagatata ttactcaaaa cagatatagc 480
 gtataaagat atagtaaatg catctcctag agtaatatc acttaacaca ttggaaacta 540
 ttatttttta gatttgaata tnaatgttat tttttaaaca cttgttatga gttacttggg 600
 attacatttt gaaatcagtt cattccatga tgcantattc tgggattaga ttaagaaaga 660
 cggaaaa 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 tacactgate taaaggacat atatataacc 60
 ctttaaaaaa aaaatcactg cctcattctt atttcaagat gaatttctat acagactaga 120
 tgtttttctg aagatcaatt agacattttg aaaatgattt aaagtgtttt ctttaatgtt 180
 ctctgaaaac aagtttcttt ttagttttta accaaaaaag tgcccttttt gtcactggat 240
 tctcctagca ttcattgattt ttttttcata caatgaaatt aaaattgcta aaatcatgga 300
 ctggctttct ggttggattt caggtaagat gtgtttaagg ccagagcttt tctcagtatt 360
 tgattttttt ccccaatatt tgatttttta aaaatatata catnggtgct gcatttatat 420
 ctgctgggtt aaaattctgt catatttcac ttctagcctt ttagttatgg caaatcatat 480
 ttacttttta cttaaagcat ttggttattt ggantatctg gttctannet aaaaaaanta 540
 attctatnaa ttgaantttt ggtactcnnn catatttggg 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	gtctccccc	ttgctctatg	aaactgcaca	ttggtcattg	360
tgaatatttt	tttttttgcc	aaggctaate	caattattat	tatcacattt	accataattt	420
atrrtgtoca	ttgatgtatt	tattttgtaa	atgtatcttg	gtgctgctga	attttctatat	480
tttttgtaca	taatgcnttt	anatatacct	atcaagtttg	ttgataaatg	acncaatgaa	540
gtgnncnncn	ttgngnggtg	aatttaatat	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

cgctctaagc	acttagacta	catcagggaa	gaacacagac	cacatccctg	tcctcatgcg	60
gcttatgttt	tctggaagaa	agtggagacc	nagtccttgg	ctttagggct	ccccggctgg	120
gggctgtgca	ntccggtcag	ggcgggaagg	gaaatgcacc	gctgcatgtg	aacttacagc	180
ccaggcggat	gccccctccc	ttagcactac	ctggcctcct	gcateccctc	gcctcatggt	240
cctcccacct	tcaaanaatg	aanaacccca	tgggcccagc	cccttgccct	ggggaaccaa	300
ggcagccttc	caaaactcag	gggctgaagc	anactattag	ggcaggggct	gactttgggt	360
gacactgccc	atccctcttc	agggcagctc	angtcaccen	ggncctctga	accagcctg	420
ttcctttgaa	aaagggcaaa	actgaaaagg	gcttttccct	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	aatgcccac	atggcagaac	60
ctgcancctt	tggncactgc	anatggaaac	ctctcagtg	cttgacatca	ccctaccctt	120
gcgggtgggtc	tccaccacaa	ccactttgac	tctgtgggtc	ctgnanggtg	gnttctcctg	180
actggcagga	tggaccttan	ccnacatate	cctctgttcc	ctctgctnag	anaaagaatt	240
cccttaacat	gatataatcc	acccatgcaa	ntngctactg	gccagctac	catttaccat	300
ttgcctacag	aatttcattc	agtctacact	ttggcattct	ctctggcgat	agagtgtggc	360
tgggctgacc	gaaaaagggtg	ccttacacac	tggccccac	cctcaaccgt	tgacncatca	420
gangcttgcc	tcctccttct	gattnncccc	catgttggat	atcaggggtg	tcnagggatt	480
ggaaaagaaa	caaaac					496

<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 ggtttcnggg gtggctcttg ccaactggga agaagccgtg gtgtctctac      120
ctgttcaact cngtttggtg ctgggggatc aactnggggc tatggaagcg gctnaactgt      180
tgttttgggt gaagggctgg taattggctt tgggaagtng cttatngaag ttggcctngg      240
gaagttgcta ttgaaagtng cnttggaagt ngntttgggt ggggggtttt ctggtggcct      300
ttgttnaatt tgggtgcttt gtnaatggcg gccccctcnc ctgggcaatg aaaaaaatca      360
ccnatgcngn aaacctcnac nnaacagcct gggcttcctt cacctcgaaa aaagttgctc      420
cccccccaaa aaaggncaan cccctcaann tggaangttg aaaaaatcct cgaatgggga      480
ncccnaaaac aaaaancccc cntttcccn gnaanggggg aaataccncc cccccactta      540
cnaaaaccct tntaaaaaac cccccgggaa aaaaaa      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 tgtgtcccgga gagtaaggag agaagctact attgattaga      60
gcctaaccce ggtaactgc aagaagaggc gggatacttt cagctttcca tgtaactgta      120
tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaact gaatccact      180
tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tgggtatgatg      240
tgcacacttg ctagactcan aaaaaatact actctcataa atgggtggga gtattttggt      300
gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg      360
gacatttagt tagtgctttt tatataccag gcatgatgct gagtgcact cttgtgtata      420
tttccaaatt tttgtacagt cgctgcacat atttgaaatc atatattaag acttccaaaa      480
aatgaagtec ctggtttttc atggcaactt gatcagtaaa ggattcncct ctgtttggta      540
cttaaaacat ctactatatn gttnanatga aattcctttt ccccnctcc cgaaaaaana      600
aagtggtggg gaaaaaaa      619

```

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

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

```

<400> 106
cattggtncct ttcatttgct ntggaagtgt nnatctctaa cagtggacaa agttcccngt      60
gccttaaact ctgtnacact tttgggaant gaaaanttng tantatgata ggttattctg      120
angtanagat gttctggata ccattanatn tgccccccngt gtcagaggct catattgtgt      180
tatgtaaagt gtatntcatt cgctactatn antcaattng aaatanggtc tttgggttat      240
gaatantnmg cagcncanct nanangctgt ctgtngtatt cattgtggtc atagcacctc      300
acancattgt aacctcnatc nagtgagaca nactagnaan ttcttagtga tggctcanga      360
ttccaaatgg nctcatntcn aatgtttaaa agttanttaa gtgtaagaaa tacagactgg      420
atgttccacc aactagtacc tgtaatgacn ggctgtgcc 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
gttgagtcctg tactaaacag taagatatct caatgaacca taaattcaac tttgtaaaaa      60
tcttttgaag catagataat attgtttggt aaatgtttct tttgtttggt aaatgtttct      120
tttaaagacc ctctatttct ataaaaactct gcatgtagag gcttgtttac ctttctctct      180
ctaaggttta caataggagt ggtgatttga aaaatataaa attatgagat tggttttcct      240
gtggcataaa ttgcatcact gtatcatttt ctttttttaa cggtaagant ttcagtttgt      300
tggaaaagtaa 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
atctttcttcc cttaattagt tnttatttat 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 agnccactt tctaanggtc tctanagctt actaancett ttgaccctt      480
accctggnta ctctgcccct ca                                502

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```

<210> 109
<211> 1308

```

<212> DNA

<213> Homo sapien

<400> 109

```

acccgaggtc tcgctaaaat catcatggat tcacttggcg ccgtcagcac tcgacttggg      60
tttgatcttt tcaaagagct gaagaaaaca aatgatggca acatcttctt ttccctgtg      120
ggcatcttga ctgcaattgg catggctctc ctggggaccc gaggagccac cgcttcccag      180
ttggaggagg tgtttctact tgaaaaagag acgaagagct caagaataaa ggctgaagaa      240
aaagaggtga ttgagaacac agaagcagta catcaacaat tccaaaagt tttgactgaa      300
ataagcaaac tctaataatga ttatgaactg aacataacca acaggctgtt tggagaaaaa      360
acatacctct tccttcaaaa atacttagat tatgttgaaa aatattatca tgcattctctg      420
gaacctgttg attttgtaaa tgcagccgat gaaagtcgaa agaagattaa ttcttgggtt      480
gaaagcaaaa caaatgaaaa aatcaaggac ttgttcccag atggctctat tagtagctct      540
accaagctgg tgcagggtgaa catggtttat tttaaagggc aatgggacag ggagttaaag      600
aaagaaaaata ctaagggaaga gaaatttttg atgaataaga gcacaagtaa atctgtacag      660
atgatgacac agagccattc ctttagcttc actttcctgg aggacttgca ggccaaaatt      720
ctagggatcc catataaaaa caacgacctc agcatgtttg tgcttctgcc caacgacatc      780
gatggcctgg agaagataat agataaaata agtcctgaga aattggtaga gtggactagt      840
ccagggcata tggagaaaag aaaggtgaat ctgcacttgc cccggtttga ggtggaggac      900
agttacgata tagaggcggt cctggctgcc atggggatgg gcgatgcctt cagtgagcac      960
aaagccgact actcggaat gtcgtcaggc tccgggttgt acgcccagaa gttcctgcac      1020
agttcctttg tggcagtaac tgaggaaggc accgaggctg cagctgccac tggcataggg      1080
tttactgtca catccgcccc aggtcatgaa aatgttctact gcaatcatcc ctctctgttc      1140
ttcatcaggc acaatgaatc caacagcatc ctcttctctc gcagattttc ttctccttaa      1200
gatgatcgtt gccatggcat tgctgctttt agcaaaaaac aactaccagt gttactcata      1260
tgattatgaa aatcgcccat tcttttaaat ggtggctcac ttgcattt      1308

```

<210> 110

<211> 391

<212> PRT

<213> Homo sapien

<400> 110

```

Met Asp Ser Leu Gly Ala Val Ser Thr Arg Leu Gly Phe Asp Leu Phe
 1          5          10          15
Lys Glu Leu Lys Lys Thr Asn Asp Gly Asn Ile Phe Phe Ser Pro Val
          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
          100          105          110
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
          145          150          155          160
Lys Asp Leu Phe Pro Asp Gly Ser Ile Ser Ser Ser Thr Lys Leu Val
          165          170          175

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Leu Val Asn Met Val Tyr Phe Lys Gly Gln Trp Asp Arg Glu Phe Lys
 180 185 190
 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
 355 360 365
 Pro Phe Leu Phe Phe Ile Arg His Asn Glu Ser Asn Ser Ile Leu Phe
 370 375 380
 Phe Gly Arg Phe Ser Ser Pro
 385 390

<210> 111
 <211> 1419
 <212> DNA
 <213> Homo sapien

<400> 111
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 ccagccacca cgtctctctc aaaaacccga ggtctcgcta aaatcatcat ggattcactt 120
 ggcgccgtca gcaactcgact tgggtttgat cttttcaaag agctgaagaa aacaaatgat 180
 ggcaacatct tcttttcccc tgtgggcata ttgactgcaa ttggcatggt cctcctgggg 240
 acccgaggag ccaccgcttc ccagttggag gaggtgtttc actctgaaaa agagacgaag 300
 agctcaagaa taaaggctga agaaaaagag gtggttaagaa taaaggctga aggaaaagag 360
 attgagaaca cagaagcagt acatcaacaa ttccaaaagt ttttgactga aataagcaaa 420
 ctactaatg attatgaact gaacataacc aacaggctgt ttggagaaaa aacatacctc 480
 ttctttcaaa aatacttaga ttatgttgaa aaatattatc atgcatctct ggaacctgtt 540
 gattttgtaa atgcagccga tgaaagtcga aagaagatta attcctgggt tgaaagcaaa 600
 acaaatgaaa aaatcaagga cttgttccca gatggctcta ttagtagctc taccaagctg 660
 gtgctggtga acatggttta ttttaaaggg caatgggaca gggagttaa gaaagaaaat 720
 actaaggaag agaaattttg gatgaataag agcacaagta aatctgtaca gatgatgaca 780
 cagagccatt ccttttagctt cactttcctg gaggacttgc aggccaaaat tctagggtt 840
 ccatataaaa acaacgacct aagcatgttt gtgcttctgc ccaacgacat cgatggcctg 900
 gagaagataa tagataaaat aagtcctgag aaattggtag agtggactag tccagggcat 960
 atggaagaaa gaaagggtgaa tctgcacttg ccccggtttg aggtggagga cagttacgat 1020
 ctgagggcgg tcctggctgc catggggatg ggcatgcct tcagtgcgca caaagccgac 1080
 tactcgggaa tgcgtcagg ctccgggttg tacgccaga agttcctgca cagttccttt 1140
 gtggcagtaa ctgaggaagg caccgaggtt gcagctgcc ctggcatagg ctttactgtc 1200

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acatccgccc caggtcacga aaatgttcac tgcaatcatc ccttcctgtt cttcatcagg 1260
cacaatgaat ccaacagcat cctcttcttc gccagatttt cttctcctta agatgatcgt 1320
tgccatggca ttgctgcttt tagcaaaaaa caactaccag tggtactcat atgattatga 1380
aaatcggtcca ttctttttaa tggtgggtca cttgcattt 1419

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

<400> 112

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

Glu Ala Ala Ala Ala Thr Gly Ile Gly Phe Thr Val Thr Ser Ala Pro
 355 360 365
 Gly His Glu Asn Val His Cys Asn His Pro Phe Leu Phe Phe Ile Arg
 370 375 380
 His Asn Glu Ser Asn Ser Ile Leu Phe Phe Gly Arg Phe Ser Ser Pro
 385 390 395 400

<210> 113
 <211> 957
 <212> DNA
 <213> Homo sapien

<400> 113
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 cctctctccc atctgtttct gtgtcttaat tgtctgtaga ccttgtaatc agtacattct 720
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 cttttctggt ctccggctgc tcagggttca tctgaagatt cgaatgaaaa gaaatgcatg 900
 tttctgctc tgccctcatt aaattgcttt taattccaaa aaaaaaaaaa aaaaaaa 957

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

<400> 114
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 Gln Gln Gln Gln Val Lys Gln Pro Ser Gln Pro Pro Pro Gln Glu Ile
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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

145
Lys

150

155

160

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

 <220>
 <221> misc_feature
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 <223> n = A,T,C or G

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 angtanagat gttctggata ccattanatn tgccccngt gtcagaggct catattgtgt 180
 tatgtaaatg gtatntcatt cgctactatn antcaattng aaatanggtc tttgggttat 240
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 acancattgt aacctcnatc nagtgagaca nactagnaan ttccctagtga tggctcanga 360
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<210> 116
 <211> 3079
 <212> DNA
 <213> Homo sapien

<400> 116
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 aaagagggtca aagtgggttta tagggggcgc tgagggtctc ccacattctc tggcctaaac 180
 cttgcaggca gatctgacca gtgggtctct ggatagctgt gccttcccta acaaaaaaat 240
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<210> 117

<211> 6921

<212> DNA

<213> Homo sapien

<400> 117

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 ctttgccagg gcttcnntnt taccaaaacn ncttctcnng gatttttaat tccccatng 540
 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 gaatccact 180
 tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tggatgatg 240
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 gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg 360
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata 420
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 aatgaagtc ctggtttttc atggcaactt gatcagtaaa ggattcnct ctgtttggta 540
 cttaaaacat ctactatatn gttanatga aattcctttt ccccnctcc cgaaaaana 600
 aagtgggtgg gaaaaaaaaa 619

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

<400> 122
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tctgtgagcga	ctccaaaggc	agcaatgaac	ttcatcaagt	tccatcgaac	tgtgactgtc	180
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caaagaaatt	cggagggcag	cactgtgaaa	tagataagtc	aaaaacctgc	tatgagggga	300
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<210> 123

<211> 2294

<212> DNA

<213> Homo sapien

<400> 123

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tgtgtgtcca	acaagtactt	ctccaacatt	cactgggtgca	actgcccata	gaaattcgga	240
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tgatttttct	gatg					2294

<210> 124

<211> 956

<212> DNA

<213> Homo sapien

<400> 124

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cagattgaga	acctcaagga	ggagctggcc	tacctgaaga	agaaccacga	ggaggagatg	180
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aaccgcaagg	atgccgagga	ttggttcttc	agcaagacag	aggaactgaa	ccgcgagggtg	360
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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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ttggaaaact	gcttttcttc	tgagaacctt	attctgaatg	tcacaaactt	taccaaactt	180
tctaagtcca	gagctaaact	agtactgttt	aagttactat	tgactgaatt	ttcttctatt	240
tctgttttagc	cagtgttacc	aaggtaagct	ggggaatgaa	gtataccaac	ttctttcaga	300
gcatttttagg	acattatggc	agcttttagaa	ggctgtcttg	tttctagcca	agggagagcc	360

agcgcagggtt	ttggatacta	gagaaagtca	tttgcttgta	ctattgccat	tttagaaagc	420
tctgatgtga	attcaaattt	tacctctgtt	acttaaagcc	aacaatttta	aggcagtagt	480
tttact						486

<210> 126
 <211> 3552
 <212> DNA
 <213> Homo sapien

<400> 126						
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<210> 127

<211> 754

<212> DNA

<213> Homo sapien

<400> 127

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accaccttct	aatactttta	atacccaatc	aaaattttatt	atacatatgt	atcatagata	660
ctcatctgta	aagctgtgct	tcaaaatagt	gatctcttcc	caacattaca	atatatatta	720
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<210> 128

<211> 374

<212> DNA

<213> Homo sapien

<400> 128

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ttccccctgcc	cttggttaagt	aactcttgat	ggagaaagga	ttaaagactc	ttatttaacc	180
aaaaaacaga	gccagcta	catttccaaa	ggttagtata	tcctgtctga	cctcttcttt	240
ggtttaattg	aataaaacta	tatgttcata	tatgtattaa	aacaactcag	aataacatct	300
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aacttaaaaa	gctg					374

<210> 129

<211> 546

<212> DNA

<213> Homo sapien

<400> 129

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cctcatttct	gcctactgat	ttccttggag	cattcatctg	aatattaccg	tttgctgtgt	180
aacctggtac	atacatagca	tgactccctg	gaatagagtg	ggctgggggtg	cttatgctgg	240
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<210> 130

<211> 5156

<212> DNA

<213> Homo sapien

<400> 130

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ttgatcggga	acttcacaga	caaactggta	atggattccg	ctgcctcaac	tgcaatgaca	240
acactgatgg	cattcactgc	gagaagtgca	agaatggctt	ttaccggcac	agagaaaggg	300
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 <211> 671
 <212> DNA
 <213> Homo sapien

<400> 131

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<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>

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

<400> 134

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 <212> DNA
 <213> Homo sapien

<400> 135						
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ccatgtatgt	gggtgaagtg	tcaccacacg	ccttctgtgg	ggccctgggc	accctgcacc	660
agctgggcat	cgtcgtcgcc	atcctcatcg	cccaggtgtt	cggcctggac	tccatcatgg	720
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agctgttccg	ctcccccgcc	taccgccagc	ccatcctcat	cgtgtgggtg	ctgcagctgt	1020
cccagcagct	gtctggcatc	aacgtgtgtc	tctattactc	cacgagcacc	ttcgagaagg	1080
cgggggtgca	gcagcctgtg	tatgccacca	ttggctccgg	tatcgtcaac	acggccttca	1140


```

ctgtcgtgtc gctgtttgtg gtggagcgag caggccggcg gaccctgcac ctcataggcc 1200
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ttgatccct gttaccaga gaatatatac attctttatc ttgacattca aggcatttct 2760
atcacatatt tgatagttgg tgttcaaaaa aacactagtt ttgtgccagc cgtgatgctc 2820
aggcttgaag tcgcattatt ttgaatgtga agggaa 2856

```

<210> 136
 <211> 356
 <212> DNA
 <213> Homo sapien

```

<400> 136
ggtggagcca aatgaagaaa atgaagatga aagagacaga cacctcagtt tttctggatc 60
aggcattgat gatgatgaag attttatctc cagcaccatt tcaaccacac caccggcttt 120
tgaccacaca aaacagaacc aggactggac tcagtggaa ccaagccatt caaatccgga 180
agtgtacttt cagacaacca caaggatgac tgatgtagac agaaatggca ccactgctta 240
tgaaggaaac tggaaaccag aagcacaccc tcccctcatt caccatgagc atcatgagga 300
agaagagacc ccacattcta caagcacaat ccaggcaact cctagtagta caacgg 356

```

<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
gcaggtggag aagacathtt attgttctct gggctctctg aggccattg gtggggctgg 60

```

gtcactggct	gcccccgaa	cagggcgctg	ctccatggct	ctgcttgtgg	tagtctgtgg	120
ctatgtctcc	cagcaaggac	agaaactcag	aaaaatcaat	cttcttatcc	tcattcttgt	180
cctttttctc	aaagacatcg	gcgaggtaat	ttgtgccctt	tttacctcgg	cccgcgacca	240
cgctaaggcc	aaantttccag	acanayggcc	gggcgggtnc	nataggggan	cccaacttgg	300
ggacccaaac	tctggcgcg	aaacacangg	gcataagctt	gnttcctgtg	gggaaa	356

<210> 138
 <211> 353
 <212> DNA
 <213> Homo sapien

<400> 138						
aggtccagtc	ctccacttgg	cctgatgaga	gtggggagtg	gcaagggacg	tttctcctgc	60
aatagacact	tagatttctc	tcttgtggga	agaaaccacc	tgtccatcca	ctgactcttc	120
tacattgatg	tggaaattgc	tgctgctacc	accacctcct	gaagaggctt	ccctgatgcc	180
aatgccagcc	atcttggcat	cctggccctc	gagcaggetg	cggttaagtag	cgatctcctg	240
ctccagccgt	gtctttatgt	caagcagcat	cttgtactcc	tggttctgag	cctccatctc	300
gcacgcggagc	tcactcagac	ctcgscgcsg	mssmcgctam	gccgaattcc	agc	353

<210> 139
 <211> 371
 <212> DNA
 <213> Homo sapien

<400> 139						
agcgtggctg	cggccgaggt	ccatccgaag	caagattgca	gatggcagtg	tgaagagaga	60
agacatatcc	tacacttcaa	agctttgggtg	caattcccat	cgaccagagt	tggtccgacc	120
agccttggaa	aggtcactga	aaaatcttca	attggattat	gttgacctct	accttattca	180
ttttccagtg	tctgtaaagc	caggtgagga	agtgatccca	aaagatgaaa	atggaaaaat	240
actatttgac	acagtggatc	tctgtgccac	gtgggaggcc	gtggagaagt	gtaaagatgc	300
aggattggac	ctgcccgggc	ggccgctcga	aagccgaatt	ccagcacact	ggcggccgtt	360
actagtggat	c					371

<210> 140
 <211> 370
 <212> DNA
 <213> Homo sapien

<400> 140						
tagcgtggtc	gcggccgagg	tccatctccc	tttgggaact	agggggctgc	tggtgggaaa	60
tgggagccag	ggcagatggt	gcattccttt	gtgtccctgt	aaatgtggga	ctacaagaag	120
aggagctgcc	tgagtggta	tttctcttcc	tggtaatcct	ctggcccagc	ctcatggcag	180
aatagaggta	tttttaggct	atttttgtaa	tatggcttct	ggtcaaaatc	cctgtgtagc	240
tgaattccca	agccctgcat	tgtacagccc	cccactcccc	tcaccaccta	ataaaggaat	300
agttaacact	caaaaaaaaa	aaaaaacctg	cccgggcggc	cgctcgaaag	cgaattcca	360
gcacactggc						370

<210> 141
 <211> 371
 <212> DNA
 <213> Homo sapien

<400> 141						
tagcgtggtc	ggggccgagg	tcctctgtgc	tgcctgtcac	agcccgatgg	taccagcgca	60
gggtgtaggc	agtgccaggag	ccctcatcca	gtggcaggga	acaggggtca	tcactatccc	120

```

aaggagcttc aggggtcctgg tactcctcca cagaatactc ggagtattca gagtactcat      180
catcctcagg ggggtacccgc tcttcctcct ctgcatgaga gacgcggagc acaggcacag      240
catggagctg ggagccggca gtgtctgcag cataactagg gaggggtcgt gatccagatg      300
cgatgaactg gccctggcag gcacagtgtc gactcatctc ttggcgacct gcccgggcgg      360
ccgctcgaag c                                     371

```

```

<210> 142
<211> 343
<212> DNA
<213> Homo sapien

```

```

<400> 142
gcgttttgag gccaatggtg taaaaggaaa tatcttcaca taaaaactag atggaagcat      60
tgtcagaaac ctctttgtga tgtttgcttt caactcacag agttgaacat tccttttcat      120
agagcagttt tgaaacactc tttttagtaa ttgcaagcg gatgattgga tcgctatgag      180
gtcttcattg gaaacgggat acctttacat aaaaactaga cagtagcatt ctcagaaatt      240
tctttgggat gtgggcattc aaccacaga ggagaacttc atttgataga gcagttttga      300
aacacccttt ttgtagaatc tacaggtgga catttagagt gct                               343

```

```

<210> 143
<211> 354
<212> DNA
<213> Homo sapien

```

```

<400> 143
aggctctgatg gcagaaaaac tcagactgtc tgcaacttta cagatgggtgc attggttcag      60
catcaggagt gggatgggaa ggaaagcaca ataacaagaa aattgaaaga tgggaaatta      120
gtggtggagt gtgtcatgaa caatgtcacc tgtactcgga tctatgaaaa agtagaataa      180
aaattccatc atcaactttg acaggagtta attaagagaa tgaccaagct cagttcaatg      240
agcaaactc cactactgtt ctttcttttt ttttctatta ctgtgttcaa ttatctttat      300
cataaacatt ttacatgcag ctatttcaa gtgtgttgga ttaattagga tcat                               354

```

```

<210> 144
<211> 353
<212> DNA
<213> Homo sapien

```

```

<400> 144
ggtcaaggac ctggggggacc cccagggtcca gcagccacat gattctgcag cagacagggg      60
cctagagcac atctggatct cageccacc cctggcaacc tgectgecta gagaactccc      120
aagatgacag actaagtagg attctgccat ttagaataat tctggtatcc tgggcgttgc      180
gttaagttgc ttaactttca ttctgtctta cgatagtctt cagaggtggg aacagatgaa      240
gaaaccatgc cccagagaag gttaagtgc ttctcttta tggagccagt gttccaacct      300
aggtttgcct gataccagac ctgtggcccc acctcccatg caggtctctg tgg                               353

```

```

<210> 145
<211> 371
<212> DNA
<213> Homo sapien

```

```

<400> 145
caggtctgtc ataaactggt ctggagtttc tgacgactcc ttgttcacca aatgcaccat      60
ttcctgagac ttgctggcct ctccgttgag tccacttggc tttctgtcct ccacagctcc      120
attgccactg ttgatcacta gctttttctt ctgccacac cttcttcgac tgttgactgc      180
aatgcaaact gcaagaatca aagccaaggc caagagggat gccaaagatga tcagccattc      240

```

```

tggaatttgg ggtgtcctta taggaccaga ggttgtgttt gctccacett cttgactccc 300
atgtgagacc tcggccgcga ccacgctaag ccgaattcca gcacactggc ggcccgttac 360
tagtggatcc g 371

```

```

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

```

```

<400> 146
ggtcctccgt cctcttccca gaggtgtcgg ggcttggccc cagcctccat cttcgtctct 60
caggatggcg agtagcagcg gctccaaggc tgaattcatt gtcggaggga aatataaaact 120
ggtacggaag atcgggtctg gctccttcgg ggacatctat ttggcgatca acatcaccaa 180
cggcgaggaa gtggcagtga agctagaatc tcagaaggcc aggcaccccc agttgctgta 240
cgagagcaag ctctataaga ttcttcaagg tggggttggc atccccaca tacgggtgta 300
tggtcaggaa aaagactaca atgtactagt catggatctt ctggggaccta gcttc 355

```

```

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

```

```

<400> 147
ggtctgttac aaaatgaaga cagacaacac aacatttact ctgtggagat atcctactca 60
tactatgcac gtgctgtgat tttgaacata actcgtccca aaaacttgtc acgatcatcc 120
tgacttttta gggtggctga tccatcaatc ttgcactcaa ctgttacttc ttcccagtg 180
ttgttaggag caaagctgac ctgaacagca accaatggct gtagataccc aacatgcagt 240
tttttcccat aatatgggaa atattttaag tctatcattc cattatgagg ataaactgct 300
acatttggtg tatcttcatt ctttgaaaca caatctatcc ttggcactcc ttcag 355

```

```

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

```

```

<400> 148
aggtctctct cccctctccc ctctcctgcc agccaagtga agacatgctt acttcccctt 60
caccttcctt catgatgtgg gaagagtgtc gcaacccagc cctagccaac accgcatgag 120
agggagtgtg ccgaggggctt ctgagaaggt ttctctcaca tctagaaaga agcgcttaag 180
atgtggcagc cctctctctt caagtggctc ttgtcctgtt gccctgggag ttctcaaatt 240
gctgcagcag cctccatcca gctgaggat gacatcaata cacagaggaa gaagagtcag 300
gaaaagatga gagaagttac agactctcct gggcgacccc gagagcttac cattcctcag 360
acttcttca 369

```

```

<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

```

actagtcaaa	aatgctaaaa	taatttgga	gaaaatattt	tttaagtagt	gttatagttt	60
catgtttatc	ttttattatg	ttttgtgaag	ttgtgtcttt	tcactaatta	cctatactat	120
gccaatattt	ccttatatct	atccataaca	tttatactac	atttgtaana	naatatgcac	180
gtgaaactta	acactttata	aggtaaaaa	gaggtttcca	anattttaata	atctgatcaa	240
gttcttggtta	tttccaaata	gaatggactt	ggtctgttaa	gggctaagga	gaagaggaag	300
ataagggttaa	aagttgttaa	tgaccaaaca	ttctaaaaga	aatgcaaaaa	aaaagtttat	360
tttcaagcct	tcgaactatt	taaggaaagc	aaaatcattt	cctaaatgca	tatcattttgt	420
gagaattttct	cattaatatc	ctgaatcatt	catttcacta	aggctcatgt	tnactccgat	480
atgtctctaa	gaaagtacta	tttcatggtc	caaacctggg	tgccatantt	gggtaaaggc	540
tttcccttaa	gtgtgaaant	atttaaaatg	aaattttcct	ctttttaaaa	attctttana	600
agggttaagg	gtgttgggga					620

<210> 150

<211> 371

<212> DNA

<213> Homo sapien

<400> 150

ggctccgatca	aaacctgcta	cctccccaa	actttactag	tgccgataaa	ctttctcaaa	60
gagcaaccag	tatcacttcc	ctgtttataa	aacctctaac	catctctttg	ttctttgaac	120
atgctgaaaa	ccacctgggc	tgcatgtatg	cccgaatttg	yaattctttt	ctctcaaatg	180
aaaatttaaat	tttagggatt	cattttctata	ttttcacata	tgtagtatta	ttatttcctt	240
atatgtgttaa	gggtgaaattt	atgggtatttg	agtgtgcaag	aaaatatatt	tttaaagcct	300
tcatttttcc	cccagtgaa	gatttagaat	tttttatgta	aatatacaga	atgttttttc	360
ttacttttat	a					371

<210> 151

<211> 4655

<212> DNA

<213> Homo sapien

<400> 151

gggacttgag	ttctgttata	ttcttaagta	gattcatatt	gtaagggtct	cggggtgggg	60
gggttgga	aatcctggag	ccagaagaaa	ggacagcagc	attgatcaat	cttacagcta	120
acatgttgta	cctggaaaac	aatgcccaga	ctcaatttag	tgagccacag	tacacgaacc	180
tggggctcct	gaacagcatg	gaccagcaga	ttcagaacgg	ctcctcgtcc	accagtcctt	240
ataacacaga	ccacgcgcag	aacagcgtca	cggcgccctc	gccctacgca	cagcccagct	300
ccaccttcga	tgctctctct	ccatcacccg	ccatccctc	caacaccgac	taccagggcc	360
cgcacagttt	cgacgtgtcc	ttccagcagt	cgagcacccg	caagtcggcc	acctggacgt	420
attccactga	actgaagaaa	ctctactgcc	aaattgcaaa	gacatgcccc	atccagatca	480
agggtgatgac	cccacctcct	cagggagctg	ttatccgcgc	catgcctgtc	tacaaaaaag	540
ctgagcacgt	cacggagggtg	gtgaagcggg	gccccaaacca	tgagctgagc	cgtgaattca	600
acgagggaca	gattgccccct	yetagtcatt	tgattcgagt	agaggggaac	agccatgccc	660
agtatgtaga	agatcccatc	acaggaagac	agagtgtgct	ggtaccttat	gagccacccc	720
agggtggcac	tgaattcacg	acagtcttgt	acaatttcat	gtgtaacagc	agttgtgttg	780
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tcttgggccc	acgtgtcttt	gaggcccggga	tctgtgcttg	cccaggaaga	gacaggaagg	900
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ttctcttgt	ctgatttctt	aggggaagga	gaagtaagag	gcttacttct	taccctaacc	2040
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tctagtgatg	atgggttcacg	ttgggggtgat	ttaatccagt	tataagaaga	agttcatgtc	2640
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taccagatac	cttatcttac	aatattgatt	gggaaaacat	ttgctgccat	tacagaggta	2820
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gaattctgat	tgatttgatt	gggatgaatg	ccatctatct	agttctaaca	gtgaagtttt	2940
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cagtaagata	tctcaatgaa	ccataaatcc	aactttgtaa	aaatcttttg	aagcatagat	3060
aatattgttt	ggtaaatggt	tcttttgttt	ggtaaatggt	tctttaaag	accctcctat	3120
tctataaaac	tctgcagtga	gaggcttggt	taccttctct	tctctaaggt	ttacaattag	3180
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<210> 152
 <211> 586
 <212> PRT
 <213> Homo sapien

<400> 152
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 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 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
 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
 225 230 235 240
 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 Val Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Val Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Leu 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
 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
 465 470 475 480
 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
 565 570 575
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
 580 585

<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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<210> 155
 <211> 153
 <212> PRT
 <213> Homo sapien

<400> 155
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 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 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

<210> 156
 <211> 128
 <212> PRT
 <213> Homo sapien

<400> 156
 Met Thr Ser Val Arg Val Ala Ala Tyr Phe Glu Asn Phe Leu Ala Ala
 1 5 10 15
 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 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 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
 115 120 125

<210> 157
 <211> 424
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(424)
 <223> n = A,T,C or G

<400> 157
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 aattcagtca ccactgttat attaccttct ccaggaaccc tccagtgggg aaggctgcga 180
 tattagattt ccttgtatgc aaagtttttg ttgaaagctg tgctcagagg aggtgagagg 240
 agaggaagga gaaaactgca tcataacttt acagaattga atctagagtc ttccccgaaa 300
 agcccagaaa cttctctgcn gnattctggct tgtccatctg gtctaagggtg gctgcttctt 360
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 tgct 424

<210> 158
 <211> 2099
 <212> DNA
 <213> Homo sapien

<400> 158
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 ccgcgcagag ccgcgcagc ggcgcggcgc cgagagcgag ttaaaacgtg caggcaccag 180
 aaggcacttc ctgtcgggtga agaagacctg tctccggtgt cacgggcatc ctgtgttttg 240
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 atctttatct tccgagtcac gatcctcgtg gtggctgccc aggaagtgtg ggggtgacgag 720
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 tacgcttaag gtggaaagtg ttcattgcac aatatatttt tactgcttct tgaatgtaga 1980

cggaacagtg tggaagcaga aggcctttttt aactcatccg tttgccaatc attgcaaaca 2040
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<210> 159
<211> 291
<212> PRT
<213> Homo sapien

<400> 159
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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
100 105 110
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
180 185 190
Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala
195 200 205
Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
210 215 220
Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys
225 230 235 240
Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile
245 250 255
Thr Gly Ser Gln Ala Lys His Phe Lys Val Lys Cys Ser Cys Val Ile
260 265 270
Arg Arg Leu Leu Ser Ser Pro Glu Gly Asn Thr Asn Leu Lys Val Pro
275 280 285
Ser Val Ala
290

<210> 160
<211> 3951
<212> DNA
<213> Homo sapien

<400> 160
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tcaagacaat	gggtataatg	gattgctcat	tgcaattaat	cctcagggtac	ctgagaatca	240
gaacctcacc	tcaaacatta	aggaaatgat	aaactgaagct	tcattttacc	tattttaatgc	300
taccaagaga	agagtatttt	tcagaaatat	aaagattttta	atacctgcca	catggaaagc	360
taataataac	agcaaaataa	aacaagaatc	atatgaaaag	gcaaatgtca	tagtgactga	420
ctggtatggg	gcacatggag	atgatccata	caccctacaa	tacagagggt	gtggaaaaga	480
gggaaaatac	attcatttca	cacctaat	cctactgaat	gataacttaa	cagctggcta	540
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tgagtataac	aatgacaaac	ctttctacat	aatgggcaaa	aatcaaatta	aagtgacaag	660
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<210> 161
 <211> 943
 <212> PRT
 <213> Homo sapien

<400> 161

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			20					25					30		
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	
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
			290			295					300				

Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser
 305 310 315 320
 Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu
 325 330 335
 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
 Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
 465 470 475 480
 Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
 485 490 495
 Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
 500 505 510
 Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
 515 520 525
 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
 545 550 555 560
 Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
 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
 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
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 725 730 735
 Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val

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<210> 162
<211> 498
<212> DNA
<213> Homo sapien
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<400> 162						
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ccaccatgcg	ccttcgggat	gagcggggcc	ctctggagca	cctctactcc	ctgcacatcc	300
ccaactgtga	caagcatggc	ctgtacaacc	tcaaacagtg	gcaagatgtc	tctgaacggg	360
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<210> 163
<211> 1128
<212> DNA
<213> Homo sapien
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<400> 163						
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gcagatacct aactcaggaa actaacaagg tggagacgta caaagagcag ccgctcaaga      480
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<210> 164
 <211> 1310
 <212> DNA
 <213> Homo sapien

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<400> 164
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ttttaatgaa tgccataata taattatcca aattgatttt cctttgtgcc cgtaaaaaata     1260
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<210> 165
 <211> 177
 <212> PRT
 <213> Homo sapien

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<400> 165
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             20             25            30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
             35             40            45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile

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

His

<210> 166
 <211> 177
 <212> PRT
 <213> Homo sapien

<400> 166
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20 25 30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
35 40 45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile
50 55 60
Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro
65 70 75 80
Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
85 90 95
Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
100 105 110
Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Lys Gly
115 120 125
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
130 135 140
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp
145 150 155 160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg
165 170 175

His

<210> 167
 <211> 3362
 <212> DNA
 <213> Homo sapien

<400> 167

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 tt 3362

<210> 168
 <211> 2784
 <212> DNA
 <213> Homo sapien

<400> 168

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2784

<210> 169

<211> 592

<212> PRT

<213> Homo sapien

<400> 169

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			20					25					30		
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		
Arg	Ser	Ala	Trp	Asp	Val	Ile	Thr	Asp	Ser	Ala	Asp	Phe	His	His	Ser
		275					280						285		
Phe	Pro	Met	Asn	Gly	Thr	Glu	Leu	Pro	Pro	Pro	Pro	Thr	Phe	Ser	Leu
		290				295					300				
Val	Glu	Ala	Gly	Asp	Lys	Val	Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser
305					310					315					320
Lys	Met	Ala	Glu	Ala	Asp	Arg	Leu	Leu	Gln	Leu	Gln	Gln	Ala	Ala	Glu
				325					330					335	
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			
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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	
Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe				
465	470	475	480	
Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln				
	485	490	495	
Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn				
	500	505	510	
Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val				
	515	520	525	
Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp				
	530	535	540	
Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg				
545	550	555	560	
Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr				
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Tyr Thr Leu Met Cys Phe His His Ala Lys Leu Leu Thr Trp Lys Leu				
	580	585	590	

<210> 170
 <211> 791
 <212> PRT
 <213> Homo sapien

<400> 170
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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

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 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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 Asp Ser Thr Trp Arg Arg Leu
 785 790

<210> 171
 <211> 1491
 <212> DNA
 <213> Homo sapien

<400> 171
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1491

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

<400> 172
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 Asn Thr Gln Arg Lys Lys Ser Gln Glu Lys Met Arg Glu Val Thr Asp
 35 40 45
 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
 65 70 75 80
 Leu Ala Ile Glu Ala Gly Phe His His Ile Asp Ser Ala His Val Tyr
 85 90 95
 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
 165 170 175
 Lys Ile Leu Phe Asp Thr Val Asp Leu Cys Ala Thr Trp Glu Ala Met
 180 185 190
 Glu Lys Cys Lys Asp Ala Gly Leu Ala Lys Ser Ile Gly Val Ser Asn
 195 200 205
 Phe Asn His Arg Leu Leu Glu Met Ile Leu Asn Lys Pro Gly Leu Lys
 210 215 220
 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
 245 250 255
 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
 325 330 335
 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
 355 360

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

<400> 173
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 tctctgaata gcataatat gatgcacgg ataggtcatt atgatttttt accatttcga 1860
 cttacataat gaaaaccaat tcatttttaa tatcagatta ttattttgta agttgtggaa 1920
 aaagctaatt gtagttttca ttatgaagtt tcccaataaa accagggtatt ctaaaaaaaa 1980
 aaaaaaaaaa 1988

<210> 174
 <211> 238
 <212> PRT
 <213> Homo sapiens

<400> 174
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 Arg Arg Pro Leu Ser Ala Val Ala Arg Pro Ala Arg Ser Ser Asp Pro
 20 25 30
 Leu Arg Ser Ala Pro Leu Gly Pro Ala Pro Pro Val Asn Met Ile Arg

35	40	45
Cys Gly Leu Ala Cys Glu Arg Cys Arg Trp Ile Leu Pro Leu Leu Leu		
50	55	60
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		
115	120	125
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		
	165	170 175
Lys Tyr Thr Gln Thr Phe Thr Leu His Ala Asn Pro Ala Val Thr Tyr		
	180	185 190
Ile Tyr Asn Trp Ala Tyr Gly Phe Gly Trp Ala Ala Thr Ile Ile Leu		
195	200	205
Ile Gly Cys Ala Phe Phe Phe Cys Cys Leu Pro Asn Tyr Glu Asp Asp		
210	215	220
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225	230	235

<210> 175
 <211> 4181
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 <223> n=A,T,C or G

<400> 175

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<211> 580

<212> PRT

<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

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

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

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 <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
 gcaaaactgg gcagaaattc tataaactct ttgctgtttt tgataacctgc tttttgtttc 360
 attttgtttt gttttgtaaa aatgataaaa cttcagaaaa t 401

<210> 178
 <211> 561
 <212> DNA
 <213> Homo sapiens

<400> 178
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 gcccgctatg ggacaggggt ctttggccag aatgagtagc tacgctatca ggaggccctg 120
 agtgagctgg ccactgcggt taaagcacga attgggagct ctcagcgaca tcaccagtca 180
 gcagccaaag acctaaactc gtcccttgag gtctcccca caaccatcca ggtgacatac 240
 ctccctcca gtcagaagag taaacgtgcc aagcacttcc ttgaattgaa gagctttaag 300
 gataactata acacattgga gactactctg tgacggagct gaaggactct tgccgtagat 360
 taagccagtc agttgcaatg tgcaagacag gctgcttgcc gggccgccc cgggaacatct 420
 ggcccagcag gccagactg tatccatcca agtcccctgt gtatocagag ttcttagagc 480
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 gactattttc cccagtagc g 561

<210> 179
 <211> 521
 <212> DNA
 <213> Homo sapiens

<400> 179
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 gcatgaagac tggcttgtct cagtgtttca acctcaccag ggtgtgtctt tggctccacac 180
 ctgcctccct gttagtgcg tatgacagcc cccatcaaat gaccttggcc aagtcacggt 240
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 acgtgagcag tcagcaccag ttctgcacca gcagcgcctc cgtcctagtg ggtgttctct 360
 tttctcctgg ccctgggtgg gctagggcct gattcgggaa gatgccttg caggaggagg 420
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atgtgggaaa cagatctaaa tctcatttta tgctgtattt t

521

<210> 180

<211> 417

<212> DNA

<213> Homo sapiens

<400> 180

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tcttggggccg cctggcgccg atcgtggcta aacaggtact gctggggccg aaggtggtgg 120
tcgtacgctg tgaaggcatc aacatttctg gcaatttcta cagaaacaag ttgaagtacc 180
tggctttcct cgcgaagcgg atgaacacca acccttcccg aggccctac cacttccggg 240
ccccagccg catcttctgg cggaccgtgc gaggtatgct gcccacaaa accaagcgag 300
gccaggccgc tctggaccgt ctcaagggtg ttgacggcat cccaccgcc taccacaaga 360
aaaagcggat ggtggttctt gctgcctca aggtcgtgcg tctgaagcct acaagaa 417

<210> 181

<211> 283

<212> DNA

<213> Homo sapiens

<220>

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<222> (35)

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

<400> 181

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caagaactca agtgtaactg tgataaaata acctttccca ggtatattgg caggtatgtg 120
tgtaattctca gaatacacag gtgacataga tatgatatga caactggtaa tgggtggattc 180
atttacattg tttacacttc tatgaccagg ccttaaggga aggtcagttt tttaaaaaac 240
caagtagtgt cttcctacct atctccagat acatgtcaaa aaa 283

<210> 182

<211> 401

<212> DNA

<213> Homo sapiens

<400> 182

atattcttgc tgcttatgca gctgacattg ttgcctccc 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 gtctcttgag 300
gctgcaagtc tgtcctatct 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)

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

<400> 183

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gtgtcggaat cactggtaaa tgttggtga gaacaatccc tccccttgca cttgtgaaaa 300
cactttgagc gctttaagag attancctga gaaataatta aatatctttt ctcttcaaaa 360
aaaaaa 366
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<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 tatttgagg 120
taaaatgtta gtctacatag atgggtgatt gtaactttat tgccattaaa agatttcaaa 180
ttgcattcat gcttctgtgt acacataatg aaaaatgggc aaataatgaa gatctctcct 240
tcagtctgt ctgtttaatt ctgctgtctg ctcttctcta atgctgcgtc cctaattgta 300
cacagtttag tgatatctag gagtataaag ttgtcgccca tcaataaaaa tcacaaagtt 360
ggtttaaaaa 370
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<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
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<210> 186

<211> 309

<212> DNA

<213> Homo sapiens

<400> 186

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gccagtgagt gacagtcatg agggagtgtc tcttcttggg gaggaaagaa ggtagagcct 180
ttctgtctga atgaaaggcc aaggctacag tacagggccc cgccccagcc aggggtgtta 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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tocaacctcg ggccagtgtc ttcaggcttt actggggacc tgcgagctgg cctaattgtg 120
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tggcctgcaa gccaggccat ccctggggcgc cacagacgag ctccgagcca ggtcaggcct 180
cggaggccac aagctcagcc tcaggcccag gcactgattg tggcagaggg gccactaccc 240
aaggtctagc taggcccag acctagttac ccagacagtg agaagcccct ggaaggcaga 300
aaagttggga gcatggcaga caggggaaggg aaacattttc agggaaaaga catgtatcac 360
atgtcttcag aagcaagtca ggtttcatgt aaccgagtgt cctcttgcgt gtccaaaagt 420
agcccagggc tgtagcacag gcttcacagt gattttgtgt tcagccgtga gtcacac 477

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<210> 188

<211> 220

<212> DNA

<213> Homo sapiens

<400> 188

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cagatgttca agaggaagtt gctattgcat tgattttaat atttgtacat aaacactgat 180
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<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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ccatcattaa gcacnnttt caaaattata gccattcatg atttactttt tccagatgac 120
tatcattatt ctagtccctt gaatttgtaa ggggaaaaaa aacaaaaaca aaaacttacg 180
atgcactttt ctccagcaca tcagatttca aattgaaaat taaagacatg ctatggtaat 240
gcacttgcta gtactacaca ctttgtacaa caaaaaacag aggcaagaaa caacggaaaag 300
agaaaagcct tctttgttg gcccttaaac tgagtcaaga tctgaaatgt agagatgatc 360
tctgacgata cctgtatgtt cttattgtgt aaataaaatt gctggtatga aatgaca 417

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<210> 190

<211> 497

<212> DNA

<213> Homo sapiens

<400> 190

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gcactgoggc gctctcccgt cccgoggtgg ttgctgctgc tgccgctgct gctgggcctg 60
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acggctccga aggatgccta catgttcttg tggctctatt atgccacaa ctctgcaag 180
aacttctcag aactgcccct ggtcatgttg cttcagggcg gtccaggcgg ttctagcact 240
ggatttgga aacttgagga aattggggccc cttgacagtg atctcaaacc acggaaaacc 300
acctggctcc aggetgccag tctcctatct gtggataatc ccgtgggcac tgggttcagt 360
tatgtgaatg gtagtggtgc ctatgccaaag gacctggcta tgggtggcttc agacatgatg 420
gttctcctga agaccttctt cagttgccac aaagaattcc agacagttcc attctacatt 480
ttctcagagt cctatgg 497

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<210> 191
 <211> 175
 <212> DNA
 <213> Homo sapiens

<400> 191
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 ctacttgagt acaaggattt gagcctgtta cattcactgc tgaatttttag gctcctggaa 120
 gataccagc attcaataga gaccacacaa taaatatatg tcaaataaaa aaaaa 175

<210> 192
 <211> 526
 <212> DNA
 <213> Homo sapiens

<400> 192
 agtaaacatt attatTTTTT ttatatttgc aaaggaaaca tatctaattcc ttcctataga 60
 aagaacagta ttgctgtaat tctttttctt ttcttctca tttcctctgc cccttaaaaag 120
 attgaagaaa gagaaacttg tcaactcata tccacgttat ctagcaaagt acataagaat 180
 ctatcactaa gtaatgtatc ctccagaatg tgttggttta ccagtgcacac ccataattca 240
 tcacaaaatt aaagcaagaa gtccatagta atttatttgc taatagtga tttttaatgc 300
 tcagagtttc tgagggtcaaa ttttatcttt tcacttacaa gctctatgat cttaaataat 360
 ttacttaatg tattttgggtg tattttcctc aaattaatat tgggtgttcaa gactatatct 420
 aattcctctg atcactttga gaaacaaact tttattaaat gtaaggcact tttctatgaa 480
 ttttaaatat aaaaataaat attgttctga ttattactga aaaaaa 526

<210> 193
 <211> 552
 <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
 tccattgtgg tggaattgcg tctctggtaa aggcgtgcag gtgttgccg cggcctctga 60
 gctgggatga gccgtgctcc cgggtggaagc aaggagccc agccggagcc atggccagta 120
 cagtggtagc agttggactg accattgctg ctgcaggatt tgcaggccgt tacgttttgc 180
 aagccatgaa gcatatggag cctcaagtaa aacaagtttt tcaaagccta ccaaaatctg 240
 ccttcagtgg tggctattat agagggtgggt ttgaacccaa aatgacaaan cgggaagcan 300
 cattaatact aggtgtaagc cctactgcc aataagggaa aataagagat gctcatcgac 360
 gaattatgct tttaaatcat cctgacaaag gaggatctcc ttatatagca nccaaaatca 420
 atgaagctaa agatttacta naagggtcaag ctaaaaaatg aagtaaattg atgatgaatt 480

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 ctccctcca taggaatttc tcccaggaaa gaaatatatc 180
cccatctccg tttcatatca gaactaccgt ccccgatatt cccttcagag agattaaaga 240
ccagaaaaaa gtgagcctct tcatctgcac ctgtaatagt ttcagttcct atttcttcc 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 gtatttgtgt tttggccttg aaagtagcaa 60
gtgaccagaa tctgccatgg caacaggctt taaaaaagac ccttaaaaag acactgtctc 120
aactgtggtg ttagcaccag ccagctctct gtacatttgc tagctttag ttttctaaga 180
ctgagtaaac ttcttatttt tanaaagggg aggctggntt gtaactttcc ttgtacttaa 240
ttgggtaaaa gtcttttcca caaaccacca tctattttgt gaactttgtt agtcactttt 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 ctagtctctg tgtaagtgtg 120
aatactacaa aaacttattt atactgttct tatgtcattt gttatattca tagatttata 180
tgatgatatg acatctggct aaaaagaaat tattgcaaaa ctaaccacta tgtaactttt 240
tataaatact gtatggacaa aaaatggcat tttttatatt aaattgttta gctctggcaa 300
aaaaaaaaaa ttttaagagc tgggtactaat aaaggattat tatgactgtt aaaaaaa 357

<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 ttttaagtgt gttttgggag tagaaaaacta 60
aagcaacaat acttcctctt gacagctttg attggaatgg ggttattaga tcattcacct 120
tggtcctaca ctttttagga tgcttggtga acataacacc acttataatg aacatccctg 180
gttcctatat tttgggctat gtgggtagga attgttactt gttactgcag cagcagccct 240
agaaagtaag cccagggtct cagatctaag ttagtccaaa agctaaatga tttaaagtca 300
agttgtaatg ctaggcataa gcactctata atacattaaa ttataggccg agcaattagg 360
gaatgtttct gaaacattaa acttggtatt atgtcactaa aattctaaca caaacttaaa 420
aaatgtgtct catacatatg ctgtactagg cttcatcatg catttctaaa tttgtgtatg 480
atgtgaatat atgaaagaat ttatacaaga gtgttattta aaattattaa aaataaatgt 540
atataatttg tacctattgt aaaaa 565

<210> 198
<211> 484
<212> DNA
<213> Homo sapiens

<400> 198
tatgtaagta ttggtgtctg ctttaaaaaa ggagaccag acttcacctg tccttttttaa 60
acatttgaga acagtgttac tctgagcagt tgggccacct tcaccttacc cgacagctga 120
ctgttggtatg tgtccattgt cgcagtttg gctgttgccc ggacaggaca ggacctccat 180
tggtgcgcagc agcaggtggc aggggtgtgg cttgaggtgg gtggcagcgt ctgggtcctcc 240
tctctggtgc tttctgagag ggtctctaaa gcagagtgtg gttggcctgg gggaaggcag 300
agcacgtatt tctccctct agtacctctg ctttgtgag tgttccctct ggctttctga 360
agggcagcag actcttgagt atactgcaga ggacatgctt tatcagtagg tcttgagggc 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
 gcttatgttt tttgttttaa cttttgtttt ttaacattta gaatattaca ttttgtatta 60
 tacagtacct ttctcanaca ttttgtanaa ttcatttcgg cagctcacta ggattttgct 120
 gaacattaaa aagngtgata gcgatattag ngccaatcaa atggaaaaaa ggtagtctta 180
 ataaacaana cacaacgttt ttatacaaca tactttaaaa tattaanaaa actccttaat 240
 attgtttcct attaatgtatt attctttggg caanattttc tgatgctttt gattttctct 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
 gcttttttga ggaattacag ggaagctcct ggaattgtac atggatatct ttatccctag 60
 ggggaaatca aggagctggg caccctaat tctttatgga agtgttttaa actattttta 120
 ttttattaca agtattacta gagtagtggt tctactotaa gatttcaaaa gtgcatttaa 180
 aatcatacat gttccgcct gcaaatatat tggtattttg gtggagaaaa aaatagtata 240
 ttctacataa aaaattaaag atattaacta agaaaaaaa 279

<210> 201
 <211> 569
 <212> DNA
 <213> Homo sapiens

<400> 201
 taggtcagta ttttttagaaa ctcttaatag ctcatactct tgataccaaa agcagccctg 60
 attgttaaag cacacacctg cacaagaagc agtgatggtt gcatttacat ttcttgggtg 120
 cacaaaaaaa aattctcaaa aagcaaggac ttacgctttt tgcaaagcct ttgagaagtt 180
 actggatcat aggaagctta taacaagaat ggaagattct taaataactc actttctttg 240
 gtatccagta acagtagatg ttcaaaaatat gttagctgatt aataccagca ttgtgaacgc 300
 tgtacaacct tgtggttatt actaagcaag ttactactag cttctgaaaa gtagcttcat 360
 aattaatgtt atttatacac tgccctccat gacttttact ttgccctaag ctaatctcca 420
 aaatctgaaa tgctactcca atatcagaaa aaaaggggga ggtggaatta tatttctctg 480
 gatttttaaga gtacagagaa tcatgcacat ctctgattag ttcatatatg tctagtgtgt 540
 aataaaagtc aaagatgaac tctcaaaaa 569

<210> 202
 <211> 501

<212> DNA

<213> Homo sapiens

<400> 202

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attaataggc ttaataattg ttggcaagga tccttttgc ttttttggca tgcaagctcc 60
tagcatctgg cagtggggcc aagaaaataa ggtttatgca tgtatgatgg ttttcttctt 120
gagcaacatg attgagaacc agtgtatgtc aacagggtgca tttgagataa ctttaaataga 180
tgtacctgtg tggctctaagc tggaatctgg tcaccttcca tccatgcaac aacttggtca 240
aattcttgac aatgaaatga agctcaatgt gcatatggat tcaatccac accatcgatc 300
atagcaccac ctatcagcac tgaaaactct tttgcattaa gggatcattg caagagcagc 360
gtgactgaca ttatgaaggc ctgtactgaa gacagcaagc tgtagtaca gaccagatgc 420
tttcttggca ggctcggtgt acctcttggg aaacctcaat gcaagatagt gtttcagtgc 480
tggcatatct tgggaattctg 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 tggctcttgag atgtcttctc gttaangaga tgggcctttt ggaggtaaaag 60
gataaaaatg atgagttctg tcatgattca ctattntata acttgcatga cctttactgt 120
gttagctctt tgaatgttct tgaaatttta gactttcttt gtaaacaaat gatatgtcct 180
tatcattgta taaaagctgt tatgtgcaac agtgtggaga ttccttgtct gatttaataa 240
aatacttaaa cactgaaaaa a 261
```

<210> 204

<211> 421

<212> DNA

<213> Homo sapiens

<400> 204

```
agcatctttt ctacaacggt aaaattgcag aagtagctta tcattaaaaa acaacaacaa 60
caacaataac aataaatcct aagtgtaaat cagttattct acccctacc aaggatatca 120
gectgttttt tccctttttt ctccctggga taattgtggg cttcttccca aatttctaca 180
gectctttcc tcttctcatg cttgagcttc cctgtttgca cgcattgctg 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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tactctcaca atgaaggacc tggaatgaaa aatctgtgtc taaacaagtc ctcttttagat 60
tttagtgcaa atccagagcc agcgtcgggt gcctcgagta attctttcoat gggtagcttt 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 tgaattttta 460
```

<210> 206

<211> 481

<212> DNA

<213> Homo sapiens

<400> 206

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tgtggtggaa ttggggacgc ccccagaccc tgactttttc ctgctggggc cgtctcctcc 60
tgcggaagca gtgacctctg acccctggtg accttcgctt tgagtgcctt ttgaacgctg 120
gtcccgcggtg acttggtttt ctcaagctct gtctgtccaa agacgctccg gtcgaggtcc 180
cgctgcccct ggggtggatac ttgaacccca gagccccctc tgtgctgctg tgtccggagg 240
cgcccttccc atctgcctgc ccaccggag ctctttccgc cggcgcaggg tcccaagccc 300
acctcccgcc ctgagtcctg cgtgtgtcgt ctgggcacgt cctgcacaca caatgcaagt 360
cctggcctcc gcgcccgcgc gccacgcga gccgtacctg ccgccaactc tgttatttat 420
ggtgtgaccc cctggaggtg cctcggccc accggggcta tttattgttt aattttattg 480
t 481
```

<210> 207

<211> 605

<212> DNA

<213> Homo sapiens

<400> 207

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accttttttg gattcagggc tcttcacaat taaaatgagt gtaatgaaac aagggtgaaaa 60
tatagaagca tccctttgta tactgttttg ctacttacag tgtacttggc attgctttat 120
ctcaactggat tctcaggtga ggattttctga gatcttaata taagctccaa agttgtctac 180
ttttttgata ctaggggtgt ccttttgttt tacagagcag ggtcacttga tttgctagct 240
ggtggcagaa ttggcaccat taccaggtc tgactgacca ccagtcagag gcactttatt 300
tgtatcatga aatgatttga aatcatttga aagcagcgaa gtctgataat gaatgccagc 360
tttctctgtg ctttgataac aaagactcca aatattctgg agaacctgga taaaagtttg 420
aagggctaga ttgggatttg aagacaaaat tgtaggaaat 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 tggattcccg tcgtaactta aagggaaact ttcacaatgt ccggagccct 60
tgatgtcctg caaatgaagg aggaggatgt ccttaagttc cttgcagcag gaacccactt 120
agggtggcacc aatcttgact tccagatgga acagtacatc tataaaagga aaagtgatgg 180
catctatata ataaatctca agaggacctg ggagaagctt ctgctggcag ctctgtgcaat 240
tgttgocatt gaaaacctg ctgatgtcag tgttatatcc tccaggaata ctggccagag 300
ggctgtgctg aagtttgctg ctgccactgg agccactcca attgctggcc gcttcactcc 360
```

```

tggaaaccttc actaaccaga tccaggcagc cttccgggag ccacggcttc ttgtgggttac 420
tgacccacagg gctgaccacc agcctctcac ggaggcatct tatgttaacc tacctaccat 480
tgcgctgtgt aacacagatt ctctctgcg ctatgtggac attgccatcc catgcaacaa 540
caaggagct cactcagtg gtttgatgtg gtggatgctg gctcgggaag ttctgcgcat 600
gcgtggcacc atttcccggtg 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 ctccaagag 60
caaatccaca ttctctttga gttctgcagc ttctgtgtaa atagggcagc tgcgtctat 120
gccgtagaat cacatgatct gaggaccatt catggaagct gctaaatagc ctagtctggg 180
gagtcctcca taaagttttg catggagcaa acaaacagga ttaactagg tttggttcct 240
tcagccctct aaaagcatag ggcttagcct gcaggcttcc ttgggcttcc tctgtgtgtg 300
tagttttgta aacactatag catctgttaa gatccagtgt ccatggaaac cttcccat 360
gccgtgactc tggactatat cagtttttgg aaagcagggt tcctctgcct gctaacaagc 420
ccacgtggac cagtctgaat gtctttcctt tacacctatg tttttaata 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
nggcccgcg gcccagggtg gggatgcacc gccgcggggt gggagctggc gccatcgcca 120
agaagaaact tgcagaggcc aagtataagg agcaggggac ggtcttggct gaggaccagc 180
tagcccagat gtcaaagcag ttggacatgt tcaagaccaa cctggaggaa ttggccagca 240
aacacaagca ggagatccgg aagaatcctg agttccgtgt gcagttccag gacatgtgtg 300
caaccattgg cgtggatccg ctggcctctg gaaaaggatt ttggtctgag atgctgggcg 360
tgggggactt ctattacgaa ctagggtgcc aaattatcga agtgtgcctg gcgctgaagc 420
atcggaatgg aggtctgata actttggagg aactacatca acaggtgttg aaggaaggg 480
gcaagttcgc ccaggatgtc agtcaagatg acctgatcag agccatcaag aaa 533

```

<210> 211

<211> 451

<212> DNA

<213> Homo sapiens

<400> 211

```

ttagcttgag ccgagaacga ggcgagaaag ctggagaccg aggagaccgc ctagagcgga 60
gtgaacgggg aggggaccgt ggggaccggc ttgatcgtgc gcggacacct gctaccaagc 120
ggagcttcag caagggaagtg gaggagcgga gtagagaacg gccctcccag cctgaggggc 180
tgcgcaaggc agctagcctc acggaggatc gggaccgtgg gcgggatgcc gtgaagcgag 240
aagctgccct acccccagtg agccccctga agggcgctct ctctgaggag gagttagaga 300
agaaatccaa ggctatcatt gaggaatatc tccatctcaa tgacatgaaa gaggcagtcc 360
agtgcgtgca ggagctggcc tcacctcct tgctcttcat ctttgtacgg catgggtgctg 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

```

gtgattattc ttgatcaggg agaagatcat ttagatttgt tttgcattcc ttanaatgga 60
gggcaacatt ccacagctgc cctggctgtg atgagtgtcc ttgcaggggc cggagtagga 120
gcactggggg gggggcgga ttgggggttac tcgatgtaag ggattccttg ttgttggtt 180
gagatccagt gcagttgtga tttctgtgga tcccagcttg gttccaggaa ttttgtgtga 240
ttggcttaaa tccagttttc aatcttcgac agctgggctg gaacgtgaac tcagtagctg 300
aacctgtctg acccggtcac gttcttgat cctcagaact ctttgcctt gtcgggggtg 360
gggtgggaac tcacgtgggg agcgggtggc gagaaaatgt aaggattctg gaatacatat 420
tccatgggac tttccttccc tctctgctt 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

```

ctaattagaa acttgctgta ctttttnttt tcttttaggg gtcaaggacc ctctttatag 60
ctnccatttg cctacaataa attattgcag cagtttgcaa tactaaaata ttttttatag 120
actttatatt tttccttttg ataaagggat gctgcatagt agagttggtg taattaaact 180
atctcagccg tttccctgct ttccttctg ctccatatgc ctcatgtcc ttccagggag 240

```

```

ctctttttaat cttaaagttc tacatttcat gctcttagtc aaattctggt accttttttaa 300
taactcttcc cactgcatat ttccatcttg aattggnggt tctaaattct gaaactgtag 360
ttgagataca gctattttaat atttctggga gatgtgcatc cctcttcttt gtggttgccc 420
aagggtggtt tgcgtaactg anactccttg atatgcttca gagaatttag gcaaactg 480
gccatggccg tgggagtact gggagtaaaa t 511

```

<210> 214

<211> 521

<212> DNA

<213> Homo sapiens

<400> 214

```

agcattgcca aataatccct aattttccac taaaaatata atgaaatgat gttaagcttt 60
ttgaaaagtt taggttaaac ctactgttgt tagattaatg tatttggtgc tcccccttat 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 agggctttgc cctttttctg taagtctctt gggatcctgt 420
gtagaagctg ttctcattaa acaccaaaca gttaagtcca ttctctggta ctagctacaa 480
attcggtttc 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

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gagcggagag cggaccngtn agagccctga gcagccccac cgccgcccgc ggcctagttt 60
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ccatgagcag cgaggccgag acccagcagc cgcccgccgc ccccccgcc gcccccggc 180
tcagcgccgc cgacaccaag cccggcacta cgggcagcgg cgcagggagc ggtggccgg 240
gcggcctcac atcgccggcg cctgccggcg gggacaagaa ggtcatcgca acgaagggtt 300
tgggaacagt aaaatggttc aatgtaagga acggatatgg tttcatcaac aggaatgaca 360
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<210> 216

<211> 425

<212> DNA

<213> Homo sapiens

<400> 216

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aacaggccaa tcttgaaggt actccctgtt tgetgcagaa tgtcagatat tttggatgtt 180
gcataagagt cctatttgcc ccagttaatt caacttttgt ctgctgttt tgtggactgg 240
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aattgacaat atatatgcat gtgtttaaac caaatccaga aagcttaaac aatagagctg 360
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<210> 217

<211> 181

<212> DNA

<213> Homo sapiens

<400> 217

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actttggctt tttcagtggg agaatatgtt gaagggttca ttttgttcta gaaaaaaaaa 180
a                                           181

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<210> 218

<211> 405

<212> DNA

<213> Homo sapiens

<400> 218

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caggccttcc agttcactga caaacatggg gaagtgtgce cagctggctg gaaacctggc 60
agtgatacca tcaagcctga tgtccaaaag agcaaagaat atttctccaa gcagaagtga 120
gcgctgggct gtttttagtg caggetgogg tgggcagcca tgagaacaaa acctcttctg 180
tatttttttt ttccattagt aaaacacaag acttcagatt cagccgaatt gtggtgtctt 240
acaaggcagg cttttcctac agggggtgga gagaccagcc tttcttctt tggtagggaat 300
ggcctgagtt ggcgttgtgg gcaggctact ggtttgtatg atgtattagt agagcaaccc 360
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<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

```

aaaaataaaa aggaaagaac cctcttnaan aaaaaa

216

<210> 220

<211> 380

<212> DNA

<213> Homo sapiens

<400> 220

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atttcacctt tgagggaac tgattagatg ggttggtgtt gtgttctgat ggagaaaaca 180
gcacccaag gactcagaag atgattttta cagttcagaa cagatgtgtg caatattggt 240
gcatgtaata atgttgagtg gcagtcaaaa gtcatgattt ttatcttagt tcttcattac 300
tgcattgaaa aggaaaacct gtctgagaaa atgcctgaca gtttaattta aaactatggt 360
gtaagtcttt gacaaaaaaa                                     380

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<210> 221

<211> 398

<212> DNA

<213> Homo sapiens

<400> 221

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cccagccccg tttcctttta ttttgagct aatgccagct gcgtgtctag ttttgagtgc 240
agtaaaatag aatcagcaaa tcaactcttat ttttcacct tttccggtat tttttgggtt 300
gtttctgtgg gagcagtgtg caccaactct tctgtatat tgcccttttg ctggaaaatg 360
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<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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gtgaagattt caaaacctga gagcactttt tctttgttta gaattatgag aaaggcacta 180
gatgacttta ggatttgcac ttttcccttt attgcctcat ttcttgtgac gccttggttg 240
ggagggaat ctgtttattt tttcctacaa ataaaaagct aagattctat atcgcaaaaa 300
a                                     301

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<210> 223

<211> 200

<212> DNA

<213> Homo sapiens

<400> 223

gtaagtgctt aggaagaaac ttgcaaaca tttaatgagg atacactgtt cattttttaa 60
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 agattttctac aggagacagt ggttttattt ggattgtctt ctgtaatagg tttcaataaa 180
 gctggatgaa cttaaaaaaa 200

<210> 224

<211> 385

<212> DNA

<213> Homo sapiens

<400> 224

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 gctgtaactg caagacctgg acaagagatt cgtcagcgaa ctgcagctca aagaaacctt 120
 tctccaacac cagcaagccc taaccagggc cctcctccac aagttccagt atctcctgga 180
 ccaccaaagg acagtctctgc cctgggtgga cccccagaaa ggactgttac tccagcccta 240
 tcatcaaagt tgttaccaag acatcttgga tccctgcta cttcagtgcc tggaatgggt 300
 aaacagagca cttaatgtta ttacagttt atattgtttt ctctgggttac caataaaacg 360
 ggccattttc aggtggtaaa aaaaa 385

<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

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
	530	535
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

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<211> 9

<212> PRT
<213> Homo sapien

<400> 227
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1 5

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<400> 228
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1 5

<210> 229
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<212> PRT
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<400> 229
Lys Leu Leu Gly Asn Cys Leu Pro Thr Val
1 5 10

<210> 230
<211> 10
<212> PRT
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<400> 230
Arg Leu Thr Gly Gly Leu Lys Phe Phe Val
1 5 10

<210> 231
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<212> PRT
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<400> 231
Ser Leu Gln Ala Leu Lys Val Thr Val
1 5

<210> 232
<211> 20
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<213> Homo sapiens

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5 10 15

Phe Ser Phe Ala
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<210> 233
<211> 21
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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
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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

<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
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<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
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<210> 240
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<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

<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
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<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
5 10 15

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
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<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

	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
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<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
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<400> 248
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Gly Ala Asp Val
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<210> 249
<211> 20
<212> PRT
<213> Homo sapiens

<400> 249
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5 10 15

Glu Thr Gly Asp

20

<210> 250
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 250
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 5 10 15

Leu Thr Phe Arg
 20

<210> 251
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 251
 Leu Gln Ala Leu Lys Val Thr Val Thr Ser Arg Ala Ser Asn Ser Ala
 5 10 15

Val Pro Pro Ala
 20

<210> 252
 <211> 153
 <212> PRT
 <213> Homo sapien

<400> 252
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 1 5 10 15
 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 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

<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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agacaagaaa	gagaatggaa	caaaattatt	ataatgaatt	ctgcagatat	ccatcacact	7860
ggcgccgct	cgagcaccac	caccaccacc	actgagatcc	ggctgctaac	aaagcccga	7920
aggaagctga	gttggtgctg	gccaccgctg	agcaataaact	agcataaccc	cttggggcct	7980
ctaaacgggt	cttgaggggt	ttttgtctga	aaggaggaac	tatatccgga	t	8031

<210> 255

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

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

<400> 255

gtggccagng	actagaaggg	gaggcgccgc	gggaccatgg	cggcggcgcc	ggacgagcgg	60
agtccanagg	acggagaaga	cgaggaagag	gaggagcagt	tggttctggg	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	taaattgcat	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

tggtggncct	gggatgggga	accgcggtgg	cttccgngga	ggtttcggca	ntggcatccg	60
gggcgggggt	cgcgcccgng	gacggggccg	gggccnangc	cgngganctc	gcggangcaa	120
ggccgaggat	aaggagtggg	tgcccgtcac	caacttgggc	cgcttgncca	aggacatgaa	180
nancaagccc	ctgnaggaga	tctatntctt	cttccctgcc	ccattaagga	atcaagagat	240
catttgattt	cttccctggg	gcctctctca	aggatnaggt	ttttgaagat	tatgccagtg	300
canaaannan	accccgttgc	cngtccatc	tnaccccaac	ncttccaagg	gcnatttttg	360
tttaggcttc	attncngggg	ggaaccttaa	cccaatttgg	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	gctgttggat	tttaaaattt	120
ttaaaatata	tgctaagtaa	tttgctatgt	cttctcccac	actatcaata	tgcttgcctc	180
taacaggctc	cccactttct	tttaatgtgc	tggtatgagc	tttggacatg	agataaccgt	240
gcctgttcag	agtgtctaca	gtaagagctg	gacaaaactc	ggagggacac	agtctttgag	300
acagctcttt	tggttgcttt	ccacttttct	gaaaggttca	cagtaacctt	ctagataata	360
gaaactccca	gttaaagcct	angctancaa	tttttttagt	t		401

<210> 258

<211> 401

<212> DNA

<213> Homo sapien

```

<400> 258
ggagcgctag gtcggtgtac gaccgagatt aggggtgctg ccagctccgg gagggcgcgg      60
tgagggggccg ggcccaagct gccgacccga gccgatcgtc agggctcgcca gcgcctcagc      120
tctgtggagg agcagcagta gtcggagggt gcaggatatt agaaatggct actccccagt      180
caattttcat ctttgcaatc tgcattttta tgataacaga attaattctg gcctcaaaaa      240
gctactatga tatcttaggt gtgccaaaat cggcatcaga gcgccaaatc aagaaggcct      300
ttcacaagtt ggccatgaag taccacctg acaaaaataa gaccagatg ctgaagcaaa      360
attcagagag attgcagaag catatgaaac actctcagat g                               401

```

```

<210> 259
<211> 401
<212> DNA
<213> Homo sapien

```

```

<400> 259
attgggtttg gagggaggat gatgacagag gaatgccctt tggccatcac ggttttgatt      60
ctccagaata ttgtgggttt gatcatcaat gcagtcatgt taggctgcat tttcatgaaa      120
acagctcagg ctcacagaag ggcagaaact ttgattttca gccgccatgc tgtgattgcc      180
gtccgaaatg gcaagctgtg cttcatgttc cgagtgggtg acctgaggaa aagcatgac      240
attagtgcct ctgtgcgcac ccagggtggtc aagaaaacaa ctacacctga aggggaggtg      300
gttcctatcc accaactgga cattcctgtt gataacccaa tcgagagcaa taacattttt      360
ctgggtggccc 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 gaggggggana tgaataggga tggagaggga natagtggat gagcaggggca      60
canggagagg aancagaaag gagaggcaag acaggggagac acacancaca nangangana      120
caggtggggg ctgggggtggg gcatggagag ccttttnangt cncccaggcc accctgctct      180
cgctggnctg ttgaaaccca ctccatggct tcctgccact gcagttgggc ccagggtctg      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 tggctctgct      60
tcacctccc ctgacctgag tagtcgccat ggcacagggt ctcagaggca ctgngactga      120

```

```

cttcocctgga tttgatgagc gggctgatgc anaaactctt cgggaaggcta tgaaaggctt 180
gggcacagat gaggagagca tctgactct gttgacatcc cgaagtaatg ctcagegcca 240
ggaaatctct gcagctttta agactctgtt tggcagggat cttctggatg acctgaaatc 300
agaactaact ggaaaatttg aaaaattaat tgtggctctg atgaaaccct ctcggcttta 360
tgatgcttat gaactgaaac atgccttgaa gggagctgga a 401

```

```

<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 ttttgnctt tcatatatca aaggagatta tgtgaaacta 60
tttttaataa ctgtaaagtg acatatagtt ataagatata tttctgtaca gtagagaaag 120
agtttataac atgaagaata ttgtaccatt atacattttc attctcgatc tcataagaaa 180
ttcaaaagaa taatgataga ggtgaaaata tgtttacttt ctctaaatca agcctagttg 240
tcaactcaaa aattatgntg catagtttta ttttgaattt aggttttggg actacttttt 300
tccancttca atgagaaaat aaaatctaca actcaggagt tactacagaa gttctaanta 360
tttttttgct aannagcnaa aaatataaac 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 tcttgggagg aagaggcagc tacggcggcg 120
gcggcggttg cggctagggc ggccggcgaat aaaggggccc ccgccgggtg atgcggtgac 180
cactgcggca ggcccaggag ctgagtgggc cccggccctc agcccgtccc gncggacccc 240
ctttcctcaa ctctccatct tctcctgccg accgagatcg ccgaggcggn ctcaggctcc 300
ctanccccc tcccgtccct tcccccccc cgtccccgcc ccggggggccg ccgccacccc 360
cctcccacca tggtctgaa ganaatccac aaggaattga a 401

```

```

<210> 264
<211> 401
<212> DNA
<213> Homo sapien

```

```

<400> 264
aacaccagcc actccaggac cectgaaggc ctctaccagg tcaccagtgt tctgcgccta 60
aagccacccc ctggcagaaa cttcagctgt gtgttctgga ataactcagc gagggaaact 120
actttggcca gcattgacct tcaaagtcag atggaaccca ggaccatcc aacttggctg 180
cttcacattt tcatccctc ctgcattcatt gctttcattt tcatagccac agtgatagcc 240
ctaagaaaac aactctgtca aaagctgtat tcttcaaaag acacaacaaa aagacctgtc 300

```

accacaacaa agaggggaagt gaacagtgcgt gtgaatctga acctgtgggc ttgggagcca 360
gggtgacctg atatgacatc taaagaagct tetggactct 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
gccacttccgt gtggacatgg gcagagcgct gctgccagtt cctggtagcc ttgaccacna 60
cgctggggggg tctttgtgat ggatcatgggt ctcatcttga cttggggggtg tgggattcaa 120
gttagaagtt tctagatctg gccgggcgca gtggctcaca cctgtaatcc cagcacttta 180
ggaggctgag gcaggcggtat catgaggtca ggagatcgag accgtcctgg ctaacacagt 240
gaaaccccggt 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 caatttctat acagngaata taaatgagac 60
gacagcaaaa ttttcatgaa atgtaaaata tttttatagt ttgttcatac tatatgaggt 120
tctatttttaa atgactttct ggattttaaa aaatttcttt aaatacaatc atttttgtaa 180
tattttatttt atgcttatga tctagataat tgcagaatat cattttatct gactctgtct 240
tcataagaga gctgtggcgg 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 gatccctcttc ggggtgagcc agggtcggcg cgcgcggctg tctcanaact 120
catgcagctg ttcccgcgag gctgtttga ggacgcgctg ccgcccatcg tgctgaggag 180
ccaggtgtac agccttctgc ctgacaggac cgtggccgac cggcagctga aggagcttca 240
agagcanggg gagacaaaat cgtccagctg ggcttcnact tggatgccca tggaanttat 300

```
tctttcnctt ganggactta cnnngggaccc aagaanccct tncaaggggc ccttngtggga 360
tgggncccgga aaccccnnta tttgcccttg ggggggncca a 401
```

```
<210> 268
<211> 223
<212> DNA
<213> Homo sapien
```

```
<400> 268
tcgccatggt ggccaggctg gtcttgaact cctgaacttta agtgatccac ccgcctcaac 60
ctcccaaagt gctgggatta caggtgtgag ccaccgcgc tgccctgata catactttta 120
gaatcaagta gtcacgcact tttctgttc atttttctaa aaagtaaata taaaatggt 180
ttgttttttg tttttttgt ttgtttgtt ctgtttttt ttt 223
```

```
<210> 269
<211> 401
<212> DNA
<213> Homo sapien
```

```
<400> 269
actatgtaaa ccacattgta ctttttttta ctttggcaac aaatatttat acatacaaga 60
tgctagtcca tttgaatatt tctcccaact tatccaagga tctccagctc taacaaaatg 120
gtttattttt atttaaatgt caatagtgtt tttttaaaat ccaaatacaga ggtgcaggcc 180
accagttaaa tgcggtctat caggttttgt gccttaagag actacagagt caaagctcat 240
ttttaaagga gtaggacaaa gttgtcacag gtttttgttg ttgtttttat tgcccccaaa 300
attacatggt aatttccatt tatatcaggg attctattta cttgaagact gtgaagttgc 360
cattttgtct cattgttttc ttgacataa 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
tggtctgttg ttcacctcag cactgcttgg tatctgcacc ctacctctct ttagaggctg 60
ccttgtaaac tgaaaaatgc acctgacttc gagcaagact ctttccttag gttctggatc 120
tgtttgagcc ccattggcact gagctggaat ctgagggtct tgttccaagg atgtgatgat 180
gtggggagaat gttctttgaa agagcagaaa tccagtctgc atggaaacag cctgtagagn 240
agaagtttcc agtgataagt gttcactgtt ctaaggaggt acaccacagc tacctgaatt 300
ttcccaaaat gagtgtctct 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 ccagagctg cacagggttt ggcccaagtt 60
tctaaggagag gcacttctc ccctcgccca tcaagtccag ccctgctgg ctggtgctg 120
```

```

agccccctcag acagccccct gccccgcagg cctgccttct cagggacttc tgcgggggct 180
gaggcaagcc atggagtgag acccaggagc cggacacttc tcaggaaatg gcttttccca 240
acccccagcc cccaccgggt ggttcttctt gttctgtgac tgtgtatagt gccaccacag 300
cttatggcat ctcattgagg acaaaaaaa 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 nacttctctg actatcctgg agacccccct cgtttccacg 60
nncatnatat cnetcatngc tgggcccntn angacacnat cccactccaa cacctgngng 120
atgctggnen cctnggaacc ancntcagaa ngacctgnt cntntgtnt cgcgaanctg 180
aagnnaangc gggntacacc tncntgcant ggnccacnct gcnggggaact ntacacacct 240
acgggatgtg gctgcgccan gagccaagag cntttctgga tgattcccca gcctcttggn 300
agggantcta caacattgct nnntacctt ntcenncnegc nnntnntgga ntacaggngn 360
tnntaacact acatcttttt tactgncen tnccttggtgg 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 ggcctcccca tcgtccaccg caaatgcttc taaacggact cagcagatgc 180
gtagattttg ctgcatgggt taattgagaa tagaaatttg cccctggcaa atgcacacac 240
ctcatgctag cctcacgaaa ctggaataag ccttcgaaaa gaaattgtcc ttgaagcttg 300
tatctgatat cagcaactgga ttgtagaact tgttgctgat tttgacctg tattgaagtt 360
aactgttccc cttggtatta acgtgtcagg gctgagtgnt c 401

```

<210> 274

<211> 401

<212> DNA

<213> Homo sapien

<400> 274

```

ccaccacac ccaccgggcc ctggttcgcc tcttctccgg gageccagtc gcgccaccgc 60
cgccgcccag gccatcgcca ccttcgcag ccatgtccac caggtecggt tctctgtctt 120
cctaccgcag gatgttcggc ggcccgggca ccgcgagccg gccgagctcc agccggagct 180
acgtgactac gtccaccgcc acctacagcc tgggcagcgc gctgcgcccc agcaccagcc 240
gcagcctcta cgctcgtcc ccgggcggcg tgtatgccac gcgctcctct gccgtgcgcc 300
tgccggagcag cgtgcccggg gtgcggctcc tgcaggactc ggtggacttc tcgctggccg 360

```

acgccatcaa caccgagttc aagaacaccc gcaccaacga g 401

<210> 275
 <211> 401
 <212> DNA
 <213> Homo sapien

<400> 275
 ccacttccac cactttgtgg agcagtgcct tcagcgcgaac ccggatgcca ggtatccctg 60
 ctggcctggg cctgggcttc gggagagcag aggggtgctca ggagggttaag gccaggggtg 120
 gaaggggactt acctcccaaa ggttctgcag gggaaatctgg agctacacac aggagggatc 180
 agctcctggg tgtgtcagag gccagcctgg ggagctctgg ccactgcttc ccatgagctg 240
 agggagaggg agaggggacc cgaggctgag gcataagtgg caggatttctg ggaagctggg 300
 gacacggcag tgatgctgag 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 ntaccottga gccacctaag ttagaagaaa ttggaaatca agaagttgtc 60
 attgttgaag aagcacagag ttcagaagac tttaacatgg gctcttcctc tagcagccag 120
 tatactttct gtcagccaga aactgtattt tcctctcagc ctagtgatga tgaatcaagt 180
 agtgatgaaa ccagtaatca gccagtcctt gccttttagac gacgccgtgc taggaagaag 240
 accgtttctg cttcagaatc tgaagaccgg ctagttgggtg aacaagaaac tgaaccttct 300
 aaggagttga gtaaacgtca gttcagtagt ggtctcaata agtgtgttat acttgctttg 360
 gtgattgcaa tcagcatggg atttgccat 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 cagctatggtt attcatgcca aaataaaaagc 60
 tgtgcagagg agtggctgca atgaggtcac aacgggtggg gatgtaaaag agatcttcaa 120
 gtctcatca cccatccctc gaactcaagt cccgctcatt acaaatctct cttgccagt 180
 tccacacatc ctgccccatc aagatgttct catcatgtgt taagagnggc gctcaaggat 240
 gatgcttctt gaaaattgct tagttgaaaa atggagagat cagcttagta aaagatccat 300
 acagtgggaa gagaggctgc aggaacagcg ganaacagtt caggacaaga agaaaacagc 360
 cgggcgcacc agtcgtagta atccccccaa accaaaggga a 401

<210> 278

<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 aaatcettgt caagatccct acattctaac accagagaac 120
 cgatgtgttt gccagtcctc aaatgccatg tgccgagAAC tgccccagtc aatagtctac 180
 aaatacatga gcatccgate tgataggtct gtgccatcag acatcttcca gatacaggcc 240
 acaactatTT atgccaacac catcaatact ttccggatta 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 ctctgatata tacctaagtn aacanaacat taatacctaa gtaaacataa 60
 cattacttgg aggggttgcag nttctaantg aaactgtatt tgaaactttt aagtatactt 120
 taggaaacaa gcatgaacgg cagtctagaa taccagaaac atctacttgg gtagcttggn 180
 gccattatcc tgtggaatct gatatgtctg gnagcatgtc attgatggga catgaagaca 240
 tctttggaaa tgatgagatt atttctgtg ttaaaaaaaa aaaaaatctt aaattcctac 300
 aatgtgaaac tgaaactaat aattttgatc ctgatgtatg ggacagcgta tctgtaccag 360
 gctctaaata acaaaagnta gggngacaag nacatgttcc t 401

<210> 280
 <211> 326
 <212> DNA
 <213> Homo sapien

<400> 280
 gaagtggaaT tgtataattc aattcgataa ttgatctcat gggctttccc tggaggaaag 60
 gttttttttg ttgttttttt ttttaagaact tgaaacttgt aaactgagat gtctgtagct 120
 tttttgccca tctgtagtgt atgtgaagat ttcaaaacct gagagcactt tttctttgtt 180
 tagaattatg agaaaggcac tagatgactt taggatttgc atttttccct ttattgcctc 240
 atttcttgtg acgccttggt ggggagggaa atctgtttat tttttcctac aaataaaaaa 300
 ctaagattct atatcgcaaa aaaaaa 326

<210> 281
 <211> 374
 <212> DNA
 <213> Homo sapien

```

<400> 281
caacgcggttt gcaaatattc ccttggttagc ctacttcctt acccccgaat attggtaaga      60
tcgagcaatg gcttcaggac atgggttctc ttctcctgtg atcattcaag tgctcactgc      120
atgaagactg gcttgtctca gtgtttcaac ctcaccaggg ctgtctcttg gtccacacct      180
cgctccctgt tagtgccgta tgacagcccc catcaaatga ccttggccaa gtcacgggtt      240
ctctgtggtc aaggttgggt ggctgattgg tggaaagtag ggtggaccaa aggaggccac      300
gtgagcagtc agcaccagtt ctgcaccagc agcgctcccg tcctagtggg tggtcctggt      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 aattcccgca tcctanncgc cgactcacac aaggcagagt ngccatggag      60
aaaattccag tgtcagcatt cttgctcctt gtggccctct cctacactct ggccagagat      120
accacagtca aacctgnagc caaaaaggac acaaaggact ctcgacccaa actgccccan      180
acctctcca gaggttgggg tgaccaactc atctggactc anacatatga agaagctcta      240
tataaatcca agacaagcaa caaacccctg atgattattc atcacttggg tgagtgccca      300
cacagtcaag ctttaaagaa agtgtttgct gaaaataaag aaatccagaa 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 ttccctcgtc cccccaaaaa tttgaatttt      120
tttttcaaca ctcttacacc tgttatggaa aatgtcaacc tttgtaagaa aacccaaaata      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

```

```

ctattaatcc tgccacaata tttttaatta cgtacaaaga tctgacatgt caccagggga      60
cccatttcac ccactgctct gtttgccgc 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 gtogaacttg 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 accgcagggg      120
ctgccaggtg cacagccctg gctcccgagg caggcaggca aggtgacggg actggaagcc      180
cttttcanag ccttgaggga gctggtccgt ccacaagcaa tgagtgccac tctgcagttt      240
gcaggggatg gataaacagg gaaacactgt gcattcctca cagccaacag tgtaggtctt      300
ggtgaagccc cggcgctgag ctaagctcag gctgttcag 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 ccattggca tcaccggtgc agccattggg ggcagcgggt accggtcctt      180
tcttgttcaa catagggtag gtggcagcca cgggtccaac tcgcttgagg ctgggccctg      240
ggcgctccat tttgtgttcc angagcatgt ggttctgttg cgggagcccc acgcagggcc      300
tgaggatggt ctgatgcag 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

```

<400> 287
 tgggtaccaa atttttttat ttgaaggaat ggnacaaatc aaanaactta agnggatgtt 60
 ttggtacaac ttatanaaaa ggnaaaggaa accccaacat gcatgcnctg ccttgngnac 120
 cagggaagtc accccacggc tatggggaaa ttancccgag gcttancttt cattatcact 180
 gtctcccagg gngngcttgc caaaaanata ttcncccaag ccaaattcgg gcgctcccat 240
 nttgcncaag ttggtcacgt 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 aaaaaaaatg gcactctgat taaactgcat tacagcctgc aggacacctt 120
 gggccagctt ggtttttactc tanattttcac tgctgctccc cccacttct tccacccac 180
 ttcttctctc accaacatgc aagttctttc ctccctgccc 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 agaggggtgca 120
 ggctgagggg ggaagggtta naggaaggaa ggccatcctg gatccccaca tttcagtctc 180
 anatgaggac aaagggactc ccaagcccc aaatcatcan aaaacaccaa ggagcaggag 240
 gagcttgagc aggcctcagg gagcctcana gccataccag ccaactgtcta ctcccatcc 300
 tctctccca ttcctgtctc gcttcnacc acctccagc taagccccag ctccattccc 360
 ccaatcctgg ccttgccag cttgacagtc acagtgcctg gaattccacc actgaggctt 420
 ctcccagttg gattaggacg tcgccctgtt agcatgctgc cc 462

<210> 290
 <211> 481
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(481)

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

<400> 290

tacttttcta	aactttatta	aagaaaaaag	caataagcaa	tgngnggtaaa	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	ttanaaactg	catctcctgt	gtcaaaaacca	anaatatgtt	360
tgtctaaagc	aacaggttaag	ccctcttttg	tttgatttgc	cttancaact	gcctcctgtg	420
tcaggcgctc	ctgaaccaa	atccgaattg	ccttaagcat	taccaggtaa	tcatcatgac	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

tcatagtaat	gtaaaaccat	ttgtttaatt	ctaaatcaaa	tcactttcac	aacagtgaag	60
attagtgaact	ggttaaggng	tgccactgta	catatcatca	ttttctgact	ggggtcagga	120
cctgggtccta	gtccacaagg	gtggcaggag	gaggggtggag	gctaanaaca	cagaaaacac	180
acaaaaanaaa	ggaaagctgc	cttggcanaa	ggatgaggng	gtgagcttgc	cgaaggatgg	240
tgggaagggg	gctccctgtt	ggggccgagc	caggagtccc	aagtcagctc	tectgcctta	300
cttagctcct	ggcanagggg	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	tcogtttaat	tgaaaaacct	gnaggatact	attccactcc	cccanatgag	60
gaggctgagg	anaccaaacc	cctacatcac	ctcgtagcca	cttctgatac	tettcacgag	120
gcagcaggca	aagacaattc	ccaaaacctc	nacaaaagca	attccaaggg	ctgctgcagc	180
taccaccanc	acatttttcc	tcagccagcc	cccaatcttc	tcacacagc	cctccttatg	240
gategccttc	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
ctgttcattg tttcttgaac acgtcttcaa ttttccttcc aaaatgctgc atgccacact      180
tgaggtaacg aagcanaagt atttttaaac atgacagcta anaacattca tctacagcaa      240
cctatatgct caatacatgc cgcgtgatcc tagtagtttt ttcacaacct tctacaagtt      300
tttggaaac atctgttatg atgactttca tacaccttca cctcaaaggc tttcttgcac      361
c

<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 tttatttatg attcanaaaa aatcgagcga ataactttct ctgaaaaaat      60
atattgactc tgtatanacc acagttattg gggganaagg gctggtaggt taaattatcc      120
tattttttat tctgaaaatg atattaatan aaagtcctcg ttcagctctg attataaaga      180
tacatatgcc caaaatggct ganaataaat acaacaggaa atgcaaaagc tgtaaagcta      240
agggcatgca ananaaaatc tcanaatacc caaagnngca acaaggaaagc tttggctgga      300
atttgaagtt atttcagtca tctttgtctt tggtctccatg 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
ttcttttggt ttattgataa cagaaactgt gcataattac agatttgatg aggaatctgc      60
aaataataaa gaatgtgtct actgccagca aaatacaatt attccatgcc ctctcaacat      120
acaaatatag agttcttcac accanatggc tctgggtgtaa caaagccatt ttanatgttt      180
aattgtgctt ctacaaaacc ttoanagcat gaggtagttt cttttaccta cnatattttc      240
cacatttcca ttattacact tttagtgagc taaaatcctt ttaacatagc ctgoggatga      300
tctttcacaa aagccaagcc tcatttacia agggttttatt tct                                     343

<210> 296
<211> 241
<212> DNA

```

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (241)

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

<400> 296

ttcttggata ttggttgttt ttgtgaaaaa gtttttgttt ttctttctcag tcaactgaat	60
tattttctcta ctttgccctc ctgatgcccc catgananaa cttaanataa tttctaacag	120
cttccacttt ggaaaaaaa aaaacctgtt ttctcatgg aaccccagga gttgaaagt	180
gatanatgc 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

gttggtgctg anaatgctgg agatgctcag ttctctccct cacaaggtag gccacaaatt	60
cttgggtggtg ccttcacatc tggggtcttc aggcaccagc catgcctgcc gaggagtgt	120
gtcaggacan accatgtccg tgctaggccc aggcacagcc caaccactcc tcatccaagt	180
ctctcccagg tttctgggtc cgatgggcaa ggatgacccc tccagtggct ggtacccac	240
catcccacta cccctcacat gctctcactc tccatcaggt ccccaatcct ggcttccctc	300
ttcacgaact ctcaaagaaa aggaaggata aaacctaaat aaaccagaca gaagcagctc	360
tggaaaagta caaaaagaca gccagagggtg 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 tgnntccagc tttattaaan atactttcca taaacaatca tggattttca	60
ggcaggacat gggcanacaa tcgttaacag tataacaaca ctttcaaact cccttnttca	120
atggactacc aaaaatcaaa aagccactat aaaacccaat gaagtcttca tctgatgtc	180
tgaacaggga aagttttaaag ngagggttga catttcacat ttagcatgtt gtttaacaac	240
ttttcacaag ccgacctga 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 agtgttgaag tttatattt atagcaccat tgagacattt tgaaattgga 60
 attggtaaaa aaataaaaca aaaagcattt gaattgtatt tggnggaaca gcaaaaaaag 120
 agaagtatca tttttctttg tcaaattata ctgtttccaa acatttttga 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 agataaaactt ttttgtcttt gotttatctt attagggagt 120
 tgtatgtcag tgtataaaac atactgtgtg gtataacagg cttataataat tctttaaaag 180
 gaaaaaaa 188

<210> 301
 <211> 291
 <212> DNA
 <213> Homo sapien

<400> 301
 aagattttgt tttatattt tatggctaga aagacactgt tatagccaaa atcggcaatg 60
 acactaaaga aatcctctgt gcttttcaat atgcaaatat atttcttcca agagttgecc 120
 tgggtgtgact tcaagagttc atgttaactt cttttctgga aacttccttt tcttagttgt 180
 tgtattcttg aagagcctgg gccatgaaga gcttgccctaa 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 aatggttcgc gtatcacaca 60


```

attacactac aatctgatag gagtggtaaa accagccaat ggaatccagg taaagtacaa      120
aaacgccacc ttttattgtc ctgtcttatt tctcggaag gagggttcta ctttacacat      180
ttcatgagcc agcagtggac ttgagttaca atgtgtagggt tccttggtggg tatagctgca      240
gaagaagcca tcaaattctt gaggacttga catctctcgg aaagaagcaa actagtggat      300
ccccggggt 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 aaatnaattt tatttgngtt cacagaacat actaggcgat ctgcacagtc      60
gctccgtgac agcccaccaa cccccaaccc tntacctcgc agccacccta aaggcgactt      120
caanaanatg gaaggatctc acggatctca ttctaatgg tccgccgaag tctcacacag      180
tanacagacg gagttganat gctggaggat gcagtcacct cctaaactta cgaccaccca      240
ccanacttca tcccagccgg gacgtcctcc cccacccgag tcttccccat ttcttctcct      300
actttgccgc agttccagggt gtcttgcttc caccagtcctc 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
ctcttttaca cagcctttat ttncggccct tgatcctgct cggatgctgg tggaggccct      60
tagctccgcc cgccaggctc tgtgccgcct ccccgaggc gcanattcat gaacacgggtg      120
ctcagggggt tgaggccgta ctccccagc gggagctggt cctccagggg ctccccctcg      180
aaggctcagcc anaacaggct gtctgcaca cctccagcc cgctcacttg ctgcttcagg      240
tgggccacgg 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

```

ggggctggcc	ctcacagggt	gttgagttcc	agcaggggtct	ggccaaggt	ctggtgaatc	120
tgcagcttct	cctccttggc	actggccaag	gtctcttcta	ggtcacgat	ggttttctcc	180
aactttgcc	canacctctc	ggcaaaactct	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	taagtataaaa	aaagttagac	tttcaagcct	gtaatcccag	180
cactttggga	ggctgaggca	ggtggatcac	taacattaaa	aagacaacat	tagattttgt	240
cgatttatag	caattttata	aatatataac	tttgtcactt	ggatcctgaa	gcaaaaataat	300
aaagtgaatt	tgggattttt	gtacttggtg	aaaagtttaa	cacctaaat	tcacaactag	360
tggatcccc	gggctgcagg	aattcgatat	caagcttatc	gataccgtcg	acctcgaggg	420
ggggcccggt	acccaattcg	ccctatagtg	agtcgta			457

<210> 307

<211> 491

<212> DNA

<213> Homo sapien

<400> 307

gtgcttgga	ggaacccggc	gctcgttccc	caccccgggc	ggcgcgccat	agccagccct	60
cgtcaacctc	ttcacgcac	cctcgactg	ccccaggcc	cccgccgcgc	ctccagcgcc	120
gcgagccac	cgccgcggc	gcccctctc	cttagtgcc	gccatgacga	ccgcgtccac	180
ctcgagggtg	cgccagaact	accaccagga	ctcagaggcc	gccatcaacc	gccagatcaa	240
cctggagctc	tacgcctcct	acgtttacct	gtccatgtct	tactactttg	accgcgatga	300
tgtggctttg	aagaactttg	ccaaataactt	tcttcaccaa	tctcatgagg	agagggaaca	360
tgctgagaaa	ctgatgaagc	tgcagaacca	acgagggtggc	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	catggcggtg	cctctggaga	60
aggccctgga	tgtgatggtg	tccaccttcc	acaagtactc	gggcaaagag	ggtgacaagt	120
tcaagctcaa	caagtcagaa	ctaaaggagc	tgtgaccccg	ggagctgccc	agcttcttgg	180
ggaaaaggac	agatgaagct	gctttccaga	agctgatgag	caacttggac	agcaacaggg	240
acaacgaggt	ggacttccaa	gagtactgtg	tcttctgtgc	ctgcatcgcc	atgatgtgta	300
acgaattctt	tgaaggcttc	ccagataagc	agcccaggaa	gaaatgaaaa	ctcctctgat	360
gtgggttgggg	ggtctgccag	ctggggccct	ccctgtcgcc	agtgggcact	tttttttttc	420
c						421

<210> 309

<211> 321

<212> DNA

<213> Homo sapien

<400> 309

accaaagtggc	ggatgacgcc	ggtgcagcgg	gggggcccgg	gggccctggt	ggccctggga	60
tggggaaccg	cggtggcttc	cgcggagggt	tcggcagtgg	catccggggc	cggggtcgcg	120
gccgtggacg	gggcgggggc	cgaggccggc	gagctcggcg	aggcaaggcc	gaggataagg	180
agtggatgcc	cgtcaccaag	ttgggcggct	tggtcaagga	catgaagatc	aagtccctgg	240
aggagatcta	tctcttctcc	ctgcccatta	aggaatcaga	gatcattgat	ttcttctctg	300
gggcctctct	caaggatgag	g				321

<210> 310

<211> 381

<212> DNA

<213> Homo sapien

<400> 310

ttaaccagcc	atattggctc	aataaatagc	ttcggtaagg	agttaatttc	cttctagaaa	60
tcagtgccta	tttttctctg	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	agatatattt	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
accaagtctc	gatatctttt	aaagacatag	ttcaaaaattg	cttttgaaaa	tctgtattct	180
tgaaaatata	cttggttggt	attaggtttt	taaataccag	ctaaaggatt	acctcactga	240
gtcatcagta	ccctcctatt	cagctcccca	agatgatgtg	tttttgctta	ccctaagaga	300
ggttttcttc	ttatttttag	ataattcaag	tgcttagata	aattatgttt	tctttaagtg	360
tttatggtaa	actcttttaa	agaaaattta	atatgtttata	gctgaatctt	tttggttaact	420
ttaaatcttt	atcatagact	ctgtacatat	gttcaaatta	gctgcttgcc	tgatgtgtgt	480
atcatcggtg	ggatgacaga	acaaacatat	ttatgatcat	gaataatgtg	ctttgtaa	538

<210> 312

<211> 176

<212> DNA

<213> Homo sapien

<400> 312

ggaggagcag	ctgagagata	gggtcagtga	atgcggttca	gootgctacc	tctcctgtct	60
tcatagaacc	attgccttag	aattattgta	tgacacgttt	tttggtgggt	aagctgtaag	120
gttttgttct	ttgtgaacat	gggtattttg	aggggagggg	ggaggagta	gggaag	176

<210> 313

<211> 396

<212> DNA

<213> Homo sapien

<400> 313

ccagcacc	ccccc	caggccctgg	gggacctggg	ttctcagact	gccccagaag	ccttgccatc	60
tggcgctccc	atggctcttg	caacatctcc	ccttcgtttt	tgaggggggc	atgccggggg		120
agccaccagc	ccctcactgg	gttcggagga	gagtcaggaa	gggccaaagca	cgacaaagca		180
gaaacatcgg	atctggggaa	cgcgtgtcaa	tcccttggtg	cgcaggggctg	ggcgggagag		240
actgtttctgt	tccttggtga	actgtgttgc	tgaaagacta	cctcgttctt	gtcttgatgt		300
gtcacggggg	caactgcctg	ggggcgggga	tgggggcagg	gtggaagcgg	ctccccattt		360
tataccaaag	gtgctacatc	tatgtgatgg	gtgggg				396

<210> 314

<211> 311

<212> DNA

<213> Homo sapien

<400> 314

cctcaacatc	ctcagagagg	actggaagcc	agtccttaag	ataaactcca	taatttatgg	60
cctgcagtat	ctcttcttgg	agcccaaccc	cgaggaccca	ctgaacaagg	aggccgcaga	120
ggctcctgcag	aacaaccggc	ggctgtttga	gcagaacgtg	cagcgctcca	tgccgggtgg	180
ctacatcggc	tccacctact	ttgagcgctg	cctgaaatag	ggttggcgca	taccaccccc	240
cgcacgggcc	acaagccctg	gcacccccctg	caaatatatta	ttggggggcca	tgggtagggg	300
tttgggggggc	g					311

<210> 315

<211> 336

<212> DNA

<213> Homo sapien

<400> 315

tttagaacad	ggttatcatc	caagactact	ctaccctgca	acattgaact	cccaagagca	60
aatccacatt	cctcttgagt	tctgcagctt	ctgtgtaaat	agggcagctg	tcgtctatgc	120
cgtagaatca	catgatctga	ggaccattca	tgggaagctgc	taaatagcct	agtctgggga	180
gtcttccata	aagttttgca	tggagcaaac	aaacaggatt	aaactagggt	tggttccttc	240
agccctctaa	aagcataggg	cttagcctgc	aggcttcctt	gggctttctc	tgtgtgtgta	300
gtttttgtaaa	cactatagca	tctgttaaga	tccagt			336

<210> 316

<211> 436

<212> DNA

<213> Homo sapien

<400> 316

aacatggctt	gctgacctta	agagagacgc	ttcctgcaga	acaggacctg	actacaaaga	60
atgtttccat	tggaattggt	ggtaaagact	tggagtttac	aatctatgat	gatgatgatg	120
tgtctccatt	cctggaagggt	cttgaagaaa	gaccacagag	aaaggcacag	cctgctcaac	180
ctgctgatga	acctgcagaa	aaggctgatg	aaccaatgga	acattaagtg	ataagccagt	240
ctatatatgt	attatcaaat	atgtaagaat	acaggcacca	catactgatg	acaataatct	300
atactttgaa	ccaaaagtgt	cagagtgggtg	gaatgctatg	ttttaggaat	cagtccagat	360
gtgagttttt	tccaagcaac	ctcactgaaa	cctatataat	ggaatacatt	tttctttgaa	420
agggctctgta	taatca					436

<210> 317

<211> 196

<212> DNA

<213> Homo sapien

<400> 317
 tattccttgt gaagatgata tactatTTTT gttaagcgtg tctgtattta tgtgtgagga 60
 gctgctggct tgcagtgcgc gtgcacgtgg agagctgggtg cccggagatt ggacggcctg 120
 atgctccctc cctgcctctg gtccagggaa gctggccgag ggtcctggct cctgaggggc 180
 atctgccccct 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
 gacgcttngg ccgtaacgat gatcggagac atcctgctgt tggggacgtt gctgatgaat 60
 gccggggcgg tgcctgaactt taagctgaaa aagaaggaca cncagggctt tggggaggag 120
 tncagggagc ccaacacagg tgacaacatc cgggaattct tgcctgancct cagatacttt 180
 cnaatcttca tncctctgtg gaacatcttc atgatgttct gcatgattgt gctgntcggc 240
 tcttgaatcc cancgatgaa accannaact cactttcccg ggatgccgan tctccattcc 300
 tccattcctg atgacttcaa naatgttttt gaccaaaaaa ccgacaacct tcccagaaag 360
 tccaagctcg tgggtggngg a 381

<210> 319
 <211> 506
 <212> DNA
 <213> Homo sapien

<400> 319
 ctaagcttta cgaatggggg gacaacttat gataaaaaact agagctagtg aattagccta 60
 tttgtaaaata cctttgttat aattgatagg atacatcttg gacatggaat tgttaagcca 120
 cctctgagca gtgtatgtca ggacttggtt attaggttgg cagcagaggg gcagaaggaa 180
 ttatacaggt agagatgtat gcagatgtgt ccatatatgt ccatatttac attttgatag 240
 ccattgatgt atgcattctt tggctgtact ataagaacac attaatcaaa tggaaataca 300
 ctttgctaatt attttaatgg tatagatctg ctaatgaatt ctcttaaaaa catactgtat 360
 tctgttgcgt tgtgtttcat tttaaattga gcattaaggg aatgcagcat ttaaatacaga 420
 actctgccaa tgcttttata tagaggcgtg ttgccatttt tgtcttatat gaaatttctg 480
 tcccaagaaa 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 tatccctca gcagagatgg agagctaaag 180
 tccaagagag gatccgagaa cgctctaagc ctgtccacga gctcaatagg gaagcctgtg 240
 atgactacag acttttgcgaa cgctaogcca tggtttatgg atacaatgct gcctataatc 300
 gctacttcag gaagcgccga gggaccaaact gagactgagg gaagaaaaaa a 351

<210> 321

<211> 421
 <212> DNA
 <213> Homo sapien

<400> 321
 ctccggaggcg ttcagctgct tcaagatgaa gctgaacatc tccttcccag ccaactggctg 60
 ccagaaaactc attgaagtgg acgatgaacg caaacttcgt actttctatg agaagcgtat 120
 ggccacagaa gttgctgctg acgctctggg tgaagaatgg aagggttatg tggctccgaat 180
 cagtgggtggg aacgacaaaac aagggtttccc 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 tcctcaccoc ctgaaaatgt tcgcctgctc caagtttgctc 60
 tccactccct ccttggtcaa gagcacctca cagctgctga gccgtccgct atctgcagtg 120
 gtgtgaaac gaccggagat actgacagat gagagcctca gcagcttggc agtctcatgt 180
 cccettacct cacttgctctc tagccgcagc ttccaaacca gcgccatttc aagggcacac 240
 gacacagcag ccaagttcat tggagctggg gctgccacag ttgggggtggc tggttctggg 300
 gctgggattg gaactgtgtt tgggagcctc atcattggtt atgccaggaa ccttctcttg 360
 aagcaacagc tcttctccta cgcattctg ggctttgcc tctcgagggc catggggctc 420
 tttgtctga tggtagcctt tctcatcctc tttgccatgt gaaggagccg tctccacctc 480
 ccatagttct cccgcgtctg gttggccccg tgtgttccct t 521

<210> 323
 <211> 435
 <212> DNA
 <213> Homo sapien

<400> 323
 ccgaggtcgc acgcgtgaga cttctccgcc gcagacgccg ccgcgatgag ctacgtcgcc 60
 tcctacctgc tggctgccct agggggcaac tcctccccca gcgccaagga catcaagaag 120
 atcttggaac gcgtgggtat cgaggcggac gacgaccggc tcaacaaggt tatcagttag 180
 ctgaatggaa aaaacattga agacgtcatt gccacgggta ttggcaagct tgccagtgtg 240
 cctgctggtg gggctgtagc cgtctctgct gccccaggct ctgcagcccc tgctgctggt 300
 tctgccctg ctgcagcaga ggagaagaaa gatgagaaga aggaggagtc tgaagagtca 360
 gatgatgaca tgggatttgg cttttttgat taaattcctg ctccccgtga aataaagcct 420
 ttttacacat ctcaa 435

<210> 324
 <211> 521
 <212> DNA
 <213> Homo sapien

<400> 324
 aggagatcga ctttcggtgc ccgcaagacc agggctggaa cgcgcgagatc acgctgcaga 60
 tgggtgcagta caagaatcgt caggccatcc tggcgtgcaa atccacgcgg cagaagcagc 120
 agcacctggt ccagcagcag cccccctcgc agccgcagcc gcagccgcag ctccagcccc 180
 aaccccagcc tcagcctcag ccgcaacccc agcccacac acaaccccag cctcagcccc 240

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aaccceaagcc tcagccccag cagctccacc cgtatccgca tccacatcca catccacact 300
ctcatcctca ctgcaccca caccctcacc cgcacccgca tccgcaccaa ataccgcacc 360
cacaccacaca gccgcactcg cagccgcacg ggcacccggt tctccgcagc acctccaact 420
ctgcctgaaa ggggcagctc ccgggcaaga caagggtttg aggacttgag gaagtgggac 480
gagcacatth ctattgtctt cacttggatc aaaagcaaaa c 521

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```

<210> 325
<211> 451
<212> DNA
<213> Homo sapien

```

```

<400> 325
attttcatth ccattaacct ggaagctttc atgaatatcc tcttctttta aaacatttta 60
acattattta aacagaaaaa gatgggctct ttctgggttag ttgttacatg atagcagaga 120
tatttttact tagattactt tgggaatgag agattgttgt cttgaactct ggcactgtac 180
agtgaatgtg tctgtagtgt tgttagtttg cattaagcat gtataacatt caagtatgtc 240
atccaaataa gaggcataata cattgaattg tttttaatcc tctgacaagt tgactcttcg 300
acccccaccc ccacccaaga catthtaata gtaaataagag agagagagaa gagttaatga 360
acatgaggta gtgttcact ggcaggatga cttttcaata gctcaaatca atttcagtgc 420
ctttatcact tgaattatta acttaatttg a 451

```

```

<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
cgcggtcgta agggctgagg atttttggtc cgcacgctcc tgctcctgac tcaccgctgt 60
tcgctctcgc cgaggaacaa gtcggtcagg aagcccgccg gcaacagcca tggcttttaa 120
ggataccgga aaaacacccg tggagccgga ggtggcaatt caccgaattc gaatcacctt 180
aacaagccgc aacgtaaaat ccttggaaaa ggtgtgtgct gacttgataa gaggcgcaaa 240
agaaaagaat ctcaaagtga aaggaccagt tcgaatgcct accaagactt tgagantcac 300
tacaagaaaa actccttgtg gtgaagggtc taagacgtgg gatcgtttcc agatgagaat 360
tcacaagcga ctcatgtact tgcacagtc cttctgagatt gttaagcaga ttacttccat 420
c 421

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<210> 327
<211> 456
<212> DNA
<213> Homo sapien

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<400> 327
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atgaataggt ccaaccagct gtacatttgg aaaaat 456

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<210> 328
<211> 471
<212> DNA
<213> Homo sapien

<400> 328
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<210> 329
<211> 278
<212> DNA
<213> Homo sapien

<220>
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<222> (1)...(278)
<223> n = A,T,C or G

<400> 329
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<210> 330
<211> 338
<212> DNA
<213> Homo sapien

<400> 330
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cgactctctc cctgaactct acacaacata ttttgtcacc aagaccctac ttctaacctc 180
cctgttctta tgaattcgaa cagcataccc ccgattccgc tacgaccaac tcatacacct 240
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cattacaatc tccagcattc cccctcaaac ctaaaaaa 338

<210> 331
<211> 2820
<212> DNA
<213> Homo sapiens

<400> 331
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gotcctgaac agcatggacc agcagattcg gaacggctcc tcgtccacca gtccctataa 180
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<210> 332

<211> 2270

<212> DNA

<213> Homo sapiens

<400> 332

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aaagaaagtt attaccgata caccatgtcc cagagcacac agacaaatga attcctcagt 180
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<210> 333

<211> 2816

<212> DNA

<213> Homo sapiens

<400> 333

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ccaggcccg caggtttcga cgtgtccttc cagcagtcga gcaccgcaa gtcggccacc 600
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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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gacatgcaat aaaattttaa aaataaataa aaactaatta agaaataaa 4849

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<210> 336

<211> 1386

<212> DNA

<213> Homo sapiens

<400> 336

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aacacagacc acgcgcagaa cagcgtcacg gcgccctcgc cctacgcaca gccaggtccc 180
accttcgatg ctctctctcc atcaccgcc atccctcca acaccgacta cccaggcccc 240
cacagtttcg acgtgtcctt ccagcagtcg agcaccgcca agtcggccac ctggacgtat 300
tccactgaac tgaagaaact ctactgccaa attgcaaaga catgccccat ccagatcaag 360
gtgatgacct cacctcctca gggagctgtt atccgcgcca tgcctgtcta caaaaaagct 420
gagcacgtca cggaggtggt gaagcgggtg cccaaccatg agctgagccg tgaattcaac 480
gagggacaga ttgcccctcc tagtcatttg attcgagtag aggggaacag ccatgccccag 540
tatgtagaag atcccatcac aggaagacag agtgtgctgg taccttatga gccaccccag 600
gttggcactg aattcacgac agtcttgtag aatttcatgt gtaacagcag ttgtgttgga 660
gggatgaacc gccgtccaat tttaatcatt gttactctgg aaaccagaga tgggcaagtc 720
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gacatgaatg gactcagccc cccccaggca ctccctcccc cactctccat gccatccacc 1320
tccactgca cccccacc tccgtatccc acagattgca gcattgtcag gatctggcaa 1380
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<210> 337

<211> 1551

<212> DNA

<213> Homo sapiens

<400> 337

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ccatcagaag atggtgagac aaacaagatt gagattagca tggactgtat ccgcatgcag 180
gactcggacc tgagtgacct catgtggcca cagtacacga acctggggct cctgaacagc 240
atggaccagc agattcagaa cggctcctcg tccaccagtc cctataacac agaccacgcg 300
cagaacagcg tcacggcgcc ctgcctctac gcacagccca gctccacctt cgatgctctc 360
tctccatcac ccgcctatccc ctccaacacc gactaccagag gccgcacag tttcgacgtg 420
tccctccagc agtcgagcac cgccaagtcg gccacctgga cgtattccac tgaactgaag 480
aaactctact gccaaattgc aaagacatgc ccatccaga tcaaggatg gacccacact 540
cctcagggag ctgttatccg cgccatgcct gtctacaaa aagctgagca cgtcacggag 600
gtgggtgaagc ggtgccccaa ccatgagctg agccgtgaat tcaacgaggg acagattgcc 660
cctcctagtc atttgattcg agtagagggg aacagccatg cccagtatgt agaagatccc 720

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atcacaggaa gacagagtgt gctggtacct tatgagccac cccaggttgg cactgaattc 780
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<210> 338

<211> 586

<212> PRT

<213> Homo sapiens

<400> 338

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Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Arg 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 Pro 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 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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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		
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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		
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		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 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 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		
465	470	475
		480

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
 565 570 575

Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
 580 585

<210> 339

<211> 641

<212> PRT

<213> Homo sapiens

<400> 339

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
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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 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
 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 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
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 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 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

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
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 <211> 356
 <212> PRT
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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 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
 225 230 235 240
 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 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
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
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 340 345 350
 Leu Gln Lys Gln
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 <210> 342
 <211> 680
 <212> PRT
 <213> Homo sapiens
 <400> 342
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 20 25 30
 Glu Ser Tyr Tyr Arg Ser Thr Met Ser Gln Ser Thr Gln Thr Asn Glu
 35 40 45

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

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

625 630 635 640
 Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro Arg Asp
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 Gln Arg Ile Lys Glu Glu Gly Glu
 675 680

 <210> 343
 <211> 461
 <212> PRT
 <213> Homo sapiens

 <400> 343
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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 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

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 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
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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 Arg Ile Trp Gln Val
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<210> 344

<211> 516

<212> PRT

<213> Homo sapiens

<400> 344

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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					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
 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
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 Ile Trp Gln Val
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<211> 1800

<212> DNA

<213> Homo sapiens

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 tgacattcgt atcatcactg tgcaccattg gcttctagga actccagtgg ggtaggagaa 180

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tttcatcgga ggtgtcaaca aacactccac cagcatcggg aaggtgtgga tcacagtcac 360
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<210> 346

<211> 261

<212> PRT

<213> Homo sapiens

<400> 346

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Ser Thr Ser Ile Gly Lys Val Trp Ile Thr Val Ile Phe Ile Phe Arg
          20                      25                      30

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```

Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln
          35                      40                      45

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Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
          50                      55                      60

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

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

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Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
          100                     105                     110

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Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys His Lys Val Arg Ile
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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
 180 185 190

Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala
 195 200 205

Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
 210 215 220

Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys
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Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile
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Thr Gly Phe Pro Ser
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<210> 347

<211> 1740

<212> DNA

<213> Homo sapiens

<400> 347

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 ctagtccagt atggagtggt ggagagctgt gagcaagtga aactgactc ggaaactgca 360
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 ctgggtccca cccaatttgt tggagccatc ataggaaaag aagggtgccac cattcggaac 660
 atcaccaaac agaccagtc taaaatcgat gtccaccgta aagaaaatgc gggggctgct 720
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<213> Homo sapiens

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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 Thr 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

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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
Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala		
245	250	255
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		
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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		
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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
Glu Gln Ser Glu Thr Glu Thr Val His Leu 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

Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val
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Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser
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Arg Arg Lys

<210> 349

<211> 207

<212> DNA

<213> Homo sapiens

<400> 349

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<210> 350

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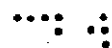
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35 40 45

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



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[51]Int. Cl⁷

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[21] 申请号 00807012.1

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C12N 15/12 C12N 15/10

C12N 15/62 C07K 16/30

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A61K 38/17 A61P 35/00

[43]公开日 2002年9月18日

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[22]申请日 2000.4.3 [21]申请号 00807012.1

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[32]1999.4.2 [33]US [31]09/285,479

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[32]1999.12.30 [33]US [31]09/476,496

[32]2000.1.10 [33]US [31]09/480,884

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[74]专利代理机构 中国国际贸易促进委员会专利商标事
务所

代理人 唐伟杰

权利要求书 13 页 说明书 221 页 附图页数 0 页

[54]发明名称 用于治疗 and 诊断肺癌的化合物和方法

[57]摘要

本发明提供用于治疗 and 诊断肺癌的化合物和方法。
本发明化合物包括含 有肺肿瘤蛋白质的至少一个部分
的多肽。本发明还提供含有该多肽、或 编码该多肽的
DNA 分子,用于免疫治疗肺癌的疫苗和药物组合物,以
及 用于制备本发明多肽的 DNA 分子。

ISSN 1008-4274

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权 利 要 求 书

1. 分离的多肽，其含有肺肿瘤蛋白质或其变体的至少免疫原性部分，其中该肿瘤蛋白质含有由选自下组的多核苷酸序列编码的氨基酸序列：

(a) 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 和 349 中所示序列；

(b) 与 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 和 349 之任一个中所示序列在中等严谨条件下杂交的序列；和

(c) (a)或(b)的互补序列。

2. 根据权利要求 1 的分离多肽，其中该多肽含有由 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 和 349 之任一个中所示多核苷酸序列、或任一个前述多核苷酸序列的互补序列编码的氨基酸序列。

3. 含有 SEQ ID NO: 110、112、114、152、155、156、159、161、165、166、169、170、172、174、176、226-252、346、348 和 350 之任一个中所示序列的分离的多肽。

4. 编码肺肿瘤蛋白质或其变体中的至少 15 个氨基酸残基的分离的多核苷酸，该变体与所述肺肿瘤蛋白质相差一或多个替代、缺失、添加和/或插入以致该变体与抗原特异性抗血清的反应能力在相当大程度得到保持，其中该肺肿瘤蛋白质含有由包含 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 和 349 之任一个中所示的序列、或任一个前述序列的互补序列的多核苷酸编码的氨基酸序列。

5. 编码肺肿瘤蛋白质或其变体的分离的多核苷酸，其中该肺肿瘤蛋白质含有由包含 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 和 349 之任一个中所示的序列、或任一前述序列的互补序列的多核苷酸编码的氨基酸序列。

6. 分离的多核苷酸，其含有 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 和 349 之任一个中所示的序列。

7. 分离的多核苷酸，其含有与 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 和 349 之任一个中的所示序列在中等严谨条件下杂交的序列。

8. 与根据权利要求 4-7 之任一项的多核苷酸互补的分离多核苷酸。

9. 含有根据权利要求 4-8 之任一项的多核苷酸的表达载体。

10. 用根据权利要求 9 的表达载体转化或转染的宿主细胞。
11. 特异地与肺肿瘤蛋白质结合的分离的抗体或其抗原结合片段，其中该肺肿瘤蛋白质含有由 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 和 349 之任一个中所示的多核苷酸序列、或任一个前述多核苷酸序列的互补序列编码的氨基酸序列。
12. 含有至少一个根据权利要求 1 的多肽的融合蛋白。
13. 根据权利要求 12 的融合蛋白，其中该融合蛋白含有在转染了编码该融合蛋白的多核苷酸的宿主细胞中增强该融合蛋白表达的表达增强子。
14. 根据权利要求 12 的融合蛋白，其中该融合蛋白含有在权利要求 1 的多肽中不存在的 T 辅助细胞表位。
15. 根据权利要求 12 的融合蛋白，其中该融合蛋白含有亲和标记物。
16. 编码根据权利要求 12 的融合蛋白的分离的多核苷酸。
17. 药物组合物，其含有生理学上可接受的载体和至少一个选自下组的成分：

- (a) 根据权利要求 1 的多肽;
- (b) 根据权利要求 4 的多核苷酸;
- (c) 根据权利要求 11 的抗体;
- (d) 根据权利要求 12 的融合蛋白; 和
- (e) 根据权利要求 16 的多核苷酸。

18. 含有免疫刺激剂和至少一个选自下组的成分的疫苗:

- (a) 根据权利要求 1 的多肽;
- (b) 根据权利要求 4 的多核苷酸;
- (c) 根据权利要求 11 的抗体;
- (d) 根据权利要求 12 的融合蛋白; 和
- (e) 根据权利要求 16 的多核苷酸。

19. 根据权利要求 18 的疫苗, 其中该免疫刺激剂是佐剂。

20. 根据权利要求 18 的疫苗, 其中该免疫刺激剂诱导主要是 I 型应答。

21. 抑制患者体内癌症发展的方法, 其包括给患者施用有效量的根据权利要求 17 的药物组合物。

22. 抑制患者体内癌症发展的方法, 包括给患者施用有效量的根据权利要求 18 的疫苗。

23. 药物组合物, 其含有表达根据权利要求 1 的多肽的抗原呈递细胞, 及可药用载体或赋形剂。

24. 根据权利要求 23 的药物组合物, 其中该抗原呈递细胞是树突

细胞或巨噬细胞。

25. 含有表达如下多肽的抗原呈递细胞和免疫刺激剂的疫苗，该多肽含有肺肿瘤蛋白质或其变体的至少免疫原性部分，其中该肿瘤蛋白质含有由选自下组的多核苷酸序列编码的氨基酸序列：

(a) 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 和 349 中所示序列；

(b) 与 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 和 349 之任一个中所示序列在中等严谨条件下杂交的序列；和

(c) (i)或(ii)的序列的互补序列。

26. 根据权利要求 25 的疫苗，其中该免疫刺激剂是佐剂。

27. 根据权利要求 25 的疫苗，其中该免疫刺激剂诱导主要是 I 型应答。

28. 根据权利要求 25 的疫苗，其中该抗原呈递细胞是树突细胞。

29. 抑制患者体内癌症发展的方法，包括给患者施用有效量的表达如下多肽的抗原呈递细胞，该多肽含有肺肿瘤蛋白质或其变体的至少免疫原性部分，其中该肿瘤蛋白质含有由选自下组的多核苷酸序列编码的氨基酸序列：

(a) 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 和 349 中所示序列；

(b) 与 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 和 349 之任一个中所示序列在中等严谨条件下杂交的序列；和
(c) 由 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 和 349 之任一个中所示多核苷酸编码的 (i) 或 (ii) 的序列的互补序列；

并藉此抑制该患者体内的癌症展。

30. 根据权利要求 29 的方法，其中该抗原呈递细胞是树突细胞。

31. 根据权利要求 21、22 和 29 之任一项的方法，其中所述癌症是肺癌。

32. 从生物样品中清除肿瘤细胞的方法，包括用特异地与肺肿瘤蛋白质反应的 T 细胞接触生物样品，其中该肿瘤蛋白质含有由选自下组的多核苷酸序列编码的氨基酸序列：

(i) 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 和 349 之任一个中所示的多核苷酸；和

(ii) 前述多核苷酸的互补序列；

其中该接触步骤在足以允许从该样品中清除表达该抗原的细胞的条件下和时间下进行。

33. 根据权利要求 32 的方法，其中该生物样品是血液或其组分。

34. 抑制患者体内癌症发展的方法，包括给患者施用经权利要求 32 的方法处理过的生物样品。

35. 刺激和/或扩增肺肿瘤蛋白质特异性 T 细胞的方法，包括在足以允许刺激和/或扩增 T 细胞的条件下和时间下，用至少一个选自下组的成

分接触 T 细胞:

(a) 含有肺肿瘤蛋白质或其变体的至少免疫原性部分的多肽, 其中该肺肿瘤蛋白质含有由选自下组的多核苷酸序列编码的氨基酸序列:

(i) 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 和 349 中所示序列;

(ii) 与 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 和 349 之任一个中所示序列在中等严谨条件下杂交的序列; 和

(iii) (i) 或 (ii) 的序列的互补序列;

(b) 编码 (a) 的多肽的多核苷酸; 和

(c) 表达 (a) 的多肽的抗原呈递细胞。

36. 分离的 T 细胞群, 其含有根据权利要求 35 的方法制备的 T 细胞。

37. 抑制患者体内癌症发展的方法, 包括给患者施用有效量的根据权利要求 36 的 T 细胞群。

38. 抑制患者体内癌症发展的方法, 包括步骤:

(a) 将自患者分离的 CD4⁺ 和/或 CD8⁺ T 细胞与至少一个选自下组的成分一起孵育:

(i) 含有肺肿瘤蛋白质或其变体的至少免疫原性部分的多肽, 其中该肺肿瘤蛋白质含有由选自下组的多核苷酸序列编码的氨基酸序列:

(1) 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 和 349 中所示序列;

(2) 与 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 和 349 之任一个中所示序列在中等严紧条件下杂交的序列；和
- (3) (1)或(2)的序列的互补序列；
 - (ii) 编码(i)的多肽的多核苷酸；和
 - (iii) 表达(i)的多肽的抗原呈递细胞；
- 以便 T 细胞获得增殖；和
- (b) 给该患者施用有效量的该增殖 T 细胞，藉此抑制该患者体内的癌症发展。

39. 抑制患者体内癌症发展的方法，包括步骤：

- (a) 将自患者分离的 CD4⁺ 和/或 CD8⁺ T 细胞与至少一个选自下组的成分一起孵育：
 - (i) 含有肺肿瘤蛋白质或其变体的至少免疫原性部分的多肽，其中该肺肿瘤蛋白质含有由选自下组的多核苷酸序列编码的氨基酸序列：
 - (1) 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 和 349 中所示序列；
 - (2) 与 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 和 349 之任一个中所示序列在中等严紧条件下杂交的序列；和
 - (3) (1)或(2)的序列的互补序列；
 - (ii) 编码(i)的多肽的多核苷酸；和
 - (iii) 表达(i)的多肽的抗原呈递细胞；
 - 以便 T 细胞获得增殖；
- (b) 克隆至少一个增殖细胞以提供克隆的 T 细胞；和
- (c) 给该患者施用有效量的该克隆 T 细胞，藉此抑制该患者体内的癌症发展。

40. 确定患者体内是否存在癌症的方法，包括步骤：

- (a) 用与肺肿瘤蛋白质结合的结合剂接触获自患者的生物样品，其

中该肿瘤蛋白质含有由 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 和 349 之任一个中所示多核苷酸序列或任一个前述多核苷酸序列的互补序列编码的氨基酸序列;

(b) 检测生物样品中与该结合剂结合的多肽的量; 和

(c) 将该多肽量与预确定的截断值进行比较, 由此确定该患者体内是否存在癌症。

41. 根据权利要求 40 的方法, 其中该结合剂是抗体。

42. 根据权利要求 43 的方法, 其中该抗体是单克隆抗体。

43. 根据权利要求 40 的方法, 其中所述癌症是肺癌。

44. 监测患者体内癌症进展趋势的方法, 包括步骤:

(a) 用与肺肿瘤蛋白质结合的结合剂接触在第一时间点上从患者获得的生物样品, 其中该肿瘤蛋白质含有由 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 和 349 之任一个中所示多核苷酸序列或任一个前述多核苷酸序列的互补序列编码的氨基酸序列;

(b) 检测生物样品中与该结合剂结合的多肽的量;

(c) 采用在随后的时间点上从该患者获得的生物样品重复步骤(a)和(b); 和

(d) 将步骤(c)中检测到的多肽量与步骤(b)中检测到的量进行比较, 由此检测该患者体内癌症的进展趋势。

45. 根据权利要求 44 的方法, 其中该结合剂是抗体。

46. 根据权利要求 45 的方法, 其中该抗体是单克隆抗体。

47. 根据权利要求 44 的方法，其中所述癌症是肺癌。

48. 确定患者体内是否存在癌症的方法，包括步骤：

(a) 用与编码肺肿瘤蛋白质的多核苷酸杂交的寡核苷酸接触获自患者的生物样品，其中该肿瘤蛋白质含有由 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 和 349 之任一个中所示多核苷酸序列或任一个前述多核苷酸序列的互补序列编码的氨基酸序列；

(b) 检测生物样品中与该寡核苷酸杂交的多核苷酸的量；

(c) 将与该寡核苷酸杂交的多核苷酸的量和预确定的截断值进行比较，由此确定该患者体内是否存在癌症。

49. 根据权利要求 48 的方法，其中与该寡核苷酸杂交的多核苷酸的量是采用聚合酶链式反应确定的。

50. 根据权利要求 48 的方法，其中与该寡核苷酸杂交的多核苷酸的量是采用杂交测定方法确定的。

51. 监测患者体内癌症进展趋势的方法，包括步骤：

(a) 用与编码肺肿瘤蛋白质的多核苷酸杂交的寡核苷酸接触从患者获得的生物样品，其中该肿瘤蛋白质含有由 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 和 349 之任一个中所示多核苷酸序列或任一个前述多核苷酸序列的互补序列编码的氨基酸序列；

(b) 检测生物样品中与该寡核苷酸杂交的多核苷酸的量；

(c) 采用在随后的时间点上从该患者获得的生物样品重复步骤(a)和(b)；和

(d) 将步骤(c)中检测到的多核苷酸量与步骤(b)中检测到的量进行

比较，由此检测该患者体内癌症的进展趋势。

52. 根据权利要求 51 的方法，其中与该寡核苷酸杂交的多核苷酸的量是采用聚合酶链式反应确定的。

53. 根据权利要求 51 的方法，其中与该寡核苷酸杂交的多核苷酸的量是采用杂交测定方法确定的。

54. 诊断试剂盒，其含有：

- (a) 根据权利要求 11 的一种或多种抗体；和
- (b) 含有报道基团的检测试剂。

55. 根据权利要求 54 的试剂盒，其中该抗体被固定在固相支持物上。

56. 根据权利要求 54 的试剂盒，其中该检测试剂含有抗免疫球蛋白、G 蛋白、A 蛋白或凝集素。

57. 根据权利要求 54 的试剂盒，其中该报道基团选自：放射性同位素、荧光基团、发光基团、酶、生物素和染料颗粒。

58. 寡核苷酸，其含有在中等严谨条件下与编码肺肿瘤蛋白质的多核苷酸杂交的 10-40 个连续核苷酸，其中该肿瘤蛋白质含有由 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 和 349 之任一个中所示多核苷酸序列或任一个前述多核苷酸序列的互补序列编码的氨基酸序列。

59. 根据权利要求 58 的寡核苷酸, 其中该寡核苷酸含有 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 和 349 之任一个中所示的 10-40 个连续核苷酸。

60. 诊断试剂盒, 其含有:

- (a) 根据权利要求 59 的寡核苷酸; 和
- (b) 用于聚合酶链式反应或杂交测定的诊断试剂。

说 明 书

用于治疗 and 诊断肺癌的化合物和方法

技术背景

一般地，本发明涉及癌症，例如肺癌的治疗和诊断。更具体地，本发明涉及含有肺肿瘤蛋白质的至少一个部分的多肽，和编码这些多肽的多核苷酸。这些多肽和多核苷酸可以用于疫苗和药物组合物中以防止和治疗肺癌，以及诊断和监测这些癌症。

发明背景

在美国，肺癌是男性和女性癌症死亡的主要原因，据报道 1994 年就估计有 172,000 个新病例。无论诊断时疾病的阶段如何，在所有的肺癌患者中，5 年的存活率仅为 13%。这与当该疾病还处于局部时检测到的病例中 46% 的 5 年存活率形成对照。然而，仅有 16% 的肺癌在该疾病扩散之前被发现。

由于通常一直要到该疾病达到晚期时才可观察到临床症状，故早期检测是困难的。目前，该疾病的诊断借助于胸部 X 射线、对痰中所含的细胞类型的分析、和支气管通道的光纤检查。治疗方案取决于该癌症的类型和阶段，包括手术、放疗和/或化疗。尽管对于肺癌的治疗已有了相当多的研究，但该疾病仍难于医治。

因此，本领域对用于肺癌的改良疫苗、治疗方法和诊断技术仍存在需要。

发明概述

简而言之，本发明提供用于诊断和治疗癌症，例如肺癌的组合物和方法。一方面，本发明提供含有肺肿瘤蛋白质或其变体的至少一个部分的多肽。某些部分和其它变体具有免疫原性，以致该变体与抗原特异性抗血清的反应能力在相当大程度得到保持。在某些实施方案中，该多肽

含有由选自下组的多核苷酸序列编码的序列：(a) 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、8、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 和 349 之任一个中所示的序列；(b) 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 和 349 之任一个中所示序列的变体；和(c) (a)或(b)序列的互补序列。在具体的实施方案中，本发明的多肽含有包括选自下组的氨基酸序列的肿瘤蛋白质的至少一个部分：SEQ ID NO: 152、155、156、165、166、169、170、172、174、176、226-252、338-334 和 346 之任意一个中的所示序列和其变体。

本发明还提供编码上述多肽的多核苷酸或其部分（例如编码肺肿瘤蛋白质的至少 15 个氨基酸残基的部分），含有这些多核苷酸的表达载体和用这些表达载体转化或转染的宿主细胞。

在其它方面，本发明提供含有上述多肽或多核苷酸和生理学上可接受载体的药物组合物。

在本发明的一个相关方面，提供用于预防或治疗用途的疫苗。这些疫苗含有上述多肽或多核苷酸和免疫刺激剂。

本发明还提供药物组合物，其含有：(a) 特异地与肺肿瘤蛋白质结合的抗体或其抗原结合片段；和 (b) 生理学上可接受的载体。

在其它方面，本发明提供药物组合物，其含有：(a) 表达上述多肽的抗原呈递细胞和 (b) 可药用载体或赋形剂。抗原呈递细胞包括树突细胞、巨噬细胞、单核细胞、成纤维细胞和 B 细胞。

在相关方面中，本发明提供疫苗，其含有 (a) 表达上述多肽的抗原

呈递细胞，和 (b) 免疫刺激剂。

在其它方面，本发明还提供含有至少一种上述多肽的融合蛋白，以及编码这些融合蛋白的多核苷酸。

在相关方面中，本发明提供含有融合蛋白或编码融合蛋白的多核苷酸，及生理学上可接受载体的药物组合物。

在其它方面，本发明还提供含有融合蛋白或编码融合蛋白的多核苷酸，及免疫刺激剂的疫苗。

在其它方面，本发明提供用于抑制患者体内癌症发展的方法，包括给患者施用上述药物组合物或疫苗。

在其它方面中，本发明还提供用于从生物样品中除去肿瘤细胞的方法，包括用特异地与肺肿瘤蛋白质反应的 T 细胞接触生物样品，其中该接触步骤在足以允许从该样品中除去表达该蛋白质的细胞的条件和时间下进行。

在相关方面，本发明提供用于抑制患者体内癌症发展的方法，包括给患者施用按上述方法处理过的生物样品。

在其它方面，本发明还提供用于刺激和/或扩增肺肿瘤蛋白质特异性 T 细胞的方法，包括在足以刺激和/或扩增 T 细胞的条件下，用以下一或多种物质接触 T 细胞：(i) 上述多肽；(ii) 编码该多肽的多核苷酸；和/或 (iii) 表达该多肽的抗原呈递细胞。本发明还提供含有按上述方法制备的 T 细胞的确定 T 细胞群。

在其它方面，本发明提供用于抑制患者体内癌症发展的方法，包括给患者施用有效量的上述 T 细胞群。

本发明还提供用于抑制患者体内癌症发展的方法，包括步骤：(a) 用以下一或多种物质与来自患者的确定 CD4⁺和/或 CD8⁺ T 细胞一起孵育：(i) 含有肺肿瘤蛋白质的至少免疫原性部分的多肽；(ii) 编码该多肽的多核苷酸；和 (iii) 表达该多肽的抗原呈递细胞；和 (b) 给患者施用有效量的该增殖 T 细胞，并藉此抑制患者体内的癌症发展。在给患者施用之前，可以，但并不必须，对增殖细胞进行克隆。

在其它方面，本发明提供用于确定患者体内是否存在癌症的方法，

包括：(a) 用与上述多肽结合的结合剂接触获自患者的生物样品；(b) 检测样品中与该结合剂结合的多肽的量；和 (c) 将该多肽量和预先确定的截断值 (cut-off value) 进行比较，由此确定患者体内是否存在癌症。在优选的实施方案中，该结合剂是抗体，更优选的是单克隆抗体。该癌症可以是肺癌。

在其它方面，本发明还提供用监测患者体内癌症进展趋势的方法。该方法包括步骤：(a) 用与上述多肽结合的结合剂接触在第一时间点上从患者获得的生物样品；(b) 检测样品中与该结合剂结合的多肽的量；(c) 采用在随后的时间点上从该患者获得的生物样品，重复步骤 (a) 和 (b)；和 (d) 将步骤 (c) 中检测到的多肽量和步骤 (b) 中检测到的量进行比较，并由此监测患者体内癌症的进展趋势。

在其它方面，本发明还提供用于确定患者体内是否存在癌症的方法，包括步骤：(a) 用与编码肺肿瘤蛋白质的多核苷酸杂交的寡核苷酸接触获自患者的生物样品；(b) 检测该样品中与该寡核苷酸杂交的多核苷酸，优选 mRNA，的水平；和 (c) 将与该寡核苷酸杂交的多核苷酸的水平与预确定的截断值进行比较，由此确定该患者体内是否存在癌症。在某些实施方案中，采用例如至少一个与编码上述多肽的多核苷酸或该多核苷酸的互补序列杂交的寡核苷酸引物，通过聚合酶链式反应，检测该 mRNA 的量。在其它实施方案中，利用与编码上述多肽的多核苷酸或该多核苷酸的互补序列杂交的寡核苷酸探针，采用杂交技术，检测该 mRNA 的量。

在相关方面，本发明提供用于监测患者体内癌症进展趋势的方法，包括步骤：(a) 用与编码肺肿瘤蛋白质的多核苷酸杂交的寡核苷酸接触获自患者的生物样品；(b) 检测该样品中与该寡核苷酸杂交的多核苷酸的量；(c) 采用在随后时间点上从该患者获得的生物样品，重复步骤 (a) 和 (b)；和 (d) 将步骤 (c) 中检测到的多核苷酸量与步骤 (b) 中检测到的量进行比较，由此监测该患者体内癌症的进展趋势。

在其它方面，本发明提供与上述多肽结合的抗体，例如单克隆抗体，以及含有这些抗体的诊断试剂盒。还提供含有上述一或多个寡核苷酸探针或引物的诊断试剂盒。

参考以下详述和附图，本发明的这些和其它方面将是明了的。本文公开的所有文献特此以参考文献的形式完整地并入，如同每篇文献单独并入一样

序列名称

SEQ ID NO: 1 是 LST-S2-2 的测定的 cDNA 序列
SEQ ID NO: 2 是 LST-S2-28 的测定的 cDNA 序列
SEQ ID NO: 3 是 LST-S2-90 的测定的 cDNA 序列
SEQ ID NO: 4 是 LST-S2-144 的测定的 cDNA 序列
SEQ ID NO: 5 是 LST-S2-133 的测定的 cDNA 序列
SEQ ID NO: 6 是 LST-S2-169 的测定的 cDNA 序列
SEQ ID NO: 7 是 LST-S2-6 的测定的 cDNA 序列
SEQ ID NO: 8 是 LST-S2-11 的测定的 cDNA 序列
SEQ ID NO: 9 是 LST-S2-17 的测定的 cDNA 序列
SEQ ID NO: 10 是 LST-S2-25 的测定的 cDNA 序列
SEQ ID NO: 11 是 LST-S2-39 的测定的 cDNA 序列
SEQ ID NO: 12 是 LST-S2-43 的第一种测定的 cDNA 序列
SEQ ID NO: 13 是 LST-S2-43 的第二种测定的 cDNA 序列
SEQ ID NO: 14 是 LST-S2-65 的测定的 cDNA 序列
SEQ ID NO: 15 是 LST-S2-68 的测定的 cDNA 序列
SEQ ID NO: 16 是 LST-S2-72 的测定的 cDNA 序列
SEQ ID NO: 17 是 LST-S2-74 的测定的 cDNA 序列
SEQ ID NO: 18 是 LST-S2-103 的测定的 cDNA 序列
SEQ ID NO: 19 是 LST-S2-N1-1F 的测定的 cDNA 序列
SEQ ID NO: 20 是 LST-S2-N1-2A 的测定的 cDNA 序列
SEQ ID NO: 21 是 LST-S2-N1-4H 的测定的 cDNA 序列
SEQ ID NO: 22 是 LST-S2-N1-5A 的测定的 cDNA 序列
SEQ ID NO: 23 是 LST-S2-N1-6B 的测定的 cDNA 序列
SEQ ID NO: 24 是 LST-S2-N1-7B 的测定的 cDNA 序列

SEQ ID NO: 25 是 LST-S2-N1-7H 的测定的 cDNA 序列
SEQ ID NO: 26 是 LST-S2-N1-8A 的测定的 cDNA 序列。
SEQ ID NO: 27 是 LST-S2-N1-8D 的测定的 cDNA 序列。
SEQ ID NO: 28 是 LST-S2-N1-9A 的测定的 cDNA 序列。
SEQ ID NO: 29 是 LST-S2-N1-9E 的测定的 cDNA 序列。
SEQ ID NO: 30 是 LST-S2-N1-10A 的测定的 cDNA 序列。
SEQ ID NO: 31 是 LST-S2-N1-10G 的测定的 cDNA 序列。
SEQ ID NO: 32 是 LST-S2-N1-11A 的测定的 cDNA 序列。
SEQ ID NO: 33 是 LST-S2-N1-12C 的测定的 cDNA 序列。
SEQ ID NO: 34 是 LST-S2-N1-12E 的测定的 cDNA 序列。
SEQ ID NO: 35 是 LST-S2-B1-3D 的测定的 cDNA 序列。
SEQ ID NO: 36 是 LST-S2-B1-6C 的测定的 cDNA 序列。
SEQ ID NO: 37 是 LST-S2-B1-5D 的测定的 cDNA 序列。
SEQ ID NO: 38 是 LST-S2-B1-5F 的测定的 cDNA 序列。
SEQ ID NO: 39 是 LST-S2-B1-6G 的测定的 cDNA 序列。
SEQ ID NO: 40 是 LST-S2-B1-8A 的测定的 cDNA 序列。
SEQ ID NO: 41 是 LST-S2-B1-8D 的测定的 cDNA 序列。
SEQ ID NO: 42 是 LST-S2-B1-10A 的测定的 cDNA 序列。
SEQ ID NO: 43 是 LST-S2-B1-9B 的测定的 cDNA 序列。
SEQ ID NO: 44 是 LST-S2-B1-9F 的测定的 cDNA 序列。
SEQ ID NO: 45 是 LST-S2-B1-12D 的测定的 cDNA 序列。
SEQ ID NO: 46 是 LST-S2-I2-2B 的测定的 cDNA 序列。
SEQ ID NO: 47 是 LST-S2-I2-5F 的测定的 cDNA 序列。
SEQ ID NO: 48 是 LST-S2-I2-6B 的测定的 cDNA 序列。
SEQ ID NO: 49 是 LST-S2-I2-7F 的测定的 cDNA 序列。
SEQ ID NO: 50 是 LST-S2-I2-8G 的测定的 cDNA 序列。
SEQ ID NO: 51 是 LST-S2-I2-9E 的测定的 cDNA 序列。
SEQ ID NO: 52 是 LST-S2-I2-12B 的测定的 cDNA 序列。
SEQ ID NO: 53 是 LST-S2-H2-2C 的测定的 cDNA 序列。

SEQ ID NO: 54 是 LST-S2-H2-1G 的测定的 cDNA 序列。
SEQ ID NO: 55 是 LST-S2-H2-4G 的测定的 cDNA 序列。
SEQ ID NO: 56 是 LST-S2-H2-3H 的测定的 cDNA 序列。
SEQ ID NO: 57 是 LST-S2-H2-5G 的测定的 cDNA 序列。
SEQ ID NO: 58 是 LST-S2-H2-9B 的测定的 cDNA 序列。
SEQ ID NO: 59 是 LST-S2-H2-10H 的测定的 cDNA 序列。
SEQ ID NO: 60 是 LST-S2-H2-12D 的测定的 cDNA 序列。
SEQ ID NO: 61 是 LST-S3-2 的测定的 cDNA 序列。
SEQ ID NO: 62 是 LST-S3-4 的测定的 cDNA 序列。
SEQ ID NO: 63 是 LST-S3-7 的测定的 cDNA 序列。
SEQ ID NO: 64 是 LST-S3-8 的测定的 cDNA 序列。
SEQ ID NO: 65 是 LST-S3-12 的测定的 cDNA 序列。
SEQ ID NO: 66 是 LST-S3-13 的测定的 cDNA 序列。
SEQ ID NO: 67 是 LST-S3-14 的测定的 cDNA 序列。
SEQ ID NO: 68 是 LST-S3-16 的测定的 cDNA 序列。
SEQ ID NO: 69 是 LST-S3-21 的测定的 cDNA 序列。
SEQ ID NO: 70 是 LST-S3-22 的测定的 cDNA 序列。
SEQ ID NO: 71 是 LST-S1-7 的测定的 cDNA 序列。
SEQ ID NO: 72 是 LST-S1-A-1E 的测定的 cDNA 序列。
SEQ ID NO: 73 是 LST-S1-A-1G 的测定的 cDNA 序列。
SEQ ID NO: 74 是 LST-S1-A-3E 的测定的 cDNA 序列。
SEQ ID NO: 75 是 LST-S1-A-4E 的测定的 cDNA 序列。
SEQ ID NO: 76 是 LST-S1-A-6D 的测定的 cDNA 序列。
SEQ ID NO: 77 是 LST-S1-A-8D 的测定的 cDNA 序列。
SEQ ID NO: 78 是 LST-S1-A-10A 的测定的 cDNA 序列。
SEQ ID NO: 79 是 LST-S1-A-10C 的测定的 cDNA 序列。
SEQ ID NO: 80 是 LST-S1-A-9D 的测定的 cDNA 序列。
SEQ ID NO: 81 是 LST-S1-A-10D 的测定的 cDNA 序列。
SEQ ID NO: 82 是 LST-S1-A-9H 的测定的 cDNA 序列。

SEQ ID NO: 83 是 LST-S1-A-11D 的测定的 cDNA 序列。
 SEQ ID NO: 84 是 LST-S1-A-12D 的测定的 cDNA 序列。
 SEQ ID NO: 85 是 LST-S1-A-11E 的测定的 cDNA 序列。
 SEQ ID NO: 86 是 LST-S1-A-12E 的测定的 cDNA 序列。
 SEQ ID NO: 87 是 L513S (T3)的测定的 cDNA 序列。
 SEQ ID NO: 88 是 L513S 重叠群 1 的测定的 cDNA 序列。
 SEQ ID NO: 89 是 L514S 的第一种测定的 cDNA 序列。
 SEQ ID NO: 90 是 L514S 的第二种测定的 cDNA 序列。
 SEQ ID NO: 91 是 L516S 的第一种测定的 cDNA 序列。
 SEQ ID NO: 92 是 L516S 的第二种测定的 cDNA 序列。
 SEQ ID NO: 93 是 L517S 的测定的 cDNA 序列。
 SEQ ID NO: 94 是 LST-S1-169 (又称 L519S) 的扩延 cDNA 序列。
 SEQ ID NO: 95 是 L520S 的第一种测定的 cDNA 序列。
 SEQ ID NO: 96 是 L520S 的第二种测定的 cDNA 序列。
 SEQ ID NO: 97 是 L521S 的第一种测定的 cDNA 序列。
 SEQ ID NO: 98 是 L521S 的第二种测定的 cDNA 序列。
 SEQ ID NO: 99 是 L522S 的测定的 cDNA 序列。
 SEQ ID NO: 100 是 L523S 的测定的 cDNA 序列。
 SEQ ID NO: 101 是 L524S 的测定的 cDNA 序列。
 SEQ ID NO: 102 是 L525S 的测定的 cDNA 序列。
 SEQ ID NO: 103 是 L526S 的测定的 cDNA 序列。
 SEQ ID NO: 104 是 L527S 的测定的 cDNA 序列。
 SEQ ID NO: 105 是 L528S 的测定的 cDNA 序列。
 SEQ ID NO: 106 是 L529S 的测定的 cDNA 序列。
 SEQ ID NO: 107 是 L530S 的第一种测定的 cDNA 序列。
 SEQ ID NO: 108 是 L530S 的第二种测定的 cDNA 序列。
 SEQ ID NO: 109 是 L531S 短形式的测定的全长 cDNA 序列。
 SEQ ID NO: 110 是推测的 SEQ ID NO: 109 编码的氨基酸序列。
 SEQ ID NO: 111 是 L531S 长形式的测定的全长 cDNA 序列。

SEQ ID NO: 112 是推测的 SEQ ID NO: 111 编码的氨基酸序列。
SEQ ID NO: 113 是 L520S 的测定的全长 cDNA 序列。
SEQ ID NO: 114 是推测的 SEQ ID NO: 113 编码的氨基酸序列。
SEQ ID NO: 115 是重叠群 1 的测定的 cDNA 序列。
SEQ ID NO: 116 是重叠群 3 的测定的 cDNA 序列。
SEQ ID NO: 117 是重叠群 4 的测定的 cDNA 序列。
SEQ ID NO: 118 是重叠群 5 的测定的 cDNA 序列。
SEQ ID NO: 119 是重叠群 7 的测定的 cDNA 序列。
SEQ ID NO: 120 是重叠群 8 的测定的 cDNA 序列。
SEQ ID NO: 121 是重叠群 9 的测定的 cDNA 序列。
SEQ ID NO: 122 是重叠群 10 的测定的 cDNA 序列。
SEQ ID NO: 123 是重叠群 12 的测定的 cDNA 序列。
SEQ ID NO: 124 是重叠群 11 的测定的 cDNA 序列。
SEQ ID NO: 125 是重叠群 13 的测定的 cDNA 序列。
SEQ ID NO: 126 是重叠群 15 的测定的 cDNA 序列。
SEQ ID NO: 127 是重叠群 16 的测定的 cDNA 序列。
SEQ ID NO: 128 是重叠群 17 的测定的 cDNA 序列。
SEQ ID NO: 129 是重叠群 19 的测定的 cDNA 序列。
SEQ ID NO: 130 是重叠群 20 的测定的 cDNA 序列。
SEQ ID NO: 131 是重叠群 22 的测定的 cDNA 序列。
SEQ ID NO: 132 是重叠群 24 的测定的 cDNA 序列。
SEQ ID NO: 133 是重叠群 29 的测定的 cDNA 序列。
SEQ ID NO: 134 是重叠群 31 的测定的 cDNA 序列。
SEQ ID NO: 135 是重叠群 33 的测定的 cDNA 序列。
SEQ ID NO: 136 是重叠群 38 的测定的 cDNA 序列。
SEQ ID NO: 137 是重叠群 39 的测定的 cDNA 序列。
SEQ ID NO: 138 是重叠群 41 的测定的 cDNA 序列。
SEQ ID NO: 139 是重叠群 43 的测定的 cDNA 序列。
SEQ ID NO: 140 是重叠群 44 的测定的 cDNA 序列。

SEQ ID NO: 141 是重叠群 45 的测定的 cDNA 序列。
SEQ ID NO: 142 是重叠群 47 的测定的 cDNA 序列。
SEQ ID NO: 143 是重叠群 48 的测定的 cDNA 序列。
SEQ ID NO: 144 是重叠群 49 的测定的 cDNA 序列。
SEQ ID NO: 145 是重叠群 50 的测定的 cDNA 序列。
SEQ ID NO: 146 是重叠群 53 的测定的 cDNA 序列。
SEQ ID NO: 147 是重叠群 54 的测定的 cDNA 序列。
SEQ ID NO: 148 是重叠群 56 的测定的 cDNA 序列。
SEQ ID NO: 149 是重叠群 57 的测定的 cDNA 序列。
SEQ ID NO: 150 是重叠群 58 的测定的 cDNA 序列。
SEQ ID NO: 151 是 L530S 的全长 cDNA 序列。
SEQ ID NO: 152 是 SEQ ID NO: 151 编码的氨基酸序列。
SEQ ID NO: 153 是 L514S 第一个变体的全长 cDNA 序列。
SEQ ID NO: 154 是 L514S 第二个变体的全长 cDNA 序列。
SEQ ID NO: 155 是 SEQ ID NO: 153 编码的氨基酸序列。
SEQ ID NO: 156 是 SEQ ID NO: 154 编码的氨基酸序列。
SEQ ID NO: 157 是重叠群 59 的测定的 cDNA 序列。
SEQ ID NO: 158 是 L763P (又称作重叠群 22) 的全长 cDNA 序列。
SEQ ID NO: 159 是 SEQ ID NO: 158 编码的氨基酸序列。
SEQ ID NO: 160 是 L762P (又称作重叠群 17) 的全长 cDNA 序列。
SEQ ID NO: 161 是 SEQ ID NO: 160 编码的氨基酸序列。
SEQ ID NO: 162 是 L515S 的测定的 cDNA 序列。
SEQ ID NO: 163 是 L524S 第一个变体的全长 cDNA 序列。
SEQ ID NO: 164 是 L524S 第二个变体的全长 cDNA 序列。
SEQ ID NO: 165 是 SEQ ID NO: 163 编码的氨基酸序列。
SEQ ID NO: 166 是 SEQ ID NO: 164 编码的氨基酸序列。
SEQ ID NO: 167 是 L762P 第一个变体的全长 cDNA 序列。
SEQ ID NO: 168 是 L762P 第二个变体的全长 cDNA 序列。
SEQ ID NO: 169 是 SEQ ID NO: 167 编码的氨基酸序列。

SEQ ID NO: 170 是 SEQ ID NO: 168 编码的氨基酸序列。
SEQ ID NO: 171 是 L773P (又称作重叠群 56) 的全长 cDNA 序列。
SEQ ID NO: 172 是 SEQ ID NO: 171 编码的氨基酸序列。
SEQ ID NO: 173 是 L519S 的扩延 cDNA 序列。
SEQ ID NO: 174 是推测的 SEQ ID NO: 174 编码的氨基酸序列。
SEQ ID NO: 175 是 L523S 的全长 cDNA 序列。
SEQ ID NO: 176 是推测的 SEQ ID NO: 175 编码的氨基酸序列。
SEQ ID NO: 177 是 LST-sub5-7A 的测定的 cDNA 序列。
SEQ ID NO: 178 是 LST-sub5-8G 的测定的 cDNA 序列。
SEQ ID NO: 179 是 LST-sub5-8H 的测定的 cDNA 序列。
SEQ ID NO: 180 是 LST-sub5-10B 的测定的 cDNA 序列。
SEQ ID NO: 181 是 LST-sub5-10H 的测定的 cDNA 序列。
SEQ ID NO: 182 是 LST-sub5-12B 的测定的 cDNA 序列。
SEQ ID NO: 183 是 LST-sub5-11C 的测定的 cDNA 序列。
SEQ ID NO: 184 是 LST-sub6-1c 的测定的 cDNA 序列。
SEQ ID NO: 185 是 LST-sub6-2f 的测定的 cDNA 序列。
SEQ ID NO: 186 是 LST-sub6-2G 的测定的 cDNA 序列。
SEQ ID NO: 187 是 LST-sub6-4d 的测定的 cDNA 序列。
SEQ ID NO: 188 是 LST-sub6-4e 的测定的 cDNA 序列。
SEQ ID NO: 189 是 LST-sub6-4f 的测定的 cDNA 序列。
SEQ ID NO: 190 是 LST-sub6-3h 的测定的 cDNA 序列。
SEQ ID NO: 191 是 LST-sub6-5d 的测定的 cDNA 序列。
SEQ ID NO: 192 是 LST-sub6-5h 的测定的 cDNA 序列。
SEQ ID NO: 193 是 LST-sub6-6h 的测定的 cDNA 序列。
SEQ ID NO: 194 是 LST-sub6-7a 的测定的 cDNA 序列。
SEQ ID NO: 195 是 LST-sub6-8a 的测定的 cDNA 序列。
SEQ ID NO: 196 是 LST-sub6-7d 的测定的 cDNA 序列。
SEQ ID NO: 197 是 LST-sub6-7e 的测定的 cDNA 序列。
SEQ ID NO: 198 是 LST-sub6-8e 的测定的 cDNA 序列。

SEQ ID NO: 199 是 LST-sub6-7g 的测定的 cDNA 序列。
SEQ ID NO: 200 是 LST-sub6-9f 的测定的 cDNA 序列。
SEQ ID NO: 201 是 LST-sub6-9h 的测定的 cDNA 序列。
SEQ ID NO: 202 是 LST-sub6-11b 的测定的 cDNA 序列。
SEQ ID NO: 203 是 LST-sub6-11c 的测定的 cDNA 序列。
SEQ ID NO: 204 是 LST-sub6-12c 的测定的 cDNA 序列。
SEQ ID NO: 205 是 LST-sub6-12e 的测定的 cDNA 序列。
SEQ ID NO: 206 是 LST-sub6-12f 的测定的 cDNA 序列。
SEQ ID NO: 207 是 LST-sub6-11g 的测定的 cDNA 序列。
SEQ ID NO: 208 是 LST-sub6-12g 的测定的 cDNA 序列。
SEQ ID NO: 209 是 LST-sub6-12h 的测定的 cDNA 序列。
SEQ ID NO: 210 是 LST-sub6-II-1a 的测定的 cDNA 序列。
SEQ ID NO: 211 是 LST-sub6-II-2b 的测定的 cDNA 序列。
SEQ ID NO: 212 是 LST-sub6-II-2g 的测定的 cDNA 序列。
SEQ ID NO: 213 是 LST-sub6-II-1h 的测定的 cDNA 序列。
SEQ ID NO: 214 是 LST-sub6-II-4a 的测定的 cDNA 序列。
SEQ ID NO: 215 是 LST-sub6-II-4b 的测定的 cDNA 序列。
SEQ ID NO: 216 是 LST-sub6-II-3e 的测定的 cDNA 序列。
SEQ ID NO: 217 是 LST-sub6-II-4f 的测定的 cDNA 序列。
SEQ ID NO: 218 是 LST-sub6-II-4g 的测定的 cDNA 序列。
SEQ ID NO: 219 是 LST-sub6-II-4h 的测定的 cDNA 序列。
SEQ ID NO: 220 是 LST-sub6-II-5c 的测定的 cDNA 序列。
SEQ ID NO: 221 是 LST-sub6-II-5e 的测定的 cDNA 序列。
SEQ ID NO: 222 是 LST-sub6-II-6f 的测定的 cDNA 序列。
SEQ ID NO: 223 是 LST-sub6-II-5g 的测定的 cDNA 序列。
SEQ ID NO: 224 是 LST-sub6-II-6g 的测定的 cDNA 序列。
SEQ ID NO: 225 是 L528S 的氨基酸序列。
SEQ ID NO: 226-251 是来源于 L762P 的合成肽。
SEQ ID NO: 252 是 L514S 的表达氨基酸序列。

SEQ ID NO: 253 是相应于 SEQ ID NO: 252 的 DNA 序列。
SEQ ID NO: 254 是 L762P 表达结构的 DNA 序列。
SEQ ID NO: 255 是克隆 23785 的测定的 cDNA 序列。
SEQ ID NO: 256 是克隆 23786 的测定的 cDNA 序列。
SEQ ID NO: 257 是克隆 23788 的测定的 cDNA 序列。
SEQ ID NO: 258 是克隆 23790 的测定的 cDNA 序列。
SEQ ID NO: 259 是克隆 23793 的测定的 cDNA 序列。
SEQ ID NO: 260 是克隆 23794 的测定的 cDNA 序列。
SEQ ID NO: 261 是克隆 23795 的测定的 cDNA 序列。
SEQ ID NO: 262 是克隆 23796 的测定的 cDNA 序列。
SEQ ID NO: 263 是克隆 23797 的测定的 cDNA 序列。
SEQ ID NO: 264 是克隆 23798 的测定的 cDNA 序列。
SEQ ID NO: 265 是克隆 23799 的测定的 cDNA 序列。
SEQ ID NO: 266 是克隆 23800 的测定的 cDNA 序列。
SEQ ID NO: 267 是克隆 23802 的测定的 cDNA 序列。
SEQ ID NO: 268 是克隆 23803 的测定的 cDNA 序列。
SEQ ID NO: 269 是克隆 23804 的测定的 cDNA 序列。
SEQ ID NO: 270 是克隆 23805 的测定的 cDNA 序列。
SEQ ID NO: 271 是克隆 23806 的测定的 cDNA 序列。
SEQ ID NO: 272 是克隆 23807 的测定的 cDNA 序列。
SEQ ID NO: 273 是克隆 23808 的测定的 cDNA 序列。
SEQ ID NO: 274 是克隆 23809 的测定的 cDNA 序列。
SEQ ID NO: 275 是克隆 23810 的测定的 cDNA 序列。
SEQ ID NO: 276 是克隆 23811 的测定的 cDNA 序列。
SEQ ID NO: 277 是克隆 23812 的测定的 cDNA 序列。
SEQ ID NO: 278 是克隆 23813 的测定的 cDNA 序列。
SEQ ID NO: 279 是克隆 23815 的测定的 cDNA 序列。
SEQ ID NO: 280 是克隆 25298 的测定的 cDNA 序列。
SEQ ID NO: 281 是克隆 25299 的测定的 cDNA 序列。

SEQ ID NO: 281 是克隆 25299 的测定的 cDNA 序列。
SEQ ID NO: 282 是克隆 25300 的测定的 cDNA 序列。
SEQ ID NO: 283 是克隆 25301 的测定的 cDNA 序列。
SEQ ID NO: 284 是克隆 25304 的测定的 cDNA 序列。
SEQ ID NO: 285 是克隆 25309 的测定的 cDNA 序列。
SEQ ID NO: 286 是克隆 25312 的测定的 cDNA 序列。
SEQ ID NO: 287 是克隆 25317 的测定的 cDNA 序列。
SEQ ID NO: 288 是克隆 25321 的测定的 cDNA 序列。
SEQ ID NO: 289 是克隆 25323 的测定的 cDNA 序列。
SEQ ID NO: 290 是克隆 25327 的测定的 cDNA 序列。
SEQ ID NO: 291 是克隆 25328 的测定的 cDNA 序列。
SEQ ID NO: 292 是克隆 25332 的测定的 cDNA 序列。
SEQ ID NO: 293 是克隆 25333 的测定的 cDNA 序列。
SEQ ID NO: 294 是克隆 25336 的测定的 cDNA 序列。
SEQ ID NO: 295 是克隆 25340 的测定的 cDNA 序列。
SEQ ID NO: 296 是克隆 25342 的测定的 cDNA 序列。
SEQ ID NO: 297 是克隆 25356 的测定的 cDNA 序列。
SEQ ID NO: 298 是克隆 25357 的测定的 cDNA 序列。
SEQ ID NO: 299 是克隆 25361 的测定的 cDNA 序列。
SEQ ID NO: 300 是克隆 25363 的测定的 cDNA 序列。
SEQ ID NO: 301 是克隆 25397 的测定的 cDNA 序列。
SEQ ID NO: 302 是克隆 25402 的测定的 cDNA 序列。
SEQ ID NO: 303 是克隆 25403 的测定的 cDNA 序列。
SEQ ID NO: 304 是克隆 25405 的测定的 cDNA 序列。
SEQ ID NO: 305 是克隆 25407 的测定的 cDNA 序列。
SEQ ID NO: 306 是克隆 25409 的测定的 cDNA 序列。
SEQ ID NO: 307 是克隆 25396 的测定的 cDNA 序列。
SEQ ID NO: 308 是克隆 25414 的测定的 cDNA 序列。
SEQ ID NO: 309 是克隆 25410 的测定的 cDNA 序列。

SEQ ID NO: 310 是克隆 25406 的测定的 cDNA 序列。
SEQ ID NO: 311 是克隆 25306 的测定的 cDNA 序列。
SEQ ID NO: 312 是克隆 25362 的测定的 cDNA 序列。
SEQ ID NO: 313 是克隆 25360 的测定的 cDNA 序列。
SEQ ID NO: 314 是克隆 25398 的测定的 cDNA 序列。
SEQ ID NO: 315 是克隆 25355 的测定的 cDNA 序列。
SEQ ID NO: 316 是克隆 25351 的测定的 cDNA 序列。
SEQ ID NO: 317 是克隆 25331 的测定的 cDNA 序列。
SEQ ID NO: 318 是克隆 25338 的测定的 cDNA 序列。
SEQ ID NO: 319 是克隆 25335 的测定的 cDNA 序列。
SEQ ID NO: 320 是克隆 25329 的测定的 cDNA 序列。
SEQ ID NO: 321 是克隆 25324 的测定的 cDNA 序列。
SEQ ID NO: 322 是克隆 25322 的测定的 cDNA 序列。
SEQ ID NO: 323 是克隆 25319 的测定的 cDNA 序列。
SEQ ID NO: 324 是克隆 25316 的测定的 cDNA 序列。
SEQ ID NO: 325 是克隆 25311 的测定的 cDNA 序列。
SEQ ID NO: 326 是克隆 25310 的测定的 cDNA 序列。
SEQ ID NO: 327 是克隆 25302 的测定的 cDNA 序列。
SEQ ID NO: 328 是克隆 25315 的测定的 cDNA 序列。
SEQ ID NO: 329 是克隆 25308 的测定的 cDNA 序列。
SEQ ID NO: 330 是克隆 25303 的测定的 cDNA 序列。
SEQ ID NO: 331-337 是 p53 肿瘤抑制基因的同系物 p63 的同种型的 cDNA 序列 (又称 L530S)。
SEQ ID NO: 338-344 分别是 SEQ ID NO:331-337 编码的氨基酸序列。
SEQ ID NO: 345 是抗原 L763P 的第二种 cDNA 序列。
SEQ ID NO: 346 是 SEQ ID NO: 345 序列编码的氨基酸序列。
SEQ ID NO: 347 是 L523S 的测定的全长 cDNA 序列。
SEQ ID NO: 348 是推测的 SEQ ID NO: 347 编码的氨基酸序列。
SEQ ID NO: 349 是编码 L773P N 端部分的 cDNA 序列。

SEQ ID NO: 350 是 L773P N 端部分的氨基酸序列。

发明详述

正如以上指出的，本发明一般指向用于治疗和诊断癌症例如肺癌的组合物和方法。本文所述组合物可以包括肺肿瘤多肽、编码这些多肽的多核苷酸、抗体等结合剂、抗原呈递细胞 (APC) 和/或免疫系统细胞（例如 T 细胞）。本发明多肽一般含有肺肿瘤蛋白质或其变体的至少一个部分（例如免疫原性部分）。“肺肿瘤蛋白质”是当采用本文提供的代表性分析方法测定时，以高于正常组织中的表达水平至少 2 倍、优选至少 5 倍的水平在肺肿瘤细胞中表达的蛋白质。某些肺肿瘤蛋白质是（在免疫测定法中，例如 ELISA 或 Western 印迹）可检测地与肺癌患者抗血清反应的肿瘤蛋白质。本发明的多核苷酸一般含有编码该多肽的全部或部分的 DNA 或 RNA 序列、或与该序列互补的序列。抗体一般是指能与上述多肽结合的免疫系统蛋白质、或其抗原结合片段。抗原呈递细胞包括表达上述多肽的树突细胞、巨噬细胞、单核细胞、成纤维细胞和 B 细胞。可以用于这些组合物的 T 细胞一般是对上述多肽具有特异性的 T 细胞。

本发明以发现的人肺肿瘤蛋白质为基础。编码具体肿瘤蛋白质的多核苷酸序列见 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 和 349。

肺肿瘤蛋白质的多核苷酸

编码本文所述肺肿瘤蛋白质、或其部分或其它变体的任何多核苷酸均包括在本发明内。优选的多核苷酸含有编码肺肿瘤蛋白质一部分的至少 15 个连续核苷酸、优选至少 30 个连续核苷酸、更优选至少 45 个连续核苷酸。更优选地，多核苷酸编码肺肿瘤蛋白质的免疫原性部分。与任何这些序列互补的多核苷酸也包括在本发明之内。多核苷酸可以是单链的（编码链或反义链）或双链的，而且可以是 DNA（基因组 DNA、cDNA 或合成的 DNA）或 RNA 分子。RNA 分子包括含有内含子并以一对一形式与

DNA 分子对应的 HnRNA 分子, 和不含内含子的 mRNA 分子。本发明多核苷酸中可以, 但不必须, 存在其它编码或非编码序列, 而且可以, 但不必须, 将多核苷酸与其它分子和/或支持材料连接在一起。

多核苷酸可以含有天然序列(即编码肺肿瘤蛋白质或其部分的内源性序列)或可以含有该序列的变体。多核苷酸变体可以含有一或多个替代、添加、缺失和/或插入, 以致所编码的多肽的免疫原性相对于天然肿瘤蛋白质得到保持。一般可以按本文所述方法评价对该编码多肽的免疫原性的影响。变体优选表现出与编码天然肺肿瘤蛋白质或其部分的多核苷酸序列有至少约 70% 的一致性、更优选至少约 80% 的一致性、最优选至少约 90% 的一致性。术语“变体”也包括异种来源的同源基因。

如果在按下述方法进行最大匹配比对后, 两个多核苷酸或多肽序列中的核苷酸或氨基酸序列相同, 则认为这两个序列是“一致的”。典型地, 两个序列之间的比较通过在比较窗中对序列进行比较以鉴定和比较局部区域的序列相似性来进行。本文所用“比较窗”是指具有至少约 20 个连续位置, 通常 30-约 75 个, 40-约 50 个连续位置的区段, 在该区段中可以在两个序列最佳对齐后比较该序列与具有相同连续位置数目的参考序列。

为了序列比较, 可以采用 Lasergene 生物信息软件包中的 Megalign 程序(DNASTAR 公司, Madison, WI), 利用默认参数进行序列的最佳比对。该程序体现了以下文献中所述的几个比对策略: Dayhoff, M. O. (1978) 蛋白质的进化改变模型 - 检测远缘关系的矩阵, 见 Dayhoff, M. O. (编)《蛋白质序列和结构图集》(Atlas of Protein Sequence and Structure), 国立生物化学研究基金会, Washington DC, 第 5 卷, 增刊 3, 第 345-358 页; Hein J. (1990) 比对和系统发生的统一方法, 第 626-645 页, 《酶学方法》(Methods in Enzymology)第 183 卷, Academic Press 公司, San Diego, CA; Higgins, D. G. 和 Sharp, P. M. (1989) CABIOS 5:151-153; Myers, E. W. 和 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. 和 Sokal, R. R. (1973)《数值分类

学 - 数值分类学的原理和实践》(Numerical Taxonomy - the Principles and Practice of Numerical Taxonomy), Freeman Press, San Francisco, CA; Wilbur, W. J. 和 Lipman, D. J. (1983) 美国国家科学院院刊 (Proc. Natl. Acad. Sci. USA) 80: 726-730.

优选地, “序列一致性百分数”通过在至少有 20 个位置的比较窗中比较两个最佳比对的序列来确定, 其中为了获得两个序列的最佳比对, 与参考序列 (不含有插入或缺失) 相比, 该比较窗中的该多核苷酸或多肽序列部分可以含有 20% 或更少, 通常 5-15%, 或 10-12% 的插入或缺失 (即间隔区)。该百分数的计算方法是: 确定这两个序列中出现相同核酸碱基或氨基酸残基的位置的数目以获得匹配位置数, 用该匹配位置数除以该参考序的总位置数 (即该窗的大小), 然后将所获结果乘以 100 以产生该序列一致性百分数。

变体还可以, 或者是作为替代方案可以, 和天然基因, 或其部分或互补序列在相当大程度上同源。这些多核苷酸变体能够在中等严紧条件下与编码天然肺肿瘤蛋白质的天然存在 DNA 序列 (或互补序列) 杂交。适合的中等严紧条件包括在 $5 \times \text{SSC}$ 、0.5% SDS、1.0mM EDTA (pH8.0) 的溶液中预洗涤; 在 $5 \times \text{SSC}$ 中 $50^\circ\text{C} - 65^\circ\text{C}$ 杂交过夜; 之后用含有 0.1% SDS 的 $2 \times$ 、 $0.5 \times$ 和 $0.2 \times \text{SSC}$ 于 65°C 20 分钟各进行 2 次洗涤。

本领域的普通技术人员将明了, 由于遗传密码的简并性, 有许多编码本文所述多肽的多核苷酸序列。这些多核苷酸中的一些与所有天然基因的核苷酸序列具有最小的同源性。然而, 由于密码子使用的差异而不同的多核苷酸是本发明所具体考虑的。而且, 含有本文提供的多核苷酸序列的基因的等位基因也属于本发明的范围。等位基因是由于一或多个突变, 例如核苷酸的缺失、添加和/或替代, 而造成改变的内源性基因。所导致的 mRNA 和蛋白质可以, 但不必, 具有改变的结构或功能。可以采用标准技术 (例如杂交、扩增和/或数据库序列比较) 鉴定等位基因。

多核苷酸可以采用多种技术中的任一种来制备。例如, 可以按以下详细描述的方法, 通过筛选微阵列 cDNA 寻找肿瘤相关表达 (即, 按本文提供的代表性分析方法测定的、在肿瘤细胞中比在正常组织中高出至少 2

倍的表达), 鉴定多核苷酸。可以采用 Synteni 微阵列 (Palo Alto, CA), 根据厂家说明书 (以及基本上按 Schena 等, 美国国家科学院院刊 93:10614-10619, 1996 和 Heller 等, 美国国家科学院院刊 94:2150-2155, 1997 中所描述的方法), 进行这些筛选。或者, 可以从表达本文所述蛋白质的细胞 (例如肺肿瘤细胞) 中制备 cDNA, 然后从该 cDNA 扩增多肽。这些多核苷酸可以通过聚合酶链式反应 (PCR) 进行扩增。对于该方法, 序列特异性引物可以基于本文所提供的序列进行设计, 并可以通过购买或合成获得。

根据熟知技术, 可以采用扩增的部分从适合的文库 (例如肺肿瘤 cDNA 文库) 中分离全长基因。在这些技术中, 可采用一或多个多核苷酸探针或适于扩增的引物筛选文库 (cDNA 或基因组文库)。优选地, 对文库进行大小筛选以包括较大分子。还可以优选随机引物产生的文库 (random primed libraries) 以鉴定基因的 5' 和上游区域。优选基因组文库以获得内含子和延伸的 5' 序列。

对于杂交技术, 可以采用熟知技术 (例如用 ^{32}P 通过切口平移或末端标记) 标记部分序列。然后通过用该标记探针杂交含有变性的细菌菌落 (或含有噬菌斑的菌苔) 的滤膜, 筛选细菌或噬菌体文库 (见 Sambrook 等, 分子克隆: 实验室手册 (Molecular Cloning: A Laboratory Manual), Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989)。筛选和扩增杂交的菌落或噬菌斑, 并分离该 DNA 用于进一步分析。可以通过例如 PCR, 采用来自该部分序列的引物和来自载体的引物, 分析 cDNA 克隆以确定额外序列的量。可以制备限制性图谱和部分序列, 以鉴定一个或多个重叠克隆。然后采用标准技术确定该完整序列, 这些技术可能涉及产生一系列缺失克隆。然后将该所获重叠序列组装成一个连续序列。可以采用熟知技术, 通过将适合的片段连接在一起, 产生全长 cDNA 分子。

作为可选择的方案, 有许多扩增技术可以用于从部分 cDNA 序列获得全长编码序列。在这些技术中, 一般通过 PCR 进行扩增。可以采用多种可从商业途径获得的试剂盒中的任一种, 实施扩增步骤。引物可以采用例如本领域熟知的软件来设计。引物优选长 22-30 个核苷酸, 具有至少

50% 的 GC 含量，并可以在约 68℃ - 72℃ 的温度下与靶序列退火。可以按以上所述方法对扩增区域进行测序，然后将重叠的序列组装成一个连续序列。

一个这样的扩增技术是反向 PCR (见 Triglia 等, 核酸研究 (Nucl. Acids Res.) 16:8186, 1988), 该技术采用限制性酶在基因的已知区域中产生片段。然后, 通过分子内连接使该片段环化, 并作为模板与来源于该已知区域的背驰引物 (divergent primers) 一起用于 PCR。在另一个方法中, 与部分序列相邻的序列可以通过采用针对接头序列的引物和已知区域所特异的引物进行扩增来获得。典型地, 该扩增序列采用相同的接头引物和该已知区域所特异的第二个引物进行第二轮扩增。该方法的一个变体采用了从该已知区域以相反方向起始延伸的两个引物, 其描述于 WO 96/38591 中。另一种此类技术称作“cDNA 末端的快速扩增”或 RACE。该技术涉及到应用一个内部引物和一个与 polyA 区域或载体序列杂交的外部引物来鉴定已知序列的 5' 和 3' 序列。其它技术包括捕获 PCR (capture PCR) (Lagerstrom 等, PCR 方法应用 (PCR Methods Applic.) 1:111-19, 1991) 和步行 PCR (walking PCR) (Parker 等, 核酸研究 19:3055-60, 1991)。还可以采用其它利用扩增的方法以获得全长 cDNA 序列。

在某些情况下, 可以通过分析已表达序列标志 (EST) 数据库, 例如可从 GenBank 获得的 EST 数据库中提供的序列, 获得全长 cDNA 序列。一般可以采用熟知程序 (例如 NCBI BLAST 搜索程序) 搜索重叠的 EST, 并可以采用这些 EST 产生连续的全长序列。还可以通过分析基因组片段获得全长 DNA 序列。

编码肺肿瘤蛋白质的部分的一些 cDNA 分子核酸序列见 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 和 349。

多核苷酸变体一般可以通过本领域已知的任何方法来制备, 包括通过例如固相亚磷酰胺化学合成法进行化学合成。还可以采用标准诱变技术, 例如寡核苷酸指导的位点特异性诱变 (见 Adelman 等, DNA 2:183, 1983), 在多核苷酸序列中引入修饰。或者, 可以通过体外或体内转录编

码肺肿瘤蛋白质或其部分的 DNA 序列，产生 RNA 分子，前提是将该 DNA 序列插入带有适合 RNA 聚合酶启动子（例如 T7 或 SP6）的载体中。按本文所述，某些部分可以用于制备编码的多肽。此外，或作为可供选择的方案，可以给患者施用部分序列，以便体内产生该编码多肽（例如通过用编码肺肿瘤多肽的 cDNA 结构转染抗原呈递细胞，例如树突细胞，然后给该患者施用此转染的细胞）。

还可以将与编码序列互补的部分序列（即反义多核苷酸）用作探针，或用以调节基因表达。还可以将能够转录出反义 RNA 的 cDNA 结构引入组织的细胞中，以便于反义 RNA 的产生。按本文所述，可以利用反义多核苷酸抑制肿瘤蛋白质的表达。反义技术通过形成三股螺旋妨碍双螺旋充分展开以结合聚合酶、转录因子或调节分子的能力，可以用于控制基因表达（见 Gee 等，Huber 和 Carr, 《分子和免疫学方法 (Molecular and Immunologic Approaches)》，Futura Publishing Co. (Mt. Kisco, NY; 1994)）。或者，可以设计反义分子与基因控制区域（例如启动子、增强子或转录起始位点）杂交并阻断该基因的转录；或通过抑制转录本与核糖体的结合阻断翻译。

还可以将部分编码序列或互补序列设计成探针或引物以检测基因表达。探针可以用多种报道基团（例如放射性核素和酶）标记，并优选长至少 10 个核苷酸，更优选长至少 20 个核苷酸，甚至更优选长至少 30 个核苷酸。正如以上指出的，引物优选长 22-30 个核苷酸。

可以对任何多核苷酸作进一步修饰，以增加其在体内的稳定性。可能的修饰包括，但不限于，在 5' 和/或 3' 末端添加侧翼序列；在骨架中采用硫代硫酸酯或 2' O-甲基而非磷酸二酯酶键；和/或在其中包含非常规碱基，例如次黄苷、queosine、wybutosine，以及腺嘌呤、胞嘧啶、鸟嘌呤、胸腺嘧啶和尿嘧啶的乙酰基、甲基、硫代、及其它修饰形式。

可以采用成熟的重组 DNA 技术将本文所描述的核苷酸序列与各种其它核苷酸序列连接起来。例如，可以将多核苷酸克隆在多种克隆载体的任意一种中，这些载体包括质粒、噬菌粒、 λ 噬菌体衍生物和粘粒。尤其有意义的载体包括表达载体、复制载体、探针制备用载体和测序载体。

一般地，载体含有在至少一种生物体中发挥功能的复制起点、方便的限制性内切酶位点和一个或多个选择标记。其它元件将由期望的用途决定，并且将是本领域普通技术人员所明了的。

在某些实施方案中，可以对多核苷酸进行配制，以便使其能进入哺乳动物细胞中，并在其中表达。这些制剂对于治疗目的是尤其有用的，见下述。本领域普通技术人员将明了，实现多核苷酸在靶细胞中的表达有多种途径，而且可以采用任何适合的方法来进行。例如，可以将多核苷酸导入病毒载体中，这些载体例如，但不限于，腺病毒、腺相关病毒、逆转录病毒、或痘苗病毒或其它痘病毒（例如禽类痘病毒）。还可以将多核苷酸作为裸质粒载体进行施用。用于将 DNA 插入这些载体中的技术是本领域普通技术人员所熟知的。此外，逆转录病毒载体还可以转移或掺入基因作为选择标记（以帮助鉴定或筛选转导的细胞）和/或导向部分，例如针对特异靶细胞上受体的配体的编码基因，以使该载体具有靶标特异性。也可以采用抗体，通过本领域配体技术人员已知的方法，实现导向。

用于治疗目的其它制剂包括胶体分散系统，例如高分子复合物、纳米囊剂（nanocapsules）、微球体、小珠，和基于脂质的系统，包括水包油型乳剂、微胶粒、混合微胶粒、和脂质体。用作体外和体内递送载体的优选胶体系统是脂质体（即人造膜载体）。这些系统的制备和应用是本领域所熟知的。

肺肿瘤多肽

在本发明的上下文中，本文所述多肽可以含有肺肿瘤蛋白质或其变体的至少免疫原性部分。正如以上所指出的，“肺肿瘤蛋白质”是肺肿瘤细胞表达的蛋白质。作为肺肿瘤蛋白质的蛋白质与肺癌患者的抗血清之间的反应可在免疫测定（例如 ELISA）中检测到。本文所述多肽可以是任何长度。还可以存在来源于该天然蛋白质和/或异源序列的其它序列，而且这些序列可以（但不必须）也具有免疫原或抗原性质。

“免疫原性部分”在本文中用于指被 B 细胞和/T 细胞表面抗原受体

识别（即特异结合）的蛋白质部分。这些免疫原性部分一般含有肺肿瘤蛋白质或其变体的至少 5 个氨基酸残基，更优选至少 10 个、甚至更优选至少 20 个氨基酸残基。某些优选的免疫原性部分包括 N 端前导序列和/或跨膜域已经缺失的肽。其它优选的免疫原性部分可以相对于成熟蛋白质含有小的 N-和/或 C-端缺失（例如 1-30 个氨基酸，优选 5-15 个氨基酸）。

一般可以采用熟知的技术，例如 Paul，基础免疫学 (Fundamental Immunology)，第 3 版，第 243-247 页 (Raven Press, 1993) 及其中所引用的文献中总结的那些技术，鉴定免疫原性部分。这些技术包括筛选能够与抗原特异性抗体、抗血清和/或 T 细胞系或克隆反应的多肽。本文中，如果抗血清和抗体特异地与抗原结合（即在 ELISA 或其它免疫测定中它们与该蛋白质反应，而且检测不到它们与无关蛋白质的反应），则它们是“抗原特异性的”。这些抗血清和抗体可以按本文所述并采用熟知技术制备。天然肺肿瘤蛋白质的免疫原性部分是（例如在 ELISA 和/或 T 细胞反应性测定中）以基本上不低于该全长多肽的反应性的水平与这些抗血清和/或 T 细胞反应的部分。这些免疫原性部分可以在这些测定试验中以类似于或高于该全长多肽的反应性的水平反应。一般可以采用本领域普通技术人员熟知的方法，例如描述于 Harlow 和 Lane，抗体：实验室手册 (Antibodies: A Laboratory Manual)，Cold Spring Harbor Laboratory, 1988 中的那些技术，进行此筛选。例如，可以将多肽固定在固相支持物上，并用患者血清与之接触以允许该血清中的抗体与该固定化多肽结合。然后除去未结合的血清，并采用例如 ^{125}I 标记的 A 蛋白检测结合的抗体。

正如以上指出的，组合物可以含有天然肺肿瘤蛋白质的变体。本文所述多肽“变体”是指与天然肺肿瘤蛋白质相差一或多个替代、缺失、添加和/或插入以致基本上保持了多肽的免疫原性的多肽。换言之，相对于天然蛋白质，变体与抗原特异性抗血清的反应能力可以有所增强或不发生改变，或可以相对于该天然蛋白质有不足 50%、优选不足 20% 的降低。一般可以通过对一种上述多肽序列进行修饰，然后评价该修饰多肽与本文所述抗原特异性抗体或抗血清的反应性，从而鉴定这些变体。优

选的变体包括其中一或多个部分，例如 N 端前导序列或跨膜域已经被除去的那些变体。其它优选的变体包括已从成熟蛋白质的 N 和/或 C 端除去了一个小部分（例如 1-30 个氨基酸，优选 5-15 个氨基酸）的变体。

多肽变体优选表现出（按上述方法测定）与所指定的多肽有至少约 70%、更优选至少约 90%、最优选至少约 95% 的一致性。

优选地，变体含有保守替代。“保守替代”是指一个氨基酸替代具有相似性质的另一个氨基酸，以致肽化学领域的技术人员将预期该多肽的二级结构和亲水性质基本上不发生改变。一般可以基于氨基酸残基的极性、电荷、可溶性、疏水性、亲水性和/或双亲性质，进行氨基酸替代。例如，带负电荷的氨基酸包括天冬氨酸和谷氨酸；带正电荷的氨基酸包括赖氨酸和精氨酸；带有非荷电极性头部基团、具有相似亲水值的氨基酸包括亮氨酸、异亮氨酸和缬氨酸；甘氨酸和丙氨酸；天冬酰胺和谷氨酰胺；及丝氨酸、苏氨酸、苯丙氨酸和酪氨酸。可以代表保守改变的其它氨基酸组包括：(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; 和 (5) phe, tyr, trp, his. 变体可以还，或作为可替代方案，含有非保守改变。在一个优选实施方案中，变体多肽与天然多肽相差 5 个或更少个氨基酸的替代、缺失或添加。还（或者作为可选择方案）可以通过例如缺失或添加对该多肽的免疫原性、二级结构和亲水性质产生最小影响的氨基酸，修饰变体。

正如以上指出的，多肽可以在该蛋白质的 N 末端含有在翻译的同时或在翻译后指导该蛋白质转移的信号（或前导）序列。该多肽还可以和接头或其它序列偶联，以利于该多肽的合成、纯化或鉴定（例如 poly-His），或增强该多肽与固相支持物的结合。例如，可以将多肽与免疫球蛋白的 Fc 区偶联。

多肽的制备可以采用多种熟知技术中的任意一种。采用本领域普通技术人员已知的多种表达载体中的任何一种，可以容易地从本文所述的 DNA 序列制备这些序列编码的重组多肽。可以在任何一种用含有编码重组多肽的 DNA 分子的表达载体转化或转染的适合宿主细胞中实现表达。适

合的宿主细胞包括原核细胞、酵母、高等真核细胞和植物细胞。优选地，该宿主细胞采用大肠杆菌、酵母或哺乳动物细胞系例如 COS 或 CHO。首先可以采用可商业购买获得的滤器，浓缩来自将重组蛋白或多肽分泌至培养基中的适合宿主/载体系统的上清液。浓缩后，可以将该浓缩物应用到适合的纯化基质例如亲和基质或离子交换树脂上。最后，可以采用一或多个反相 HPLC 步骤进一步纯化重组多肽。

还可以通过合成手段，采用本领域普通技术人员熟知的技术，制备具有少于约 100 个氨基酸、一般少于约 50 个氨基酸的多肽部分和其它变体。例如，可以采用任何一种商业可获得的固相技术，例如 Merrifield 固相合成法，通过将氨基酸顺序地添加到生长的氨基酸链上，合成这些多肽。见 Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. 用于自动合成多肽的仪器可从供应商例如 Perkin Elmer/Applied BioSystems Division (Foster City, CA) 处购买获得，并可以按厂家说明书进行操作。

在某些具体的实施方案中，多肽可以是含有多个上述多肽的融合蛋白，或含有至少一个上述多肽及无关序列（例如已知的肿瘤蛋白质）的融合蛋白。融合伴侣（fusion partner）可以例如协助提供 T 辅助细胞表位（免疫学融合伴侣），优选人类所识别的 T 辅助细胞表位，或可以协助使该蛋白质比该原来的重组蛋白以更高的产量表达（表达增强子）。某些优选的融合伴侣既是免疫学融合伴侣又是表达增强融合伴侣。可以选择其它融合伴侣，以便增加该蛋白质的可溶性或使该蛋白质能被导向期望的细胞内区室。再其它融合伴侣包括利于该蛋白质纯化的亲和标记物。

融合蛋白一般可以采用包括化学偶联在内的标准技术制备。优选地，将融合蛋白表达为重组蛋白质，以便使其相对于非融合蛋白在表达系统中的产生水平提高。简而言之，可以单独地将编码这些多肽成分的 DNA 序列组装起来，然后连接至适合的表达载体中。将编码一个多肽成分的 DNA 序列的 3' 末端与编码第二多肽成分的 DNA 序列的 5' 末端，在有或无肽接头时相连，以便这些序列的阅读框同相。这就使得可以翻译成保留了这两个多肽成分的生物学活性的单个融合蛋白质。

可以采用肽接头序列将该第一和第二多肽成分分开一段足够长的距离，以保证每一个多肽都折叠成其二级和三级结构。该多肽接头序列可以采用本领域熟知的标准技术并入融合蛋白中。可以基于以下因素选择适合的肽接头序列：(1) 其能够采取柔性伸展构象；(2) 不能采取能与该第一和第二多肽的功能性表位相互作用的二级结构；和(3) 缺乏可以和该多肽的功能性表位反应的疏水或带电荷残基。优选的肽接头序列含有 Gly、Asn 和 Ser 残基。其它近中性氨基酸，例如 Thr 和 Ala 也可以用于该接头序列中。可以用作接头的有用氨基酸序列包括那些公开于如下文献中的序列：Maratea 等，基因(Gene) 40:39-46, 1985；Murphy 等，美国国家科学院院刊 83:8258-8262, 1986；美国专利 4,935,233 和美国专利 4,751,180。接头序列一般可以长 1-约 50 个氨基酸。当该第一个和第二个多肽具有能够用以分开这些功能域并防止空间干扰的非必需 N 端氨基酸区域时，则无需接头序列。

将这些相连的 DNA 序列可操作地与适当的转录或翻译调节元件连接在一起。负责 DNA 表达的调节元件仅置于编码该第一多肽的 DNA 序列的 5' 端。同样，终止翻译所必需的终止密码子和转录终止信号仅存在于编码该第二多肽的 DNA 序列的 3' 端。

本发明还提供含有本发明多肽及无关免疫原性蛋白质的融合蛋白。优选地该免疫原性蛋白质能够引起回忆应答。这些蛋白质的实例包括破伤风、结核和肝炎蛋白(见例如 Stoute 等，New Engl. J. Med., 336:86-91 (1997))。

在优选的实施方案中，免疫学融合伴侣来源于 D 蛋白，即革兰氏阴性细菌流感嗜血杆菌 B 的一种表面蛋白质(WO 91/18926)。优选地，D 蛋白的衍生物含有该蛋白质的大约三分之一(first third)(例如 N 端的头 100-110 个氨基酸)，而且可以对 D 蛋白衍生物进行脂化。在某些优选实施方案中，N 端包括了 D 脂蛋白融合伴侣的头 109 个残基，以提供具有额外外源性 T 细胞表位的多肽并增强其在大肠杆菌中的表达水平(由此起到表达增强子的作用)。该脂类尾部保证了该抗原向抗原呈递细胞的最佳呈递。其它融合伴侣包括来自流感病毒的非结构蛋白 NS1(血凝素)。

尽管可以采用包括 T 辅助细胞表位在内的不同片段，但典型地采用此 N 端 81 个氨基酸。

在另一个实施方案中，该免疫学融合伴侣是称作 LYTA 的蛋白质，或其部分（优选 C 端部分）。LYTA 来源于肺炎链球菌 (*Streptococcus pneumoniae*)，该细菌合成一种称作酰胺酶 LYTA 的 N-乙酰基-L-丙氨酸酰胺酶（由 *LytA* 基因编码；基因 (Gene) 43:265-292, 1986）。LYTA 是一种特异降解该肽聚糖骨架中某些键的自溶素。该 LYTA 蛋白的 C 端区域负责与胆碱或某些胆碱类似物例如 DEAE 的亲合。该性质已被利用来开发表达融合蛋白的大肠杆菌表达 C-LYTA 的质粒。对在氨基端含有该 C-LYTA 片段的杂合蛋白的纯化已有描述（见生物技术 (Biotechnology) 10:795-798, 1992）。在一个优选的实施方案中，可以将 LYTA 的重复部分掺入融合蛋白中。重复部分存在于从第 178 个残基起始的 C 端区域中。尤其优选的重复部分包括第 188 - 305 位残基。

一般地，本文所述多肽（包括融合蛋白）和多核苷酸是分离的。“分离的”多肽或多核苷酸是从其最初环境中被分离出来的多肽或多核苷酸。例如，如果将天然存在的蛋白质和其自然系统中的一些或全部共存物质分开，则该蛋白质是“分离的”。优选地，这些多肽有至少约 90% 的纯度，更优选至少约 95% 的纯度，最优选至少约 99% 的纯度。例如，如果将多核苷酸克隆在非其自然环境一部分的载体中，则该多核苷酸被认为是分离的。

结合剂

本发明还提供特异地与肺肿瘤蛋白质结合的药剂，例如抗体和其抗原结合片段。在本文中，如果抗体或其抗原结合片段（在例如 ELISA 中）以可检测得到的水平与肺肿瘤蛋白质反应，而在相似条件下不能检测到其与无关蛋白质的反应时，则被认为与肺肿瘤蛋白质“特异结合”。本文所用“结合”是指两个独立分子之间的非共价联接以致形成复合物。结合能力可以通过例如测定形成该复合物的结合常数来评价。结合常数是当用各成分的浓度乘积除该复合物的浓度时获得的值。一般地，在本文

的上下文中，当形成复合物的结合常数大于约 10^3L/mol 时，两个化合物被认为是“相结合的”。该结合常数可以采用本领域熟知的方法测定。

采用本文提供的代表性测定方法，结合剂还能够区分患者是否患有癌症，例如肺癌。换言之，与肺肿瘤蛋白质结合的抗体或其它结合剂将在至少约 20% 患有该病的患者中产生指示癌症存在的信号，而将在至少约 90% 未患该病的个体中产生指示癌症不存在的信号。为了确定结合剂是否满足此要求，可以按本文所述方法测定在来自（用标准临床检验确定的）患有和未患癌症的患者的生物样品（例如血液、血清、痰、尿和/或肿瘤活检组织）中是否存在与该结合剂结合的多肽。很明显，分析的患病和未患病样品的数量应当具有统计学显著性。每个结合剂都应满足以上标准；然而，本领域普通技术人员将知道，可以联合使用多个结合剂以提高灵敏度。

满足以上要求的任何药剂都可以是结合剂。例如，结合剂可以是含有或不含有肽成分的核糖体、RNA 分子或多肽。在一个优选实施方案中，结合剂是抗体或其抗原结合片段。抗体的制备可以采用本领域普通技术人员已知的多种技术中的任意一种。见例如 Harlow 和 Lane, 抗体：实验室手册, Cold Spring Harbor Laboratory, 1988. 一般地，可以通过细胞培养技术制备抗体，包括按本文所述制备单克隆抗体，或通过用抗体基因转染适合的细菌或哺乳动物细胞宿主，以便使得可以产生重组抗体。在一项技术中，首先给多种哺乳动物（例如小鼠、大鼠、家兔、绵羊或山羊）中的任一种注射含有本发明多肽的免疫原。在该步骤中，可以将本发明的多肽不经修饰用作免疫原。或者，尤其是对于相对短的多肽，如果将该多肽与载体蛋白质，例如牛血清白蛋白或匙孔蠔血蓝蛋白，连接在一起，则可以引起极佳的免疫应答。给该动物宿主注射该免疫原，并优选地根据预先确定的时间表掺入一或多次加强免疫，然后定期采取该动物的血液。然后可以从抗血清中，通过例如采用与适合固相支持物偶联的该多肽进行亲和层析，纯化对该多肽具有特异性的多克隆抗体。

对目的抗原多肽具有特异性的单克隆抗体可以采用例如 Kohler 和 Milstein 的技术 (Eur. J. Immunol. 6:511-519, 1976), 及其改良方

法来制备。简而言之，这些方法涉及制备能够产生具有期望特异性（即与目的多肽的反应性）的抗体的永生化细胞系。可以从例如获自按上述方法免疫的动物的脾细胞制备这些细胞系。然后通过例如和骨髓瘤细胞融合伴侣，优选与该免疫动物同基因的骨髓瘤细胞，融合，使该脾细胞永生化。可以采用多种融合技术。例如，可以将该脾细胞和骨髓瘤细胞与非离子去污剂混合几分钟，然后以低密度铺在支持杂种细胞而不支持骨髓瘤细胞生长的选择培养基上。优选的筛选技术采用了 HAT（次黄嘌呤、氨基喋呤、胸苷）筛选。在足够长的时间之后，通常为约 1-2 周，可观察到杂种集落。选择单集落，并测试其培养物上清液与本发明多肽的结合活性。优选具有高反应性和特异性的杂交瘤。

可以从培养的杂交瘤集落的上清液中分离单克隆抗体。此外，还可以采用各种技术增加产量，例如将该杂交瘤细胞系注射入适合脊椎动物宿主例如小鼠的腹腔内。然后可以从腹水或血液中收获单克隆抗体。可以通过常规技术例如层析、凝胶过滤、沉淀和抽提从这些抗体中除去杂质。本发明多肽可以用于纯化方法的例如亲和层析步骤中。

在某些实施方案中，可能优选采用抗体的抗原结合片段。这些片段包括 Fab 片段，它们可以采用标准技术制备。简而言之，可以通过在 A 蛋白珠柱上通过亲和层析从兔血清中纯化免疫球蛋白（Harlow 和 Lane, 抗体：实验室手册，Cold Spring Harbor Laboratory, 1988），然后通过木瓜蛋白酶消化产生 Fab 和 Fc 片段。该 Fab 和 Fc 片段可以在 A 蛋白珠柱上通过亲和层析分离。

可以将本发明的单克隆抗体与一或多种治疗剂偶联在一起。在此方面适合的治疗剂包括放射性核素、分化诱导剂、药物、毒素和它们的衍生物。优选的放射性核素包括 ^{90}Y 、 ^{123}I 、 ^{125}I 、 ^{131}I 、 ^{186}Re 、 ^{188}Re 、 ^{211}At 和 ^{212}Bi 。优选的药物包括氮甲喋呤、及嘧啶和嘌呤的类似物。优选的分化诱导剂包括佛波酯和丁酸。优选的毒素包括蓖麻毒素、相思豆毒素、白喉毒素、霍乱毒素、gelonin、假单胞菌外毒素、志贺氏菌毒素和美洲商陆抗病毒蛋白。

治疗剂可以与适合的单克隆抗体直接或间接地（即通过接头基团）

偶联（例如共价键合）。当药剂和抗体均具有能够与另一个反应的取代基时，它们之间的直接反应是可能的。例如，一个上的亲核基团，例如氨基或巯基，可以和另一个上的含有羰基的基团例如酐或酰基卤，或含有容易离去的基团（例如卤素）的烷基反应。

或者，可能期望将治疗剂和抗体通过接头基团偶联。接头基团能够作为间隔起作用使抗体和药剂分隔开，以便避免对结合性能的干扰。接头基团还可以用于增强药剂或抗体上取代基的化学反应性，由此增加偶联效率。化学反应性的增强还可以促进药剂、或药剂上功能基团的应用，否则将不可能实现这种应用。

本领域技术人员将明了，有多种功能相同和相异的双功能或多功能试剂（例如描述于 Pierce 化学制品公司 (Rockford, IL) 的产品目录中的那些）可以用作该接头基团。可以通过例如氨基、羧基、巯基或氧化糖残基实现偶联。有许多文献描述过该方法学，例如 Rodwell 等的美国专利 4,671,958。

当治疗剂游离于本发明治疗偶联物的抗体部分而更为有效时，可能期望采用在内化进行细胞过程中或之后可切割的接头基团。已有过许多不同的可切割接头基团的描述。在细胞内从这些接头基团处释放出药剂的机制包括由二硫键还原（例如 Spitler 的美国专利 4,489,710）、光不稳定键的辐射（例如 Senter 等的美国专利 4,625,014）、衍生的氨基酸侧链的水解（例如 Kohn 等的美国专利 4,638,045）、血清补体介导的水解（例如 Rodwell 等的美国专利 4,671,958）、和酸催化的水解（例如 Blattler 等的美国专利 4,569,789）引起的断裂。

可能期望将一个以上的药剂与抗体偶联。在一个实施方案中，一个药剂的多个分子与一个抗体分子偶联。在另一个实施方案中，一种以上类型的药剂可以和一个抗体偶联。无论具体的实施方案如何，可以有多种途径制备带有一个以上药剂的免疫偶联物。例如，可以将一个以上的药剂直接与一个抗体分子偶联，或可以采用提供多个连接位点的接头。或者，可以采用载体。

载体可以以多种方式携带这些药剂，包括直接或通过接头基团的共价键

合。适合的载体包括蛋白质例如白蛋白（例如 Kato 等的美国专利 4,507,234）、肽和多糖例如氨基葡聚糖（例如 Shih 等的美国专利 4,699,784）。载体还可以通过非共价结合或通过包入例如脂质体囊中（例如美国专利 4,429,008 和 4,873,088）携带药剂。特异用于放射性核素药剂的载体包括放射性卤化小分子和螯合化合物。例如美国专利 4,735,792 公开了代表性的放射性卤化小分子和它们的合成。可以从螯合化合物形成放射性核素螯合物，这些螯合化合物包括那些含有氮和硫原子作为结合金属、或金属氧、放射性核素的供体原子的螯合化合物。例如，Davison 等的美国专利 4,673,562 公开了代表性的螯合化合物和它们的合成。

可以采用多种途径施用这些抗体和免疫偶联物。典型地，可以静脉内、肌内、皮下或在切除肿瘤床（bed of a resected tumor）中给药。很明显，该抗体/免疫偶联物的精确剂量将随所用的抗体、肿瘤上的抗原密度、和抗体的清除率而改变。

T 细胞

免疫治疗组合物可以还，或者作为替代方案可以，含有肺肿瘤蛋白质特异性 T 细胞。这些细胞一般可以在体外或离体采用标准程序制备。例如，可以采用商业上可获得的细胞分离系统，例如可从 Nexell Therapeutics 公司 (Irvine, CA) 获得的 Isolex™ 系统，从患者的骨髓、外周血、或骨髓或外周血组分分离 T 细胞（也参见美国专利 5,240,856；美国专利 5,215,926；WO 89/06280；WO 91/16116 和 WO 92/07243）。或者，可以从相关或无关的人、非人哺乳动物、细胞系或培养物获得 T 细胞。

可以用肺肿瘤多肽、编码肺肿瘤多肽的多核苷酸和/或表达该多肽的抗原呈递细胞 (APC) 刺激 T 细胞。该刺激在足以产生对该多肽特异的 T 细胞的条件和时间下进行。优选地，将肺肿瘤多肽或多核苷酸置于递送载体中，例如微球体中，以利于特异性 T 细胞的产生。

如果 T 细胞特异增殖、分泌细胞因子或杀伤被覆肺肿瘤多肽或表达编码该多肽的基因的靶细胞，则该 T 细胞被认为是肺肿瘤多肽特异的。T

细胞的特异性可以采用多种标准技术中的任一种进行评价。例如，在铬释放测定或增殖测定中，相对于阴性对照，在裂解和/或增殖方面超过 2 倍的刺激指数增加指示 T 细胞的特异性。这些测定可以按例如 Chen 等，癌症研究 (Cancer Res.) 54:1065-1070, 1994 中的描述进行。或者，可以通过各种已知技术检测 T 细胞的增殖。例如，可以通过测量 DNA 合成速率的增加（例如通过用含氘胸苷脉冲标记 T 细胞培养物并测量掺入 DNA 中的含氘胸苷的量），检测 T 细胞的增殖。和肺肿瘤多肽（100ng/ml - 100 μ g/ml，优选 200 ng/ml - 25 μ g/ml）接触 3-7 天应导致 T 细胞增殖的至少 2 倍增加。正如采用标准细胞因子测定方法所测量的，在该测定方法中细胞因子（例如 TNF 或 IFN- γ ）释放水平增加 2 倍指示 T 细胞的激活（见 Coligan 等，当代免疫学实验指南 (Current Protocols in Immunology)，第 1 卷，Wiley Interscience (Greene 1998)），按以上所述接触 2-3 小时应导致 T 细胞的激活。响应肺肿瘤多肽、多核苷酸或表达该多肽的 APC 而激活的 T 细胞可以是 CD4⁺ 和/或 CD8⁺ 的。可以采用标准技术扩增肺肿瘤蛋白质特异性 T 细胞。在优选的实施方案中，这些 T 细胞来源于患者、或相关或无关的供体，并在刺激和扩增后被用于该患者。

对于治疗目的，可以在体外或体内扩增响应肺肿瘤多肽、多核苷酸或 APC 而增殖的 CD4⁺ 或 CD8⁺ T 细胞的数量。可以有多种途径来实现这些 T 细胞的体外增殖。例如，可以在添加了或未添加 T 细胞生长因子（例如白介素 2）和/或合成肺肿瘤多肽的刺激细胞的情况下，将这些 T 细胞重新暴露于肺肿瘤多肽或相应于该多肽免疫原性部分的短肽中。或者，可以通过克隆大量扩增在存在肺肿瘤蛋白质时增殖的一或多种 T 细胞的数量。克隆细胞的方法是本领域所熟知的，包括有限稀释。

药物组合物和疫苗

在某些方面，可以将本文所公开的多肽、多核苷酸、T 细胞和/或结合剂掺入药物组合物或免疫原性组合物（即疫苗）中。药物组合物含有一或多种这些化合物及生理学上可接受载体。疫苗可以含有一或多种这

些化合物和免疫刺激剂。免疫刺激剂可以是增强或加强针对外源性抗原的免疫应答的任何物质。免疫刺激剂的例子包括佐剂、生物可降解微球体（例如 polylactic galactide）和脂质体（所述化合物被掺入其中；见例如 Fullerton, 美国专利 4,235,877）。疫苗的制备一般描述于例如 M.F. Powell 和 M.J. Newman 编, “疫苗的设计（亚单位和佐剂方法）（Vaccine Design (the subunit and adjuvant approach)”, Plenum Press (NY, 1995)。属于本发明范围的药物组合物和疫苗还可以含有其它化合物, 这些化合物可以具有或没有生物学活性。例如, 可以将其它肿瘤抗原的一或多个免疫原性部分并入融合多肽中或作为独立的成分存在于该组合物或疫苗中。

药物组合物或疫苗可以含有编码一或多种上述多肽的 DNA, 以便原位产生该多肽。正如以上所指出的, 该 DNA 可以存在于本领域普通技术人员已知的多种递送系统的任一种中, 包括核酸表达系统、细菌和病毒表达系统。许多基因递送技术是本领域所熟知的, 例如描述于 Rolland, Crit. Rev. Therop. Drug Carrier Systems 15:143-198, 1998, 和其中的引用文献中的那些技术。适合的核酸表达系统含有在患者中进行表达所必需的 DNA 序列（例如适合的启动子和终止信号）。细菌递送系统涉及到施用于其细胞表面表达该多肽免疫原性部分或分泌该表位的细菌（例如卡介苗 (Bacillus-Calmette-Guerrin)）。在一个优选的实施方案中, 可以采用病毒表达系统（例如痘苗病毒或其它痘病毒、逆转录病毒、或腺病毒）引入该 DNA, 这可能涉及到非致病性（缺陷性）可复制病毒的使用。适合的系统公开于例如 Fisher-Hoch 等, 美国国家科学院院刊 86:317-321, 1989; Flexner 等, Ann, N.Y. Acad. Sci. 569:86-103, 1989; Flexner 等, 疫苗 (Vaccine) 8:17-21, 1990; 美国专利 4,603,112、4,769,330 和 5,017,487; WO 89/01973; 美国专利 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, 生物技术 (Biotechniques) 6:616-627, 1988; Rosenfeld 等, 科学 (Science) 252:431-434, 1991; Kolls 等, 美国国家科学院院刊 91:215-219, 1994; Kass-Eisler 等, 美国国家科学院院刊 90:11498-11502, 1993; Guzman

等, 血液循环(Circulation) 88:2838-2848, 1993; 和 Guzman 等, Cir. Res. 73:1202-1207, 1993. 用于将 DNA 引入这些表达系统的技术是本领域普通技术人员熟知的. 这些 DNA 也可以是“裸露的”, 参见例如 Ulmer 等, 科学 259:1745-1749, 1993, 综述参见 Cohen, 科学 259:1691-1692, 1993. 可以通过将裸露的 DNA 包被在可以有效地运送入细胞的生物可降解小珠上, 增加该 DNA 的摄取.

尽管在本发明的药物组合物中可采用本领域普通技术人员已知的任何适合载体, 但载体的类型将随给药模式的改变而改变. 可以对本发明的组合物进行配制以用于适当的给药方式, 包括例如局部、口服、鼻腔、静脉内、颅内、腹膜内、皮下或肌肉内给药. 对于非胃肠道给药, 例如皮下注射, 该载体优选含有水、盐水、乙醇、脂肪、蜡或缓冲液. 对于口服用药, 可以采用以上任一种载体或固体载体, 例如甘露醇、乳糖、淀粉、硬脂酸镁、糖精钠、滑石、纤维素、葡萄糖、蔗糖、和碳酸镁. 还可采用生物可降解微球体(例如 polylactate polyglycolate)作为载体用于本发明的药物组合物. 适合的生物可降解微球体公开于例如美国专利 4,897,268 和 5,075,109.

这些组合物还可以含有缓冲液(例如中性缓冲盐水或磷酸缓冲盐水)、糖类(例如葡萄糖、甘露糖、蔗糖或葡聚糖)、甘露醇、蛋白质、多肽或氨基酸(例如甘氨酸)、抗氧化剂、螯合剂例如 EDTA 或谷胱甘肽、佐剂(例如氢氧化铝)和/或防腐剂. 或者, 可以将本发明的组合物制成冻干物. 还可以采用熟知的技术将化合物装入脂质体中.

在本发明的疫苗中可以采用多种免疫刺激剂中之任一种. 例如, 可以将佐剂包括在内. 大多数佐剂含有设计用以防止抗原快速代谢的物质, 例如氢氧化铝或矿物油, 和免疫应答的刺激剂, 例如脂质 A、百日咳博德特氏菌(*Bordetella pertussis*)或结核分支杆菌(*Mycobacterium tuberculosis*)来源的蛋白质. 可从商业途径获得适合的佐剂, 例如弗氏不完全佐剂和完全佐剂(Difco Laboratories, Detroit, MI); Merck 佐剂 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); 铝盐例如氢氧化铝凝胶(明矾)或磷酸铝;

钙、铁或锌的盐类；酰化酪氨酸的不溶性悬浮物；酰化糖；阳离子或阴离子衍生多糖；聚磷腈；生物可降解微球体；单磷酸脂 A (monophosphoryl lipid A) 和 quil A. 细胞因子，例如 GM-CSF 或白介素-2、-7 或-12，也可以用作佐剂。

在本文提供的疫苗中，优选对佐剂组合物进行设计以诱导主要是 Th1 型免疫应答。高水平的 Th1 型细胞因子（例如 IFN- γ 、TNF α 、IL-2 和 IL-12）倾向于促进诱导针对所施用抗原的细胞介导免疫应答。相反，高水平的 Th2 型细胞因子（例如 IL-4、IL-5、IL-6 和 IL-10）倾向于促进诱导体液免疫应答。在施用本文所提供的疫苗后，患者将支持包括 Th-1 和 Th-2 型应答在内的免疫应答。在应答主要是 Th-1 型的优选实施方案中，Th-1 型细胞因子的水平将比 Th2-型细胞因子的水平有更高程度的增加。这些细胞因子的水平可以采用标准测定方法容易地评价。对于细胞因子家族的综述，参见 Mosmann 和 Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

用于引起主要是 Th-1 型应答的优选佐剂包括，例如单磷酸脂 A，优选 3-脱氧酰化单磷酸脂 A (3D-MPL)，与铝盐的组合。MPL 佐剂可从 Ribi ImmunoChem Research 公司 (Hamilton, MT) 获得（见美国专利 4,436,727；4,877,611；4,866,034 和 4,912,094）。含有 CpG 的寡核苷酸（其中该 CpG 二核苷酸未被甲基化）也诱导主要是 Th1 应答。这些寡核苷酸是熟知的，并描述于例如 WO 96/02555 和 WO 99/33488。免疫刺激性 DNA 序列还描述于，例如 Sato 等，*科学* 273:352, 1996。另一优选的佐剂是皂苷，优选 QS21 (Aquila Biopharmaceuticals 公司, Framingham, MA)，其可以单独或联合其它佐剂一起使用。例如，一个增强系统包括单磷酸脂 A 和皂苷衍生物的组合，例如 WO 94/00153 中所述的 QS21 和 3D-MPL 的组合，或 WO 96/33739 中所述的用胆固醇淬灭了 QS21 并具有较小反应原性的组合物。其它优选制剂包含水包油型乳剂和生育酚。WO 95/17210 描述了一种尤其有效的在水包油型乳剂中包含 QS21、3D-MPL 和生育酚的佐剂制剂。

其它优选的佐剂包括 Montanide ISA 720 (Seppic, 法国)，SAF (Chiron, California, 美国)，ISCOMS (CSL)，MF-59 (Chiron)，SBAS

系列佐剂(例如 SBAS-2 或 SBAS-4, 可从 SmithKline Beecham, Rixensart, 比利时获得), Detox (Ribi ImmunoChem Research 公司, Hamilton, MT), RC-529 (Ribi ImmunoChem Research 公司, Hamilton, MT) 和氨烷基氨基葡萄糖苷 4-磷酸盐 (AGPs)。

本文提供的所有疫苗均可以采用将抗原、免疫应答增强剂和适合的载体或赋形剂组合在一起的熟知方法制备。本文所述组合物可以作为持续释放制剂(即, 施用后实现化合物的缓慢释放的胶囊、海绵或凝胶(例如由多糖组成的)等制剂)的部分施用。这些制剂一般可以采用熟知技术(见例如 Coombes 等, 疫苗(Vaccine) 14:1429-1438, 1996)制备, 并通过例如口服、直肠或皮下植入, 或通过期望靶位置的植入进行施用。持续释放制剂可以含有多肽、多核苷酸或抗体, 它们可以被分散在载体基质中和/或包含在控速膜包围形成的贮存池中。

用于这些制剂的载体具有生物适合性, 并还可以是可生物降解的; 优选地, 该制剂提供相对恒定水平的活性成分释放。这些载体包括 poly(lactide-co-glycolide) 微粒, 以及聚丙烯酸酯、胶乳、淀粉、纤维素和葡聚糖。其它延迟释放载体包括超分子生物载体, 它们含有一个非液体亲水核心(例如交联的多糖或寡糖)和任选的含有双亲化合物例如磷脂的外层(见例如美国专利 5, 151, 254 和 PCT 申请 WO 94/20078、WO 94/23701 和 WO 96/06638)。包含在持续释放制剂中的活性化合物的量取决于植入位置、释放速率和预期的持续时间, 以及待治疗或预防的疾病性质。

在药物组合物和疫苗中可以采用多种递送载体中的任一种, 以促进产生靶向肿瘤细胞的抗原特异性免疫应答。递送载体包括抗原呈递细胞 (APC)、例如树突细胞、巨噬细胞、B 细胞、单核细胞和可以经改造成为有效 APC 的其它细胞。这些细胞可以, 但不必须, 经遗传修饰, 以增强呈递抗原的能力、改善对 T 细胞应答的激活和/或维持、本身具有抗肿瘤作用和/或与受体在免疫学上相容(即, 匹配的 HLA 单倍型)。一般可以从多种生物学液体或器官(包括肿瘤和肿瘤周围组织)中的任一种分离 APC, 而且 APC 可以是自体的、同种异体、同系的、或异种的细胞。

本发明的某些优选实施方案采用树突细胞或其祖先细胞作为抗原呈递细胞。树突细胞是极为有效的 APC (Banchereau 和 Steinman, 自然 (Nature) 392:245-251, 1998), 而且已经显示其与生理学佐剂在引起预防性或治疗性抗肿瘤免疫方面同样有效(见 Timmerman 和 Levy, Ann. Rev. Med. 50:507-529, 1999)。一般地, 树突细胞可以基于其典型性状(在原位是星形, 而体外可见到有明显的细胞质突起(树突))、其高效摄取、加工和呈递抗原的能力、和其激活幼稚 T 细胞应答的能力来鉴定。当然, 可以对树突细胞进行改造以表达通常在体内或离体时树突细胞上并不存在的特定细胞表面受体或配体, 而且这些修饰的树突细胞是本发明所考虑的。作为树突细胞的替代物, 可以在疫苗中采用携带抗原的分泌小泡的树突细胞(称作外来体)(见 Zitvogel 等, Nature Med. 4:594-600, 1998)。

树突细胞和其祖先细胞可以从外周血、骨髓、肿瘤浸润细胞、肿瘤周围组织浸润细胞、淋巴结、脾脏、皮肤、脐带血或任何其它适合的组织或体液中获得。例如, 可以通过将细胞因子的组合例如 GM-CSF、IL-4、IL-13 和/或 $\text{TNF}\alpha$ 加入从外周血收获的单核细胞的培养物中, 离体分化树突细胞。或者, 可以通过将 GM-CSF、IL-3、 $\text{TNF}\alpha$ 、CD40 配体、LPS、flt3 配体和/或诱导树突细胞分化、成熟和增殖的其它化合物的组合加入培养基中, 使收获自外周血、脐带血或骨髓的 CD34 阳性细胞分化成树突细胞。

方便地, 树突细胞被分为“未成熟”和“成熟”细胞, 这样就允许通过一种简单的方式区分两种已良好表征的表型。然而, 不应将此命名理解为排除了所有可能的分化中间阶段。未成熟树突细胞被表征是具有强抗原摄取和加工能力的 APC, 这与 $\text{Fc}\gamma$ 受体和甘露糖受体的高表达相关联。成熟表型的典型特征是这些标记的较低表达, 但负责 T 细胞激活的细胞表面分子例如 I 型和 II 型 MHC、粘着分子(例如 CD54 和 CD11)和共刺激分子(例如 CD40、CD80、CD86 和 4-1BB)有高表达。

一般可以用编码肺肿瘤蛋白质(或其部分或其它变体)的多核苷酸转染 APC, 以便在该细胞表面表达该肺肿瘤多肽、或其免疫原性部分。按

本文所述，该转染可以离体进行，然后可以将含有该转染细胞的组合物或疫苗用于治疗目的。或者，可以给患者施用靶向树突细胞或其它抗原呈递细胞的基因递送载体，以导致在体内发生转染。例如，树突细胞的体内和离体转染一般可以采用本领域已知的任何方法进行，例如 WO 97/2447 中描述的那些方法，或者 Mahvi 等（免疫学和细胞生物学 (Immunology and Cell Biology) 75:456-460, 1997）所述的基因枪法。可以通过树突细胞或其祖先细胞与该肺肿瘤多肽、DNA（裸露的或位于质粒载体中）或 RNA；或与表达抗原的重组细菌或病毒（例如痘苗病毒、禽痘病毒、腺病毒或慢病毒载体）一起孵育，使树突细胞携带抗原。在携带之前，可以将该多肽与提供 T 细胞辅助的免疫学伴侣（例如载体分子）偶联。或者，可以用非偶联的免疫学伴侣单独地或在多肽存在的同时脉冲树突细胞。

可以将疫苗和药物组合物置于单剂量或多剂量容器中，例如密封的安瓿或小瓶中。优选将这些容器密封以保持直到使用前该制剂无菌。一般地，可以将制剂以悬浮液、溶液或乳剂的形式在油性或水性赋形剂中贮存。或者，可以将疫苗或药物组合物在冻干情况下贮存，临使用前只需加入无菌液相载体即可。

癌症治疗

在本发明的其它方面，可以将本文所述组合物用于免疫治疗癌症、例如肺癌。在这些方法中，典型地给患者使用药物组合物和疫苗。本文所用“患者”是指任何恒温动物，优选人类。患者可以患有或可以未患有癌症。因此，以上药物组合物和疫苗可以用于预防癌症的出现或治疗癌症患者。可以采用本领域普遍接受的标准（包括恶性肿瘤存在的），诊断癌症。可以在手术除去原发性肿瘤和/或实施例如施用放疗或常规化疗药物等治疗之前或之后，施用药物组合物和疫苗。

在某些实施方案中，免疫治疗可以是主动免疫治疗，其中治疗依靠施用免疫应答调节剂（例如本文公开的多肽和多核苷酸）体内刺激内源性宿主免疫系统产生抗肿瘤反应。

在其它实施方案中，免疫治疗可以是被动免疫治疗，其中治疗涉及到递送具有确定肿瘤免疫反应性、能够直接或间接地介导抗肿瘤效果的药剂（例如效应细胞或抗体），而无需依赖完整的宿主免疫系统。效应细胞的例子包括以上讨论的 T 细胞、T 淋巴细胞（例如 CD8+ 细胞毒 T 淋巴细胞和 CD4 + T 辅助肿瘤浸润淋巴细胞）、杀伤细胞（例如自然杀伤细胞和淋巴因子激活的杀伤细胞）、B 细胞和表达本文提供的多肽的抗原呈递细胞（例如树突细胞和巨噬细胞）。可以对本文所述多肽的特异性 T 细胞受体和抗体受体进行克隆、表达、和转移至其它载体或效应细胞中用于过继免疫治疗。还可以采用本文提供的多肽制备抗体或抗独特型抗体（按以上所述和美国专利 4,918,164 中的方法）用于被动免疫治疗。

一般可以按本文所述方法，通过体外培养获得用于过继免疫治疗的足量效应细胞。用于将单抗原特异性效应细胞扩增至几十亿个并保留其体内抗原识别性质的培养条件是本领域熟知的。典型地，这些体外培养条件是通常在细胞因子（例如 IL-2）和非分裂饲养细胞存在时，利用抗原进行间歇性刺激。正如以上指出的，可以采用本文提供的免疫反应性多肽快速扩增抗原特异性 T 细胞培养物，以产生足够用于免疫治疗的细胞数目。具体地，采用本领域熟知的标准技术，可以用免疫反应性多肽脉冲（pulse）抗原呈递细胞例如树突细胞、巨噬细胞、单核细胞、成纤维细胞或 B 细胞，或可以用一或多种多核苷酸转染抗原呈递细胞。例如，可以用含有适于在重组病毒或其它表达系统中增强表达的启动子的多核苷酸转染抗原呈递细胞。培养的效应细胞必需能够在体内生长和广泛分布，并且能够长期存活。研究表明，通过用补加 IL-2 的抗原进行反复刺激能够诱导相当大数量的培养效应细胞在体内生长并长期存活（见例如 Cheever 等，免疫学综述 (Immunological Reviews), 157:177, 1997)。

或者，可以将表达本文所述多肽的载体引入取自患者的抗原呈递细胞中，然后通过克隆和离体增殖后再移植回同一患者体内。可以采用本领域已知的任何手段，优选以无菌形式通过静脉内、腔内、腹膜内或肿瘤内施用，将转染的细胞重新导入该患者体内。

本文公开的治疗组合物的施用途径和频率及剂量将因人而异，而且

可以采用标准技术容易地确定。一般地，可以通过注射（例如皮内、肌肉、静脉内或皮下）、鼻腔途径（例如通过吸入）或口服，施用这些药物组合物和疫苗。优选地，可以在 52 周的一个期间中施用 1-10 个剂量。优选地，以间隔 1 个月的形式施用 6 个剂量，此后可以定期给予加强接种。替代接种方案可能对个别患者是适合的。适合的剂量为当按以上所述方法施用时，能够促进抗肿瘤免疫应答使其至少高于基础（即未处理的）水平 10-50% 的化合物的量。可以通过测量患者体内的抗肿瘤抗体，或通过能够体外杀伤该患者肿瘤细胞的细胞裂解性效应细胞的疫苗依赖性产生，监测该应答。这些疫苗还应该能够引起免疫应答，以导致与未接种的患者相比在接种的患者中出现改善的临床结果（例如，更频繁的症状缓解、完全或部分的或较长的无病存活）。一般地，对于含有一或多种多肽的药物组合物和疫苗，一个剂量中存在的每种多肽的量为每 kg 宿主约 25 μ g - 5mg。适合的剂量大小将随患者的体积而改变，但典型地在约 0.1ml - 约 5ml 之间。

一般地，适当的剂量和治疗方案提供足以获得治疗和/或预防益处的量的活性成分。可以通过确定与未治疗患者相比经治疗的患者出现改善的临床效果（例如更频繁的症状缓解、完全或部分的或较长的无病存活），监测该应答。预先存在的抗肺肿瘤蛋白质的免疫应答的增加一般与改善的临床效果相关联。一般可以采用标准增殖、细胞毒或细胞因子测定，评价这些免疫应答，这些测定可以采用在治疗前和从患者获得的样品进行。

癌症检测方法

一般地，可以基于从患者获得生物样品（例如血液、血清、痰、尿和/或肿瘤活检组织）中一或多种肺肿瘤蛋白质和/或编码这些蛋白质的多核苷酸的存在，检测该患者是否患有癌症。换言之，可以采用这些蛋白质作为标志指示是否存在癌症例如肺癌。此外，还可以采用这些蛋白质检测其它癌症。一般本文提供的结合剂可以检测生物样品中与该药剂结合的抗原的水平。多核苷酸引物和探针可以用于检测编码肿瘤蛋白质

的 mRNA 的水平，该水平也指示了癌症的存在与否。一般地，肺肿瘤序列在肿瘤组织中应比在正常组织中高至少 3 倍的水平存在。

对于采用结合剂检测样品中的多肽标志而言，有多种本领域普通技术人员已知的测定形式可以使用。见例如 Harlow 和 Lane，抗体：实验室手册，Cold Spring Harbor Laboratory, 1988。一般地，患者体内是否存在癌症可以通过以下步骤确定：(a) 用结合剂接触从患者获得的生物样品；(b) 检测样品中与该结合剂结合的多肽的水平；和 (c) 将该多肽水平与预先确定的截断值进行比较。

在一个优选的实施方案中，该测定涉及采用固定在固相支持物上的结合剂结合并从样品剩余物中分离该多肽。然后采用含有报道基团并特异与该结合剂/多肽复合物结合的检测试剂检测该结合的多肽。这些检测试剂可以含有例如，与该多肽特异结合的结合剂、或与该结合剂特异结合的抗体或其它药剂，例如抗免疫球蛋白、G 蛋白、A 蛋白或凝集素。或者，可以利用竞争测定法，在该方法中用报道基团标记多肽，并在固定化结合剂与样品一起孵育后，允许该多肽和该结合剂结合。该样品中的成分对该标记多肽与该结合剂结合的抑制程度指示了该样品与该固定化结合剂的反应性。适合用于这些测定方法的多肽包括以上所述的全长肺肿瘤蛋白质和其与该结合剂结合的部分。

所述固相支持物可以是本领域普通技术人员已知的可以附着该肿瘤蛋白的任何材料。例如，该固相支持物可以是微量滴定板中的测试孔或硝酸纤维素或其它适合的膜。或者，该支持物可以是小珠或圆盘，例如玻璃、玻璃纤维、胶乳、或塑料例如聚苯乙烯或聚氯乙烯。该支持物还可以是磁性颗粒或光导纤维传感器，例如公开于美国专利 5,359,681 中的那些。可以采用本领域技术人员已知的各种技术将结合剂固定在固相支持物上，这些技术在此类专利和科学文献中有详细的描述。在本发明的上下文中，术语“固定”既指非共价连接例如吸附，又指共价结合（其可以是抗原和该支持物上的官能团之间的直接连接，或可以通过交联剂形成的连接）。优选通过吸附固定在微量滴定板孔中或膜上。在这些情况下，可以通过在适合缓冲液中使结合剂与固相支持物接触适当长的时

间来实现吸附。该接触时间随温度而改变，但典型的在约 1 小时至约 1 天之间。一般地，用约 10ng - 约 10 μ g 量、优选约 100ng - 约 1 μ g 量的结合剂接触一个塑料微量滴定板孔（例如聚苯乙烯或聚氯乙烯），就足以固定足量的结合剂。

一般地，可以首先通过用既可以和支持物又可以和结合剂上的官能团，如羟基或氨基，反应的双功能剂与该支持物反应，实现结合剂与固体支持物的共价结合。例如，可以采用苯醌或通过支持物上的醛基和结合伴侣上胺及活性氢的缩合，使该结合剂与具有适当聚合物包衣的支持物共价结合（见例如 Pierce 免疫技术产品目录和手册 (Pierce Immunotechnology Catalog and Handbook), 1991, A12-A13)。

在某些实施方案中，该测定方法是双抗体三明治测定。该测定的操作方式可以是首先使固定在固相支持物上（通常是微量滴定板的孔中）的抗体与样品接触，以便该样品中的多肽可以与该固定的抗体结合。然后，从该固定的多肽-抗体复合物中除去未结合的样品，并加入含有报道基团的检测试剂（优选能够与该多肽上的不同部位结合的二抗）。然后采用适于该特定报道基团的方法，确定与该固相支持物保持结合的检测试剂的量。

更具体地，一旦该抗体按以上所述被固定在该支持物上后，典型地封闭该支持物上的剩余蛋白质结合位点。可以采用本领域普通技术人员已知的任何适合的封闭剂，例如牛血清白蛋白或 Tween 20TM (Sigma Chemical 公司, St. Louis, MO)。然后将该固定化抗体与样品一起孵育，并使多肽可以和该抗体结合。在孵育前可用适合的稀释剂例如磷酸缓冲盐溶液 (PBS) 稀释该样品。一般地，适合的接触时间（即孵育时间）为足以在获自患有肺癌的个体的样品中检测到多肽存在的时间段。优选地，该接触时间足以使结合水平到达结合和未结合多肽之间达到平衡时结合水平的至少大约 95%。本领域的普通技术人员将明了，通过测定一段时间内出现的结合水平，可以容易地确定达到平衡所必需的时间。在室温，约 30 分钟的孵育时间一般是足够的。

然后，通过用适当缓冲液，例如含有 0.1% Tween 20TM 的 PBS，洗

涤该固相支持物，除去未结合的样品。随后可以向该固相支持物加入含有报道基团的二抗。优选的报道基团包括以上所述的那些基团。

然后使检测试剂与该固定的抗体-多肽复合物一起孵育足够长时间以能检测到该结合多肽。适合的时间长度一般可以通过测定一段时间内出现的结合水平来确定。然后除去未结合的检测试剂，并利用该报道基团检测结合的检测试剂。用于检测该报道基团的方法取决于该报道基团的性质。对于放射性基团，一般液闪计数或放射自显影法是适合的。可以采用分光光度法检测染料、发光基团和荧光基团。可以采用偶联了一个不同的报道基团（通常是放射性基团或荧光基团或酶）的抗生物素蛋白检测生物素。酶报道基团一般可以通过加入底物（一般持续一定时间段），随后采用分光光度法或其它分析方法分析反应产物，以进行检测。

为了确定癌症（例如肺癌）是否存在，一般将所检测到的来自与该固相支持物保持结合的该报道基团的信号和相应于预确定截断值的信号进行比较。在一个优选实施方案中，用于癌症检测的截断值为当用该固定化抗体与从未患该癌症的患者获得的样品一起孵育时，所获得的信号的平均值。一般地，将所产生的信号高于该预确定截断值 3 个标准差的样品认定为癌症阳性。在另一个优选实施方案中，该截断值采用 Receiver Operator Curve，根据 Sackett 等（临床流行病学：临床医学的基础科学 (Clinical Epidemiology: A Basic Science for Clinical Medicine), Little Brown and Co., 1985, 第 106-7 页) 的方法确定。简而言之，在该实施方案中，将该诊断测试结果的每一个可能截断值所对应的成对真阳性率（即灵敏度）和假阳性率（100% 特异性）作图，然后可以从该图确定该截断值。图上最接近左上角的截断值（即包括了最大面积的值）是最准确的截断值，而产生的信号高于该方法所确定的截断值的样品可以被认为是阳性的。或者，可以沿着该图向左移动该截断值，以最小化假阳性率，或向右移动以最小化假阴性率。一般地，产生的信号高于该方法所确定的截断值的样品被认为是癌症阳性。

在一个相关的实施方案中，该测定在流过或长条测试形式上进行，其中结合剂被固定在硝酸纤维素等膜上。在该流过测试中，当样品经过

该膜时，样品中的多肽与固定化结合剂结合。然后当含有标记的第二结合剂的溶液流经该膜时，该第二结合剂将与该结合剂-多肽复合物结合。接着可以按以上所述方法检测结合的第二结合剂。在长条测试形式中，将结合了结合剂的膜的一端浸入含有样品的溶液中。该样品沿该膜迁移通过含有第二结合剂的区域并到达含有固定化结合剂的区域。在含有固定化结合剂的区域中第二结合剂的浓缩指示了癌症的存在。典型地，在该位置第二结合剂的浓缩产生能够通过肉眼观察的图形，例如线。无该图形，则指示阴性结果。一般地，对固定在该膜上的结合剂的量进行选择，以便当生物样品含有的多肽水平足以在该以上讨论形式的双抗体三明治测定中产生阳性信号时，可以产生肉眼可识别的图形。用于这些测定的优选结合剂是抗体和其抗原结合片段。优选地，固定在该膜上的抗体量在约 25ng - 约 1 μ g 之间，更优选在约 50ng - 约 500ng 之间。典型地用极少量的生物样品即能够进行这些测试。

当然，存在着适用于本发明肿瘤蛋白质或结合剂的许多其它测试方法。以上的描述仅旨在作为范例。例如，本领域的普通技术人员将明了，可以容易地对以上操作步骤进行修改，以采用肺肿瘤多肽检测生物样品中与这些多肽结合的抗体。这些抗体特异性肺肿瘤蛋白质的检测结果可以和癌症的存在相关联。

还可以，或者作为替代方案可以，基于生物样品中特异地与肺肿瘤蛋白质反应的 T 细胞的存在，检测癌症。在某些方法中，将分离自患者的含有 CD4⁺ 和/或 CD8⁺ T 细胞的生物样品与肺肿瘤多肽、编码该多肽的多核苷酸和/或表达该多肽的至少免疫原性部分的 APC 一起孵育，然后检测该 T 细胞是否被特异激活。适合的生物样品包括，但不限于，分离的 T 细胞。例如，可以根据常规技术（例如通过 Ficoll/Hypaque 密度梯度离心外周血淋巴细胞），从患者分离 T 细胞。可以将 T 细胞和多肽（例如 5-25 μ g/ml）在体外于 37 $^{\circ}$ C 一起孵育 2-9 天（典型的是 4 天）。可能期望在无肺肿瘤多肽的情况下孵育另一份 T 细胞样品以用作对照。对于 CD4⁺ T 细胞，优选通过评价该 T 细胞的增殖来检测激活。对于 CD8⁺ T 细胞，优选通过评价细胞裂解活性来检测激活。与未患病患者相比，高至少 2 倍

的增殖水平和/或高至少 20% 的细胞裂解活性指示患者患有癌症。

正如以上指出的，还可以，或者作为替代方案可以，基于生物样品中编码肺肿瘤蛋白质的 mRNA 的水平检测癌症。例如，可以在基于聚合酶链式反应的测定中采用至少两个寡核苷酸引物扩增来源于生物样品的肺肿瘤 cDNA 的部分，其中该寡核苷酸引物中的至少一个对编码该肺肿瘤蛋白质的多核苷酸是特异的（即可以与之杂交）。然后采用本领域熟知的技术，例如凝胶电泳，分离并检测该扩增的 cDNA。相似地，可以在杂交测定中采用特异与编码肺肿瘤蛋白质的多核苷酸杂交的寡核苷酸探针，检测生物样品中是否存在编码该肿瘤蛋白质的多核苷酸。

为了保证在测定条件下发生杂交，寡核苷酸引物和探针应含有与编码肺肿瘤蛋白质的多核苷酸的一部分有至少约 60%、优选至少约 75%、最优选至少 90% 一致性的寡核苷酸序列，其中该多核苷酸部分长至少 10 个核苷酸、优选至少 20 个核苷酸。优选地，寡核苷酸引物和/或探针将在本文所定义的中等严谨条件下与编码本文所公开多肽的多核苷酸杂交。可以用于本文所述诊断方法中的寡核苷酸引物和/或探针优选长至少 10-40 个核苷酸。在一个优选的实施方案中，该寡核苷酸引物含有如下 DNA 分子中的至少 10 个连续核苷酸、更优选至少 15 个核苷酸，该 DNA 分子具有 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 和 349 中所示序列。用于基于 PCR 的测定方法和杂交分析的技术是本领域熟知的（见例如 Mullis 等, Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich 编, PCR 技术 (PCR Technology), Stockton Press, NY, 1989）。

一个优选的测定法采用了 RT-PCR，其中 PCR 联合逆转录一起使用。典型地，从生物样品，例如活检组织中提取 RNA，然后将之逆转录以制备 cDNA 分子。采用至少一个特异引物进行 PCR 扩增以产生 cDNA 分子，该 cDNA 分子可以通过例如凝胶电泳进行分离和观察。可以对取自测试患者的样品和取自未患癌症的个体的样品进行扩增。该扩增反应可以在横跨两个数量级的几种 cDNA 稀释液中进行。典型地，该测试患者样品的几种稀释

液与具有同样稀释度的非癌性样品相比在表达上的两倍或更高倍的增加被认为是阳性。

在另一个实施方案中，本公开的组合物可以用作癌症进展趋势的标志。在该实施方案中，可以在不同时间进行以上所述的用于癌症诊断的测定，并评价反应性多肽或多核苷酸水平的改变。例如，可以在6个月-1年的期间内每隔24-72小时进行一次该测定，之后按需要进行。一般地，如果患者体内所检测到的多肽或多核苷酸水平随时间的过去而增加，则该患者体内的癌症处于发展状态。相反，如果反应性多肽或多核苷酸的水平保持不变或随时间的过去而减少，则该癌症并非处于发展状态。

某些体内诊断分析方法可以直接在肿瘤上进行。一个这样的分析方法涉及用结合剂接触肿瘤细胞。然后通过报道基团直接或间接地检测该结合的结合剂。这些结合剂也可以用于组织学用途中。或者，可以在这些应用中采用多核苷酸探针。

正如以上指出的，为了提高灵敏度，可以在一个指定的样品中测定多个肺肿瘤蛋白质标志。应明了，对本文所提供的不同蛋白质具有特异性的结合剂可以联合用于一个测定试验中。而且，可以同时使用多个引物或探针。肿瘤蛋白质标志可以基于常规实验来选择，以确定导致最佳灵敏度的组合。此外，或者作为可替代方案，可以将用于测定本文所提供的肿瘤蛋白质的方法和用于测定其它已知肿瘤抗原的方法结合起来。

诊断试剂盒

本发明还提供用于任一种以上诊断方法的试剂盒。这些试剂盒典型地含有进行诊断测定所必需的两种或多种成分。这些成分可以是化合物、试剂、容器和/或设备。例如，试剂盒中的一个容器可含有特异与肺肿瘤蛋白质结合的单克隆抗体或其片段。可以将这些抗体或片段附着在以上所述的固体材料上一起提供。其它的一个或多个容器可以包括用于该测定的成分，例如试剂或缓冲液。这些试剂盒可以还，或者作为替代方案可以，包括上述含有适于直接或间接检测抗体结合的报道基团的检测试

剂。

或者，可以将试剂盒设计为用于检测生物样品中编码肺肿瘤蛋白质的 mRNA 的量。这些试剂盒一般含有至少一个上述与编码肺肿瘤蛋白质的多核苷酸杂交的寡核苷酸探针或引物。例如，可以将该寡核苷酸用于 PCR 或杂交分析。该试剂盒中可以存在的其它成分包括便于检测编码肺肿瘤蛋白质的多核苷酸的第二寡核苷酸和/或诊断试剂或容器。

提供以下实施例作为举例说明，而非进行限制。

实施例 1

分离和表征编码肺肿瘤多肽的 cDNA 序列

本实施例描述了从肺肿瘤 cDNA 文库中分离编码肺肿瘤特异性多肽的 cDNA 分子。

A. 从肺鳞状细胞癌文库分离 cDNA 序列

采用 Superscript 用于 cDNA 合成的质粒系统和质粒克隆试剂盒 (BRL Life Technologies, Gaithersburg, MD 20897)，根据厂家说明书，从来自两名患者组织库的 poly A⁺ RNA 构建人肺鳞状细胞癌 cDNA 表达文库。具体地，用 polytron (Kinematica, 瑞士) 匀浆肺癌组织，然后采用 Trizol 试剂 (BRL Life Technologies) 按厂家指导提取总 RNA。然后采用寡脱氧胸苷酸纤维素，按 Sambrook 等 (分子克隆：实验室手册 (Molecular Cloning: A Laboratory Manual), Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989) 所述的方法，纯化该 poly A⁺ RNA。采用 NotI/Oligo-dT18 引物合成第一链 cDNA。合成双链 cDNA，将其与 BstXI/EcoRI 连接子 (Invitrogen, Carlsbad, CA) 连接，然后用 NotI 消化。在用 cDNA 大小分级分离柱 (BRL Life Technologies) 进行大小分级分离后，将该 cDNA 连接到 pCDNA3.1 (Invitrogen) 的 BstXI/NotI 位点中，并通过电穿孔转化 ElectroMax 大肠杆菌 DH10B 细胞 (BRL Life Technologies)。

采用同样的程序，从含有 4 个组织标本的库中制备正常的人肺 cDNA 表达文库。通过确定独立菌落的数量、带有插入片段的克隆的百分数、

插入片段的平均大小, 并通过序列分析, 对这些 cDNA 文库进行表征。该肺鳞状细胞癌文库含有 2.7×10^6 个独立菌落、100% 的克隆含有插入片段而且插入片段的平均大小为 2100 个碱基对。该正常肺 cDNA 文库含有 1.4×10^6 个独立菌落、90% 的克隆含有插入片段而且插入片段的平均大小为 1800 个碱基对。对于这两个文库, 序列分析显示, 大多数克隆含有从 mRNA 合成的全长 cDNA 序列。

采用以上肺鳞状细胞癌和正常肺 cDNA 文库, 按稍作修饰的 Hara 等所述的方法 (血液 (Blood), 84:189-199, 1994), 进行 cDNA 文库扣除。具体地, 按下述制备肺鳞状细胞癌特异性扣除 cDNA 文库。用 BamHI 和 XhoI 消化正常组织 cDNA 文库 ($80 \mu\text{g}$), 之后用 DNA 聚合酶 Klenow 片段进行补平反应。酚-氯仿抽提和乙醇沉淀后, 将该 DNA 溶解在 $133 \mu\text{l}$ H_2O 中, 热变性后与 $133 \mu\text{l}$ ($133 \mu\text{g}$) 光探测生物素 (Photoprobe biotin) (Vector Laboratories, Burlingame, CA) 混合。按厂家推荐方法, 用 270W 的太阳灯照射置于冰上的所获混合物 20 分钟。再加入 $67 \mu\text{l}$ 光探测生物素, 并重复该生物素化反应。用丁醇抽提 5 次后, 乙醇沉淀该 DNA, 并将其溶解在 $23 \mu\text{l}$ H_2O 中形成驱动 DNA (driver DNA)。

为了形成示踪 DNA (tracer DNA), 用 NotI 和 SpeI 消化 $10 \mu\text{g}$ 肺鳞状细胞癌 cDNA 文库, 酚氯仿抽提后通过 Chroma spin-400 柱 (Clontech, Palo Alto, CA)。典型地, 在经过大小选择柱后回收 $5 \mu\text{g}$ cDNA。乙醇沉淀后, 将该示踪 DNA 溶解在 $5 \mu\text{l}$ H_2O 中。将示踪 DNA 与 $15 \mu\text{l}$ 驱动 DNA 和 $20 \mu\text{l}$ $2 \times$ 杂交缓冲液 (1.5M NaCl/ 10mM EDTA/ 50mM HEPES pH7.5/ 0.2% 十二烷基硫酸钠) 混合, 用矿物油覆盖, 然后进行完全热变性。将该样品立即转移到 68°C 的水浴中, 并孵育 20 个小时 (长杂交 [LH])。然后用链霉亲和素处理该反应混合物, 之后进行酚/氯仿抽提。再重复该过程 3 次。沉淀扣除 DNA, 将其溶解在 $12 \mu\text{l}$ H_2O 中, 与 $8 \mu\text{l}$ 驱动 DNA 和 $20 \mu\text{l}$ $2 \times$ 杂交缓冲液混合, 然后 68°C 杂交 2 小时 (短杂交 [SH])。除去生物素化的双链 DNA 后, 将扣除 DNA 连接至氯霉素抗性 pBCSK+ (Stratagene, La Jolla, CA) 的 NotI/SpeI 位点中, 然后通过电穿孔转化 ElectroMax 大肠杆菌 DH10B 细胞, 产生肺鳞状细胞癌特异性扣除 cDNA 文库 (文后称作“肺

扣除文库 I”)。

除了将来自于肺扣除文库 I 的 8 个频繁多次回收的基因包括在该驱动 DNA 中外, 以类似于该肺扣除文库 I 的方式, 构建第二个肺鳞状细胞癌特异性扣除 cDNA 文库 (称作“肺扣除文库 II”), 并回收了 24,000 个独立的克隆。

为了分析这些扣除 cDNA 文库, 从这些扣除肺鳞状细胞癌特异性文库中随机挑取 320 个独立克隆, 制备质粒 DNA。在 Perkin Elmer/Applied Biosystems Division 373A 型和/或 377 型自动测序仪 (Foster City, CA) 上, 通过 DNA 测序对代表性 cDNA 克隆进行分析。在 SEQ ID NO: 1-60 中提供了分离的 60 个克隆的 cDNA 序列。采用 EMBL 和 GenBank 数据库 (Release 96) 将这些 cDNA 序列与基因库中的已知序列进行比较。对于 SEQ ID NO: 2、3、19、38 和 46 中所提供的序列, 没有发现显著同源性。发现 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 和 57-59 的序列表现出与以前鉴定的已表达序列标志 (EST) 有某种同源性。发现 SEQ ID NO: 9、28、31 和 33 的序列表现出与以前鉴定的非人类基因序列有某种同源性, 而发现 SEQ ID NO: 4、5、14、50、53、56 和 60 的序列表现出与以前在人类中鉴定的基因序列有某种同源性。

采用以上肺鳞状细胞癌 cDNA 文库作为该示踪 DNA, 而以上正常肺组织 cDNA 文库和来自正常肝和心脏的 cDNA 文库 (从由以上所述每种组织的一个样品组成的库进行构建的), 加上在肺扣除文库 I 和 II 中频繁多次回收的 20 个其它 cDNA 克隆, 作为该驱动 DNA, 重复上述扣除步骤 (肺扣除文库 III)。该正常肝和心脏 cDNA 文库含有 1.76×10^6 个独立菌落, 100% 的克隆含有插入片段而且插入片段的平均大小为 1600 个碱基对。又分离了 10 个克隆 (SEQ ID NO: 61-70)。按以上所述, 将这些 cDNA 序列与基因库中的序列进行比较, 显示 SEQ ID NO: 62 和 67 中提供的序列没有显著同源性。发现 SEQ ID NO: 61、63-66、68 和 69 的序列表现出与以前分离的 EST 有某种同源性, 而发现 SEQ ID NO: 70 中提供的序列表现出与一个以前鉴定的大鼠基因有某种同源性。

在进一步的研究中, 采用以上肺鳞状细胞癌 cDNA 文库作为该示踪 DNA, 而来自正常肺、肾、结肠、胰脏、脑、静息 PBMC、心脏、皮肤和食道组成的库的 cDNA 文库作为该驱动 DNA, 其中食道 cDNA 占该驱动材料的三分之一, 重复上述扣除步骤。由于食道富含正常上皮细胞, 包括分化的鳞状细胞, 该方法很可能富集肿瘤特异性而非组织特异性基因。在该扣除方法中确定的 48 个克隆的 cDNA 序列见 SEQ ID NO: 177-224。SEQ ID NO: 177、178、180、181、183、187、192、195-197、208、211、212、215、216、218 和 219 的序列表现出与以前鉴定的基因有某种同源性。SEQ ID NO: 179、182、184-186、188-191、193、194、198-207、209、210、213、214、217、220 和 224 的序列表现出与以前确定的 EST 有某种同源性。SEQ ID NO: 221-223 的序列表现出与任何以前确定的序列均无同源性。

B. 从肺腺癌文库分离 cDNA 序列

按以上所述方法构建人肺腺癌 cDNA 表达文库。该文库含有 3.2×10^6 个独立菌落, 100% 的克隆含有插入片段而且插入片段的平均大小为 1500 个碱基对。采用上述正常肺和正常肝和心脏 cDNA 表达文库作为驱动 DNA, 按上述方法进行文库扣除杂交。回收 2600 个独立克隆。

最初对 100 个独立克隆的 cDNA 序列分析显示有许多核糖体蛋白质基因。在此扣除杂交中分离的 15 个克隆的 cDNA 序列见 SEQ ID NO: 71-86。按上述进行这些序列与基因库中序列的比较, 显示与 SEQ ID NO: 84 中提供的序列没有显著同源性。发现 SEQ ID NO: 71、73、74、77、78 和 80-82 的序列表现出与以前分离的 EST 有某种同源性, 而发现 SEQ ID NO: 72、75、76、79、83 和 85 的序列表现出与以前鉴定的人类基因有某种同源性。

在进一步的研究中, 从转移性肺腺癌构建 cDNA 文库 (称作 mets3616A)。随机选自该文库的 25 个克隆的确定 cDNA 序列见 SEQ ID NO: 255-279。从该 mets3616 cDNA 文库中扣除制备自正常肺、肝、胰脏、皮肤、肾、脑和静息 PBMC 的库的 cDNA 文库。为了增加该扣除法的特异性,

在该驱动动物中掺入已被确定在该 mets3616A cDNA 文库中最丰富的基因例如 EF1- α 、整联蛋白 β 和抗凝蛋白 PP4, 以及以前发现的在扣除肺腺癌 cDNA 文库中差异表达的 cDNA. 从该扣除文库 (称作 mets3616A-S1) 分离的 51 个克隆的测定 cDNA 序列见 SEQ ID NO: 280-330.

在 SEQ ID NO: 255-330 的序列与公共数据库中的序列之间进行比较, 显示与 SEQ ID NO: 255-258、260、262-264、270、272、275、276、279、281、287、291、296、300 和 310 的序列没有显著同源性. SEQ ID NO: 259、261、265-269、271、273、274、277、278、282-285、288-290、292、294、297-299、301、303-309、313、314、316、320-324 和 326-330 的序列表现出与以前鉴定的基因序列有某种同源性, 而 SEQ ID NO: 280、286、293、302、310、312、315、317-319 和 325 的序列表现出与以前分离的已表达序列标志 (ETS) 有某种同源性.

实施例 2

确定肺肿瘤多肽的组织特异性

采用基因特异性引物, 通过 RT-PCR 测定实施例 1 所述的 7 种代表性肺肿瘤多肽在多种正常和肿瘤组织中的 mRNA 表达水平.

简而言之, 采用 Trizol 试剂按以上所述从多种正常和肿瘤组织中提取总 RNA. 采用 2 μ g 总 RNA 和 SuperScript II 逆转录酶 (BRL Life Technologies) 于 42°C 孵育 1 个小时, 合成第一链 cDNA. 然后采用基因特异性引物通过 PCR 扩增该 cDNA. 为了确保该 RT-PCR 的半定量性质, 采用 β -肌动蛋白作为每一个检测组织的内对照. 采用 1 μ l 1:30 的 cDNA 稀释液以使该 β -肌动蛋白模板在线性范围内扩增, 而且此 cDNA 量也具有足够的灵敏度以反映在该最初拷贝数中存在的差异. 在这些条件下, 测定来自每个组织的逆转录反应中该 β 肌动蛋白的水平. 通过 DNase 处理, 并通过保证在采用制备的第一链 cDNA 而不加入逆转录酶时为阴性 PCR 结果, 最小化 DNA 污染.

在 5 种不同类型的肿瘤组织 (来自 3 名患者的肺鳞状细胞癌、肺腺癌、来自 2 名患者的结肠癌、乳腺肿瘤和前列腺肿瘤), 和 13 种不同的

正常组织（来自 4 名供体的肺、前列腺、脑、肾、肝、卵巢、骨骼肌、皮肤、小肠、胃、心肌、视网膜和睾丸）中，检测 mRNA 的表达水平。采用 10 倍量的 cDNA，发现抗原 LST-S1-90 (SEQ ID NO: 3) 在肺鳞状细胞癌和乳腺肿瘤中以高水平表达，而在检测的其它组织中表达水平低或检测不到。

抗原 LST-S2-68 (SEQ ID NO: 15) 似乎是肺和乳腺肿瘤特异的，然而，在正常肾中也检测到其表达。抗原 LST-S1-169 (SEQ ID NO: 6) 和 LST-S1-133 (SEQ ID NO: 5) 似乎在肺组织（正常和肿瘤组织）中极为丰富，在大多数检测的正常组织中这两个基因的表达降低。LST-S1-169 和 LST-S1-133 也在乳腺和结肠肿瘤中表达。抗原 LST-S1-6 (SEQ ID NO: 7) 和 LST-S2-I2-5F (SEQ ID NO: 47) 没有表现出肿瘤或组织特异性表达，LST-S1-28 的表达稀少仅可在少数几种组织中检测到。抗原 LST-S3-7 (SEQ ID NO: 63) 表现出肺和乳腺肿瘤特异性表达，当 PCR 进行 30 个循环后仅在正常睾丸中检测到其信息。当将该循环数增至 35 时在一些正常组织中检测到较低水平的表达。发现抗原 LST-S3-13 (SEQ ID NO: 66) 在 4 个肺肿瘤中的 3 个、一个乳腺肿瘤和两个结肠肿瘤样品中表达。与在肿瘤中相比，其在正常组织中的表达较低，仅在 4 个正常肺组织的一个中和肾、卵巢和视网膜的正常组织中检测到。抗原 LST-S3-4 (SEQ ID NO: 62) 和 LST-S3-14 (SEQ ID NO: 67) 的表达稀少而且未显示出任何组织或肿瘤特异性。与 Northern 印迹分析相一致，抗原 LAT-S1-A-10A (SEQ ID NO: 78) 的 RT-PCR 结果提示，其在包括肺和结肠肿瘤在内的肺、结肠、胃和小肠组织中高表达，而在其它组织中其表达量低或无法检测到。

对上述在肺扣除文库 I、II 和 III 中分离的总共 2002 个 cDNA 片段进行菌落 PCR 扩增，并采用微阵列技术 (Synteni, Palo Alto, CA) 在肺肿瘤、正常肺、和各种其它正常和肿瘤组织中检测了它们的 mRNA 表达水平。简而言之，将这些 PCR 扩增产物以阵列格式点在载玻片上，在该阵列中每个产物占据独一个位置。从待测试的组织样品中提取 mRNA，逆转录、然后制备荧光标记的 cDNA 探针。用这些标记的 cDNA 探针探测这些微阵列，扫描载玻片并测量荧光强度。该强度与杂交强度相关。17 个非

冗余 cDNA 克隆在肺鳞状细胞癌中表现出超量表达, 在测试的正常组织 (肺、皮肤、淋巴结、结肠、肝、胰脏、乳腺、心脏、骨髓、大肠、肾、胃、脑、小肠、膀胱和唾液腺) 中的表达或检测不到, 或低于肺鳞状肿瘤 10 倍。克隆 L513S 的部分测定 cDNA 序列见 SEQ ID NO: 87 和 88; L514S 的见 SEQ ID NO: 89 和 90; L516S 的见 SEQ ID NO: 91 和 92; L517S 的见 SEQ ID NO: 93; L519S 的见 SEQ ID NO: 94; L520S 的见 SEQ ID NO: 95 和 96; L521S 的见 SEQ ID NO: 97 和 98; L522S 的见 SEQ ID NO: 99; L523S 的见 SEQ ID NO: 100; L524S 的见 SEQ ID NO: 101; L525S 的见 SEQ ID NO: 102; L526S 的见 SEQ ID NO: 103; L527S 的见 SEQ ID NO: 104; L528S 的见 SEQ ID NO: 105; L529S 的见 SEQ ID NO: 106; 和 L530S 的见 SEQ ID NO: 107 和 108。此外, SEQ ID NO: 151 中提供了 L530S 的全长 cDNA 序列, SEQ ID NO: 152 中提供了相应的推测氨基酸序列。L530S 表现出与 p53 肿瘤抑制基因的拼接变体 p63 同源。SEQ ID NO: 331-337 中提供了 7 种已知的 p63 同种型的 cDNA 序列, 而 SEQ ID NO: 338-344 中分别提供了相应的推测氨基酸序列。

由于多态性, 克隆 L531S 表现出有两种形式。测定的 L531S 的第一种全长 cDNA 序列见 SEQ ID NO: 109, 其相应的推测氨基酸序列见 SEQ ID NO: 110。测定的 L531S 的第二种全长 cDNA 序列见 SEQ ID NO: 111, 其相应的推测氨基酸序列见 SEQ ID NO: 112。除了 SEQ ID NO: 111 的序列含有一个 27bp 的插入片段外, 其与 SEQ ID NO: 109 的序列一致。类似地, L514S 也有两种不同的拼接形式; 第一种变体 cDNA 见 SEQ ID NO: 153, 其相应的氨基酸序列见 SEQ ID NO: 155。L514S 第二种变体形式的全长 cDNA 见 SEQ ID NO: 154, 其相应的氨基酸序列见 SEQ ID NO: 156。L524S (SEQ ID NO: 101) 的全长克隆产生两种变体 (SEQ ID NO: 163 和 164), 它们的相应推测氨基酸序列分别是 SEQ ID NO: 165 和 166。两种变体均表现出编码甲状旁腺激素相关肽。

分离 L519S 的全长 cDNA 的尝试导致分离获得 SEQ ID NO: 173 中提供的扩延 cDNA 序列, 其含有一个潜在的开放阅读框。SEQ ID NO: 174 中提供了 SEQ ID NO: 173 的推测的编码氨基酸序列。此外, SEQ ID NO: 100

的克隆（称作 L523S）的全长 cDNA 序列是一个已知的基因，见 SEQ ID NO: 175，而其相应的推测氨基酸见 SEQ ID NO: 176。在进一步的研究中，通过 PCR 扩增，采用从 SEQ ID NO: 175 的序列设计的基因特异性引物，从 L523S 阳性肿瘤 cDNA 文库中分离了 L523S 的全长 cDNA 序列。该测定的 cDNA 序列见 SEQ ID NO: **。该序列编码的氨基酸序列见 SEQ ID NO: **。该蛋白质与以前公开的蛋白质序列在两个氨基酸位置上，即第 158 和 410 位，不同。

按以上所述，将 L514S 和 L531S 的序列（分别是 SEQ ID NO: 87 和 88、89 和 90、及 109）与基因库中的序列进行比较，显示其与已知序列没有显著同源性。发现 L531S、L516S、L517S、L519S、L520S 和 L530S 的序列（分别是 SEQ ID NO: 87 和 88、91 和 92、93、94、95 和 96、107 和 108）表现出与以前鉴定的 EST 有某种同源性。发现 L521S、L522S、L523S、L524S、L525S、L526S、L527S、L528S 和 L529S（分别是 SEQ ID NO: 97 和 98、99、99、101、102、103、104、105、和 106）是已知基因。测定的 L520S 的全长 cDNA 序列见 SEQ ID NO: 113，其相应的推测氨基酸序列见 SEQ ID NO: 114。随后的微阵列分析显示，L520 除了在肺鳞状肿瘤中外还在乳腺肿瘤中超量表达。

进一步的分析说明，L529S (SEQ ID NO: 106 和 115)、L525S (SEQ ID NO: 102 和 120) 和 L527S (SEQ ID NO: 104) 是细胞骨架成分，并且潜在地是鳞状细胞特异性蛋白质，L529S 是连接蛋白 26，一种间隙连接蛋白质。其在肺鳞状肿瘤 9688T 中高表达，在其它两个鳞状肿瘤中适当地过量表达。然而，在正常皮肤、结肠、肝和胃中也可检测到连接蛋白 26 的较低水平表达。连接蛋白 26 在某些乳腺肿瘤中的过量表达已有报道，而且 L529S 的突变形式可以导致其在肺肿瘤中的过量表达。L525S 是 plakophilin 1，一种在皮肤的带斑粘着连接中发现的细胞桥粒蛋白质。L525S mRNA 的表达水平在测试的 4 个肺鳞状肿瘤中的 3 个和正常皮肤中有很大的提高。L527S 已被鉴定为角蛋白 6 的同种型，II 型 58Kd 角蛋白，和细胞角蛋白 13，并显示出在鳞状肿瘤中超量表达，而在正常皮肤、乳腺和结肠组织中低表达。值得注意的是，已有大量文献证明角蛋白和角

蛋白相关基因是肺癌包括 CYFRA2.1 的潜在标志 (Pastor, A. 等, Eur. Respir. J., 10: 603-609, 1997)。L513S (SEQ ID NO: 87 和 88) 在测试的几种肿瘤组织中表现出中等程度的超量表达, 其编码一个最初作为寻常性天疱疮抗原分离的蛋白质。

L520S (SEQ ID NO: 95 和 96) 和 L521S (SEQ ID NO: 97 和 98) 在肺鳞状肿瘤中高表达, 而且 L520S 在正常唾液腺中上调, 而 L521S 在正常皮肤中超量表达。两者均属于富含脯氨酸的小蛋白质家族, 并是完全分化的鳞状细胞的标志。L521S 被描述为肺鳞状肿瘤的特异标志 (Hu, R. 等, 肺癌 (Lung Cancr), 20:25-30, 1998)。L515S (SEQ ID NO: 162) 编码 IGF- β 2, 而 L516S 是醛糖还原酶的同系物, 两者均在肺鳞状肿瘤和正常结肠中以中等水平表达。值得注意的是, L516S (SEQ ID NO: 91 和 92) 在转移的肿瘤中而非原发性肺腺癌中表达上调, 这说明其在癌转移中的潜在作用, 是一个潜在的预示标志。L522S (SEQ ID NO: 99) 在肺鳞状肿瘤中以中等水平表达, 而在正常组织中表达最少。L522S 表现出属于 IV 型醇脱氢酶, 即 ADH7, 而且其表达分布情况提示其是一个鳞状细胞特异性抗原。L523S (SEQ ID NO: 100) 在肺鳞状肿瘤、人胰腺癌细胞系和胰腺癌组织中以中等程度超量表达, 这提示该基因可能是胰腺和肺鳞状细胞癌所共有的抗原。

L524S (SEQ ID NO: 101) 在测试的大多数鳞状肿瘤中超量表达, 并与甲状旁腺激素相关肽 (PTHrP) 同源, 已十分清楚地知道其引起与恶性肿瘤例如白血病、前列腺和乳腺癌相关的体液高血钙。据信 PTHrP 还与肺鳞状癌极为相关, 而与肺腺癌极少相关 (Davidson, L. A. 等, J. Pathol., 178: 398-401, 1996)。L528S (SEQ ID NO: 105) 在两个肺鳞状肿瘤中高度超量表达, 而在另两个鳞状肿瘤、一个肺腺癌和一些正常组织, 包括皮肤、淋巴结、心脏、胃和肺中适度表达。它编码与黑素细胞特异性基因 Pmel17 的前体相似的 NMB 基因, 据报道该基因优选在潜在的低转移性黑素瘤细胞系中表达。这提示, L528S 可能是黑素瘤和肺鳞状细胞癌中共有的抗原。L526S (SEQ ID NO: 103) 在测试的所有鳞状细胞肿瘤组织中均超量表达, 而且表现出与基因 (ATM) 有同源性, 该基因中的一个突变

导致共济失调毛细血管扩张该疾病是一种人类遗传疾病，除了其它症状外还导致易于引发癌症的倾向。ATM 编码的蛋白质通过对 p53 分子的直接结合和磷酸化，激活 p53 介导的细胞周期关卡。大约 40% 的肺癌与 p53 突变有关，而且推测 ATM 的超量表达是补偿 p53 功能丧失造成的结果，但不知道该超量表达是肺鳞状细胞癌的原因还是结果。此外，在转移性而非肺腺癌中也检测到 L525S (ATM) 的表达，这提示其在癌转移中起作用。

按以上所述通过实时 RT-PCR 还检测了 L523S (SEQ ID NO: 175) 的表达。在采用一系列肺鳞状肿瘤进行的第一项研究中，发现 L523S 在 4/7 肺鳞状肿瘤、2/3 头部和颈部鳞状肿瘤，及 2/2 肺腺癌中表达，而在骨骼肌、软腭和扁桃体中低水平表达。在采用肺腺癌系列进行的第二项研究中，在 4/9 原发性腺癌、2/2 肺胸腔积液、1/1 转移性肺腺癌和 2/2 肺鳞状肿瘤中观察到 L523S 的表达，而在正常组织中几乎没有观察到其表达。

L523S 在肺肿瘤和各种正常组织中的表达还采用标准技术通过 Northern 印迹分析进行了检查。在第一项研究中，发现 L523S 在许多肺腺癌和鳞状细胞癌，以及正常扁桃体中表达。在正常肺中没有观察到表达。在采用来自 Clontech 的正常组织印迹进行的第二项研究中，发现尽管 L523S 在胎盘中有强表达，但在脑、骨骼肌、结肠、胸腺、脾脏、肾、肝、小肠、肺或 PBMC 中没有观察到表达。

实施例 3

通过基于 PCR 的扣除方法分离和表征肺肿瘤多肽

从如下 cDNA 扣除文库中获得 857 个克隆，该扣除文库 (Clontech, Palo Alto, CA) 含有已扣除了来自包括肺、PBMC、脑、心脏、肾、肝、胰脏和皮肤在内的 8 种正常人组织 cDNA 的两个人肺鳞状肿瘤库的 cDNA，将这些克隆用于第一轮 PCR 扩增。按照该厂家说明书，将该文库进行第二轮 PCR 扩增。将所获 cDNA 片段亚克隆至载体 P7 - Adv 载体 (Clontech, Palo Alto, CA) 中，并转化大肠杆菌 DH5 α (Gibco, BRL)。从独立的克隆中分离 DNA，并采用 Perkin Elmer /Applied Biosystems Division 373

型自动测序仪进行测序。

对 162 个阳性克隆进行了测序。按上述方法，将这些克隆的 DNA 序列与 EMBL 和 GenBank 数据库中的序列进行比较，显示其中的 13 个克隆，下文称作重叠群 13、16、17、19、22、24、29、47、49、56-59，没有显著同源序列。测定的这些克隆的 cDNA 序列分别提供在 SEQ ID NO: 125、127-129、131-133、142、144、148-150、和 157 中。发现重叠群 1、3-5、7-10、12、11、15、20、31、33、38、39、41、43、44、45、48、50、53、54（分别是 SEQ ID NO: 115-124、126、130、134-141、143、145-147）表现出与以前鉴定的 DNA 序列有某种程度的同源性。发现重叠群 57 (SEQ ID NO: 149) 是 1998 年 7 月 27 日提交的美国专利申请 09/123,912 中所公开的克隆 L519S (SEQ ID NO: 94)。就本发明者所知，以前从未报道过这些序列在肺肿瘤中有差异超量表达。

按上述方法通过 RT-PCR 确定在肺肿瘤组织、正常肺组织 (n=4)、静息 PBMC、唾液腺、心脏、胃、淋巴结、骨骼肌、软腭、小肠、大肠、支气管、膀胱、扁桃体、肾、食道、骨髓、结肠、肾上腺、胰脏和皮肤（所有组织均来自人类）中代表性克隆的 mRNA 表达水平。除非另行指出否则在每一类组织的一个样品中，按以上所述，采用微阵列技术检查表达水平。

发现重叠群 3 (SEQ ID NO: 116) 在测试的所有头部和颈部鳞状细胞肿瘤 (17/17) 中均以高水平表达，在大多数 (8/12) 肺鳞状肿瘤中有表达，(7/12 高表达，2/12 中等水平表达，2/12 低表达)，而在 2/4 正常肺组织中表现出表达阴性，且在剩余的两个样品中表现出低表达。重叠群 3 在皮肤和软腭中表现出以中等水平表达，而在静息 PBMC、大肠、唾液腺、扁桃体、胰脏、食道和结肠中表达水平较低。发现重叠群 11 (SEQ ID NO: 124) 在测试所有头部和颈部鳞状细胞肿瘤 (17/17) 中均有表达：14/17 高表达，3/17 中等水平表达。此外，肺鳞状肿瘤中也表现出有 3/12 高水平表达，4/12 中等水平表达。对于 3/4 的正常肺样品，重叠群 11 是阴性的，而剩余样品仅有低表达。重叠群 11 对唾液腺、软腭、膀胱、扁桃体、皮肤、食道和大肠表现出低至中等的反应性。在测试的所有头部和颈部鳞

状细胞肿瘤(17/17)中发现重叠群 13 (SEQ ID NO:125) 的表达: 12/17 高表达, 5/17 中等水平表达。重叠群 13 在 7/12 的肺鳞状肿瘤中表达, 其中 4/12 高表达而 3 个样品中有中等水平的表达。对正常肺样品的分析显示 2/4 的为表达阴性, 而剩余的两个样品中有低至中等水平的表达。重叠群 13 确实表现出对静息 PBMC、唾液腺、膀胱、胰腺、扁桃体、皮肤、食道和大肠有低至中等的反应性, 而且在软腭中有高表达。发现重叠群 16 (SEQ ID NO: 127) 在一些头部和颈部鳞状细胞肿瘤(6/17)和一个肺鳞状肿瘤中有中等水平的表达; 而在测试的所有正常肺样品中均未表现出有任何表达。重叠群 16 确实表现出对静息 PBMC、大肠、皮肤、唾液腺和软腭有低的反应性。重叠群 17 (SEQ ID NO: 128) 表现出在测试的所有头部和颈部鳞状细胞肿瘤(17/17)中均表达: 5/17 的为高表达, 12/17 的为中等水平表达。在肺鳞状肿瘤中的表达水平显示, 一个肿瘤样品有高水平表达, 而 3/12 的为中等水平表达。重叠群 17 对于 2/4 正常肺样品是阴性的, 在剩余的样品中仅有低水平表达。此外, 还在食道和软腭中发现低水平的表达。发现重叠群 19 (SEQ ID NO: 129) 在测试的大多数头部和颈部鳞状细胞肿瘤(11/17)中都有表达: 其中两个样品有高水平的表达, 6/17 的表现出中等水平的表达, 而在 3/17 的样品中发现低水平的表达。在肺鳞状肿瘤中的测试仅显示出在 3/12 的样品中有中等水平的表达。在 2/4 正常肺样品中表达水平为阴性, 其它两个样品仅有低表达。重叠群 19 在食道、静息 PBMC、唾液腺、膀胱、软腭和胰腺中表现出低的表达水平。

重叠群 22 (SEQ ID NO: 131) 表现出在测试的大多数头部和颈部鳞状细胞肿瘤(13/17)中存在表达, 这些样品中的 4 个有高水平的表达, 6/17 的有中等水平的表达, 而在 3/17 的样品中有低水平表达。在测试的 3/12 肺鳞状肿瘤组织中发现有中等至高的表达水平, 在两个正常肺样品中为表达阴性而在其它两个样品中有低水平表达(n=4)。重叠群 22 在皮肤、唾液腺和软腭中表现出低水平的表达。相似地, 在测试的大多数头部和颈部鳞状细胞肿瘤(13/17)中发现有重叠群 24 (SEQ ID NO: 132) 的表达, 其中 3 个样品为高表达, 在 6/17 的样品中为中等水平表达, 而在 4/17

的样品中为低水平表达。在测试的 3/12 肺鳞状肿瘤组织中发现有中等至高的表达水平，在 3 个正常肺样品中表达为阴性而在一个样品中有低水平的表达 (n=4)。重叠群 24 在皮肤、唾液腺和软腭中表现出低水平的表达。重叠群 29 (SEQ ID NO: 133) 在测试的几乎所有头部和颈部鳞状细胞肿瘤 (16/17) 中都有表达：4/17 的为高表达水平，11/17 的为中等表达水平，而在一个样品中为低表达水平。而且，在 3/12 的肺鳞状肿瘤中也有适度表达，尽管 2/4 的正常肺样品中表达为阴性。重叠群 29 在大肠、皮肤、唾液腺、胰腺、扁桃体、心脏和软腭中表现出低至中等的表达水平。重叠群 47 (SEQ ID NO: 142) 在测试的大多数头部和颈部鳞状细胞肿瘤 (12/17) 中都有表达：10/17 的为中等水平表达，而在两个样品中为低水平的表达。在肺鳞状肿瘤中，一个样品中有高水平表达，而在另两个样品中为中等表达水平 (n=13)。重叠群 47 在 2/4 的正常肺样品中为阴性，而在剩余的两个样品中有中等水平的表达。而且，重叠群 47 在大肠和胰腺中表现出中等表达水平，而在皮肤、唾液腺、软腭、胃、膀胱、静息 PBMC 和扁桃体中表现出低表达水平。

重叠群 48 (SEQ ID NO: 143) 在测试的所有头部和颈部鳞状细胞肿瘤 (17/17) 中均有表达：8/17 的有高水平的表达而 7/17 的有中等水平的表达，而在两个样品中为低水平的表达。在 3 个肺鳞状肿瘤样品 (n=13) 中表达水平从高至中等。重叠群 48 在 4 个正常肺样品的其中 1 个中为阴性，而剩余样品表现出有低或中等水平的表达。重叠群 48 在软腭、大肠、胰腺和膀胱中表现出中等表达水平，而在食道、唾液腺、静息 PBMC 和心脏中表现出低表达水平。重叠群 49 (SEQ ID NO: 144) 在测试的 6/17 头部和颈部鳞状细胞肿瘤中以低至中等的水平表达。在 3 个肺鳞状肿瘤样品 (n=13) 中表达水平中等。重叠群 49 在 2/4 的正常肺样品中为阴性，而剩余样品表现出低的表达水平。皮肤、唾液腺、大肠、胰腺、膀胱和静息 PBMC 中表现出中等的表达水平，软腭、淋巴结和扁桃体中表现出低表达水平。重叠群 56 (SEQ ID NO: 148) 在测试的 3/17 头部和颈部鳞状细胞肿瘤中以低至中等的水平表达，而 13 个肺鳞状肿瘤样品中的 3 个表现出低至中等的表达水平。值得注意的是，在 1 个腺癌肺肿瘤样品 (n=2) 中

检测到低的表达水平。重叠群 56 在 3/4 的正常肺样品中为阴性，而且仅在大肠中表现出中等表达水平，在唾液腺、软腭、胰腺、膀胱和静息 PBMC 中表现出低的表达水平。重叠群 58，又称 L769P，(SEQ ID NO: 150) 在测试的 11/17 头部和颈部鳞状细胞肿瘤中以中等水平表达，而在另外的 1 个样品中以低水平表达。13 个肺鳞状肿瘤样品中的 3 个表现出低至中等的表达水平。重叠群 58 在 3/4 的正常肺样品中为阴性，而在 1 个样品中有低水平的表达。在皮肤、大肠和静息 PBMC 中表现出中等表达水平，在唾液腺、软腭、胰腺和膀胱中表现出低的表达水平。重叠群 59 (SEQ ID NO: 157) 在某些头、颈、和肺鳞状肿瘤中表达。在唾液腺和大肠中也检测到重叠群 59 的低表达水平。

重叠群 22 (又称 L763P) 的全长 cDNA 序列见 SEQ ID NO: 158，其相应的推测氨基酸序列见 SEQ ID NO: 159。对 L763P 的实时 RT-PCR 分析揭示，其在 3/4 的肺鳞状肿瘤和 4/4 的头部和颈部鳞状肿瘤中有高水平表达，而在正常的脑、皮肤、软腭和气管中观察到低的表达水平。随后的数据库搜索显示，SEQ ID NO: 158 的序列含有一个导致在其相应的蛋白质序列出现移码的突变。SEQ ID NO: 345 中提供了 L763P 的第二种 cDNA 序列，而在 SEQ ID NO: 346 中提供了相应的氨基酸序列。除了 SEQ ID NO: 159 的 C 端 33 个氨基酸之外，SEQ ID NO: 159 和 346 的序列是一致的。

合并了重叠群 17、19 和 24 的全长 cDNA 序列，称作 L762P，序列见 SEQ ID NO: 160，其预测的相应氨基酸序列见 SEQ ID NO: 161。对 L762P 进行的进一步分析确定其是 I 型膜蛋白，并对另两个变体进行了测序。变体 1 (SEQ ID NO: 167，其相应氨基酸序列见 SEQ ID NO: 169) 是 SEQ ID NO: 160 的另一种拼接形式，导致 503 个核苷酸的缺失和该表达蛋白质中一个短片段的缺失。变体 2 (SEQ ID NO: 168，其相应氨基酸序列见 SEQ ID NO: 170) 与 SEQ ID NO: 160 相比在 3' 编码区缺失了两个核苷酸，结果产生该表达蛋白质的分泌形式。L762P 的实时 RT-PCR 分析揭示，在 3/4 的肺鳞状肿瘤和 4/4 的头部和颈部肿瘤中有超量表达，而在正常皮肤、软腭和气管中观察到有低水平的表达。

重叠群 56 (SEQ ID NO: 148) 的全长 cDNA 序列, 又称 L773P, 见 SEQ ID NO: 171, 其推测的氨基酸序列见 SEQ ID NO: 172. 发现 L733P 与二羟基脱氢酶在该基因的 3' 部分一致, 而具有不同的 5' 序列. 因此, 其 N 端的 69 个氨基酸是独一无二的. 编码该 69 个 N 端氨基酸的 cDNA 序列提供在 SEQ ID NO: 349 中, 而该 N 端氨基酸序列提供在 SEQ ID NO: 350 中. 实时 PCR 显示, L773P 在肺鳞状肿瘤和肺腺癌中以高水平表达, 而在正常组织中却检测不到其表达. L773P 的随后 Northern 印迹分析说明, 该转录本在鳞状肿瘤中有差异超量表达, 而且在原发性肿瘤组织中检测到约 1.6Kb 的片段, 在原发性头和颈部肿瘤组织中检测到约 1.3Kb 的片段.

随后的微阵列分析显示, 重叠群 58, 又称 L769S (SEQ ID NO: 150), 除了在肺鳞状肿瘤中还在乳腺肿瘤中超量表达.

实施例 4

多肽合成

可以在 Perkin Elmer/Applied Biosystems Division 430A 肽合成仪上, 采用 FMOC 化学和 HPTU(O-苯并三唑-N,N,N',N'-四甲基脲鎓六氟磷酸盐)活化, 合成多肽. 可以在该肽的氨基端连接一个 Gly-Cys-Gly 序列, 以提供进行偶联、与固定化表面结合、或标记该肽的方法. 从固相支持物上将该肽切割下来可以采用如下切割混合物来实现: 三氟乙酸: 乙二硫醇: 苯甲硫醚: 水: 酚 (40:1:2:2:3). 切割 2 小时后, 可以在冷甲基叔丁基醚中沉淀该多肽. 然后将该肽沉淀溶解在含有 0.1% 三氟乙酸 (TFA) 的水中, 并冻干, 再用 C18 反相 HPLC 纯化. 可以采用 0% - 60% 梯度的乙腈 (含 0.1% TFA) 水溶液洗脱该肽. 将该纯化组分冻干后, 可以采用电喷射或其它类型的质谱测定以及通过氨基酸分析, 对该肽进行特性分析.

实施例 5

制备抗肺癌抗原的抗体

按以下制备抗肺癌抗原 L514S、L528S 和 L531S (分别是 SEQ ID NO: 155、225 和 112) 的抗体。

用按以上所述在大肠杆菌中表达并纯化的重组蛋白质免疫兔。对于最初的免疫, 皮下(S.C.)注射 400 μ g 抗原和胞壁酰二肽(MDP)。4 周之后用混合了弗氏不完全佐剂(IFA)的 200 μ g 抗原经皮下对动物进行加强免疫。作为诱导高抗体滴度应答所必需的, 随后 S.C. 注射混有 IFA 的 100 μ g 抗原进行加强。采用纯化的蛋白质进行 ELISA 测定, 以测定取自免疫兔的血清的抗原特异性反应活性。采用与固相支持物连接的纯化蛋白质, 从高滴度多克隆血清中亲和纯化抗 L514S、L528S 和 L531S 的多克隆抗体。

在 5 个肺肿瘤样品、5 个正常肺组织样品、和正常结肠、肾、肝、脑和骨髓上, 采用抗 L514S 多克隆抗体进行免疫组织化学分析。具体地, 将组织样品在甲醛溶液中固定 24 小时, 然后包埋在石蜡中, 并切成 10 微米厚的切片。对组织切片进行透化处理并与抗体孵育 1 小时。与 HRP 标记的抗小鼠孵育后, 通过与 DAB 色素原的孵育观察 L514S 的免疫反应性。发现 L514S 在肺肿瘤组织中以高水平表达, 而在正常肺、脑或骨髓中几乎没有或没有观察到表达。在结肠和肾中观察到轻微的染色。在正常肝中观察到染色, 但在该组织中没有检测到 mRNA, 这使该结果值得怀疑。

实施例 6

用肽抗原免疫小鼠和 CTL 细胞系的增殖

按下述鉴定来自肺癌抗原 L762P (SEQ ID NO: 161) 针对 HLA-A2/Kb 限制性 CD8⁺ T 细胞的免疫原性肽。

采用通过与 HLA-A*0201 的已知肽结合基序进行匹配检验以预测可能与 HLA-A*0201 结合的肽序列的计算机程序(Ruper 等(1993), 细胞(Cell) 74: 929; Rammensee 等(1995)免疫遗传学(Immunogenetics) 41: 178-228), 预测该肺癌抗原 L762P (SEQ ID NO: 161) 中 HLA-A2 结合肽的位置。按上述方法制备相应于该预测的 HLA-A*0201 结合肽选定子集的一系列 19 个合成肽。

按进行了如下修改的 Thebald 等(美国国家科学院院刊 92: 11993-11997, 1995) 的所述方法, 用这些合成肽免疫表达人 HLA-A2/Kb 转基因的小鼠(由 L. Sherman 博士, The Scripps Research Institute, La Jolla, CA 提供)。用在弗氏不完全佐剂中乳化的 $50\mu\text{g}$ L726P 肽和 $120\mu\text{g}$ 来源于乙型肝炎病毒的 I-Ab 结合肽免疫小鼠。3 周后处死这些动物, 并制备单细胞悬浮液。然后将这些细胞以 7×10^6 个细胞/ml 的密度重悬在含有 10% FCS、2mM 谷氨酰胺(Gibco BRL)、丙酮酸钠(Gibco BRL)、非必需氨基酸(Gibco BRL)、 $2 \times 10^{-5}\text{M}$ 2-巯基乙醇、50U/ml 青霉素和链霉素的完全培养基(RPMI-1640; Gibco BRL, Gaithersburg, MD)中, 并在存在辐射(3000 rads)过的 L726P 肽- ($5\mu\text{g}/\text{ml}$)和 $10\text{mg}/\text{ml}$ B2-微球蛋白- ($3\mu\text{g}/\text{ml}$) LPS 母细胞(在存在 $7\mu\text{g}/\text{ml}$ 硫酸葡聚糖和 $25\mu\text{g}/\text{ml}$ LPS 时培养 3 天的 A2 转基因脾细胞)的情况下进行培养。6 天后, 用 $2.5 \times 10^6/\text{ml}$ 经肽脉冲的辐射(20,000 rads)过的 EL4A2Kb 细胞(Sherman 等, 科学(Science), 258:815-818, 1992), 和 $5 \times 10^6/\text{ml}$ 辐射(3000 rads)过的 A2/Kb 转基因脾饲喂细胞, 对细胞(5×10^5 个/ml)进行再次刺激。将细胞在 10U/ml IL-2 存在的情况下培养。一周一次按所述方法反复刺激细胞, 为克隆该细胞系作准备。

用辐射(20,000 rads)过的经 L762P 肽脉冲的 EL4 A2Kb 肿瘤细胞(1×10^4 个细胞/孔)作为刺激物, 而辐射(3000 rads)过的 A2/Kb 转基因脾细胞作为饲喂物(5×10^5 个细胞/孔), 通过极限稀释分析克隆肽特异性细胞系, 将之培养在存在 10U/ml IL-2 存在的情况下。第 7 天, 按前述对细胞进行再次刺激。在第 14 天, 分离生长的克隆并维持培养。

对 L762P-87 (SEQ ID NO: 226; 相应于 SEQ ID NO: 161 的第 87-95 位氨基酸)、L726P-145 (SEQ ID NO: 227; 相应于 SEQ ID NO: 161 的第 145-153 位氨基酸)、L762P-585 (SEQ ID NO: 228; 相应于 SEQ ID NO: 161 的第 585-593 位氨基酸)、L762P-425 (SEQ ID NO: 229; 相应于 SEQ ID NO: 161 的第 425-433 位氨基酸)、L762P(10)-424 (SEQ ID NO: 230; 相应于 SEQ ID NO: 161 的第 424-433 位氨基酸)、和 L762P(10)-458 (SEQ ID NO: 231; 相应于 SEQ ID NO: 161 的第 458-467 位氨基酸) 具有特异性

的细胞系，表现出其对抗 L762P 肽脉冲的 EL4-A2/K^b 肿瘤靶细胞的反应性明显高于其对抗对照肽脉冲的 EL4-A2/K^b 肿瘤靶细胞的反应性（按特异裂解百分数测定的）。

实施例 7

鉴定来源于肺癌抗原 L762P 的 CD4 免疫原性 T 细胞表位

按下述方法制备抗原 L762P (SEQ ID NO: 161) 特异性 CD4 T 细胞系。

合成横跨约 50% 的该 L762P 序列的一系列 28 个重叠肽。为了进行抗原接触，将 4-5 个肽组合成一个库，以 20 μ g/ml 的浓度对树突细胞脉冲 24 小时。然后洗涤该树突细胞，并在 96 孔 U 型底板中将其与阳性筛选的 CD4⁺ T 细胞混合。每个肽库产生 40 个培养物。每周一次用携带这些肽库的新鲜树突细胞反复刺激这些培养物。总共 3 个刺激周期后，另外停止处理细胞 1 周，并采用 γ -干扰素 ELISA 和增殖测定试验测试细胞对肽库脉冲的抗原呈递细胞 (APC) 的特异性。对于这些测定试验，采用携带有该相关肽库或无关肽的贴壁单核细胞作为 APC。就每一个库，鉴定通过细胞因子释放和增殖表现出特异识别 L762 肽库的 T 细胞系。重点放在鉴定具有增殖应答的 T 细胞上。对表现出 L762P 特异性细胞因子分泌和增殖，或仅表现出强增殖的 T 细胞系进行再扩增，以检测其对来自这些库的各个肽的识别，以及其对重组 L762P 的识别。重组 L762P 来源于大肠杆菌，该物质经过部分纯化并表现出内毒素阳性。这些研究采用了 10 μ g 每种肽、10 或 2 μ g 无关肽，以及 2 或 0.5 μ g L762P 蛋白质或无关的纯度相同的大肠杆菌产生的重组蛋白。每个库中的许多 L76P 来源肽都诱导显著的 γ 干扰素产生和 CD4 T 细胞的增殖。这些肽的氨基酸序列见 SEQ ID NO: 232-251。这些肽分别相应于 SEQ ID NO: 161 的第 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 和 586-605 位氨基酸。

用 10 μ g/ml 相关肽进行刺激，进一步扩增对各个 L762P 来源肽表现出特异性的 CD4 T 细胞系。刺激后 2 周，采用增殖和 IFN- γ ELISA 测定

检测识别此特定肽的 T 细胞系。许多之前鉴定的 T 细胞继续表现出 L762P 肽特异性活性。在该相关肽上进一步对这些细胞系的每一个进行扩增，并在扩增两周后在滴定试验中测试每个细胞系对该 L762P 肽的特异识别，以及对重组大肠杆菌来源 L762P 蛋白的识别。对于这些实验，用该相关 L762P 来源肽、或无关 mammaglobin 来源肽、重组大肠杆菌来源的 L762P (大约 50% 的纯度)、或无关大肠杆菌来源的蛋白质，脉冲自体贴壁单核细胞。发现大多数 T 细胞系表现出对该相关肽的低亲和性，原因是当 L762P 肽被稀释后特异增殖和 IFN- γ 比值极大地降低。然而，鉴定了 4 个甚至在 0.1 $\mu\text{g/ml}$ 肽时仍表现出显著活性的细胞系。这些细胞系（称作 A/D5、D/F5、E/A7 和 E/B6）的每一个均还表现出响应该大肠杆菌来源的 L762P 蛋白制备物，而不响应该无关蛋白制备物的特异增殖。SEQ ID NO: 234、249、236 和 245 中分别提供了这些细胞系所识别的 L762P 来源肽的氨基酸序列。在所有这些细胞系中均没有检测到蛋白质特异性 IFN- γ 。在经 0.1 (A/D5 和 E/A7) 或 1 (D/F5) $\mu\text{g/ml}$ 该相关肽脉冲的自体贴壁单核细胞上，克隆 A/D5、E/A7 和 E/B6 细胞系。在细胞生长后，测试其对该相关肽的特异性。对于 A/D5 和 E/A7，鉴定了许多对该相关肽具有特异性的克隆。

实施例 8

肺肿瘤特异性抗原的蛋白质表达

a) 在大肠杆菌中表达 L514S

将肺肿瘤抗原 L514 (SEQ ID NO: 89) 亚克隆在表达载体 pE32b 的 NcoI 和 NotI 位点中，并采用标准技术转化大肠杆菌。从 SEQ ID NO: 89 的第 3-153 位表达出该蛋白质。表达的氨基酸序列和其相应 DNA 序列分别见 SEQ ID NO: 252 和 253。

b) L762P 的表达

采用卡那霉素抗性，将带有 6 $\times$ His 尾的肺肿瘤抗原 L762P (SEQ ID NO: 161) 第 32-944 位氨基酸亚克隆在修饰的 pET28 表达载体中，并采用标

准技术用其转化 BL21 CodonPlus. 观察到低至中等水平的表达。该 L762P 表达结构的测定 DNA 序列见 SEQ ID NO: 254.

从以上所述, 应明了, 尽管为了举例说明的目的本文中描述了本发明的具体实施方案, 但可以对其进行各种修改而不偏离本发明的精神和范围。因此, 本发明仅受所附权利要求的限制。

序列表

<110> Corixa 公司等.

<120> 用于治疗 and 诊断肺癌的化合物和方法

<130> 210121.45501PC

<140> PCT

<141> 2000-04-03

<160> 350

<170> FastSEQ for Windows Version 3.0

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gttaatatgt ttgtaaactc atgtacagtt ttttttgggg gggaagcaat gggaangta	240
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<211> 380

<212> DNA

<213> 人

<400> 2

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ggataaatto ccagttctaga ttattagcct ttgttaacca tcaagcacct agaagaagaa	300
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tgtnggaaga nannnnnnn ccccccctnc tncnncctng cngctnnnc cncntgtngg 660
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gccaatattt	ccttatatct	atocataaca	tttatactac	atttgtaaga	gaatatgcac	180
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<213> 人

<220>

<221> misc feature

<222> (1)...(670)

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aaacanttcc	aanttcgaag	tcacccnaat	ctcctggaac	aatgaacatn	aatatnttct	600
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<220>

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cacctagcat	tgccctactta	gccccctgaa	ttaacagagc	ccaattgaga	caaacccttg	180
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689

<210> 9
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 <212> DNA
 <213> 人

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gaaaaaagcg aggcctttttt gccaccttgg taaaggccag ttcactgcta tagaactgct 180
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<210> 11
 <211> 602
 <212> DNA
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<400> 11
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cagttttgca taattataat cggcattgta catagaaagg atatggctac cttttgttaa 300
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tcttgggata ctgtgttagaa ctgttctcat taaacaccaa acagttaagt ccattctctg 480
gtactagcta caaattcggt ttcatattct acttaacaat ttaataaac tgaaatattt 540
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aa

602

<210> 12
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 <212> DNA
 <213> 人
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gcatgcattt gtaacatgat tagtagattt gaatatatag atgtagtatn ttgggtatct 180
aggtgtttta tcattatgta aaggaattaa agtnaaggac ttgtagtgtg tttttattaa 240
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cntntccaat ngacaatcga gtttccnnnc tccngnaacc tngccgnnnn cnggccnnnc 600
cantntgnta accccgcgcc cggatcgctc tcnnntcgtt ctncncnana ngggntttcn 660
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 <212> DNA
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 <220>
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gtttactagc tagctttaca atatgccaaa aaaggatttc tccctgacct catccgtggt 300
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actatgcggtt gaactgcaat ggtttggctg gggnccttga acaatttaat cncatacatc 600
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679

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ttaaaaaagg gcctgaaaaa aggggagcca caaatctgtc tgcttcccca cnttantent 180
tggcaaatna gcattctgtc tcnttggctg cngcctcanc ncaaaaaanc ngaactcnat 240
cnggccagg aatacatctc ncaatnaacn aaattganca aggcnnntggg aaatgccnga 300
tgggattatc ntccgcttgt tgancttcta agtttctntc ccttcattcn accctgccag 360
ccnagttctg ttagaaaaat gcengaattc naacnccggg tttctactc ngaatttaga 420
tctncanaaa ctctcctggc acnattcnaa ttnanggnca cgnacanatn ccttccatna 480
anncncccc acntttgana gccangacaa tgactgcntn aantgaaggc ntgaaggaa 540
aacttttga ggaaaaaaaa ctttgtttcc ggcccttccc aacncttctg tgttnancac 600
tgccttctng naacctgga agcccnngna cagtgttaca tgttgttcta nnaaacngac 660
ncttnaatnt cnatcttccc nanaacgatt ncncc
679

```

```

<210> 16
<211> 669
<212> DNA
<213> 人

```

```

<220>
<221> misc feature
<222> (1)...(669)
<223> n = A,T,C or G

```

```

<400> 16
cgccgaagca gcagcgcagg ttgtcccccgt ttccctccc ccttcccttc tccggttgcc 60
ttcccgggcc ccttacactc cacagtcccg gtcccgccat gtcccagaaa caagaagaag 120
agaaccctgc ggaggagacc ggcgaggaga agcaggacac gcaggagaaa gaaggtattc 180
tgccgtgagag agctgaagag gcaaaagctaa aggccaaaata cccaagccta ggacaaaagc 240
ctggaggctc cgacttccctc atgaagagac tccagaaagg gcaaaagtac tttgactcng 300
gagactacaa catggccaaa gccaacatga agaataagca gctgccaaagt gcangaccag 360
acaagaacct ggtgactggt gatcacatcc ccaccccaca ggatctgccc agagaaagtc 420
ctcgtctcgt accagcaagc ttgcgggtgg ccaagttgaa tgatgctgcc ggggctctgc 480
canatctgag acgcttccct cctgccccca cccgggtcct gtgctggctc ctgcccttcc 540
tgcttttgca gccangggtc aggaagtggc ncnnggtngtg gctgggaaagc aaaacccctt 600
cctgttggtg tcccacccat ggagcccccig gggcgagccc angaacttga ncccttttgt 660

```

tntcttnc

669

<210> 17
 <211> 697
 <212> DNA
 <213> 人
 <220>
 <221> misc_feature
 <222> (1)...(697)
 <223> n = A,T,C or G

<400> 17
 gcaagatatg gacaactaag tgagaaggta atnctctact gctctagntn ctcnnggenn 60
 gacgcgctga ggagannnac gctggcccan ctgcccggca cacacgggga tcntggtnat 120
 gccctgccan gggancccca ncnctcggan cccatntcac acccgnnccn tncgcccacn 180
 ncctggeten cncngcceng nccagctcnc gnccccctcc gccnnnctcn ttnnctctc 240
 cncncctccc ncnachacct cctacccncc gctcccctcc cagccccccc ccgcaancct 300
 ccacnacncc ntenhncga ancnccnctc gcncctengcc ccngccccct gccccccgcc 360
 cncnacnccg cgnctccccg cgcncgcncg ctccccccct cccacnacag ncnaccccg 420
 agncaacgnc tccgcccncct gacgccccnn cccgcccggc tcaccttcac ggncconacg 480
 ccccgcctnc nccnctgcnc gccgncnngg cgcgccgcc cncnccngtn cchncngnng 540
 cccnngcngn angcnctgc cncnangncc gngccggnen ncacctccg nccnccgcc 600
 cgcgcgctgg gggctcccgc cncgcggntc antcccncc cntnccgcca ctntccgntc 660
 cnnnctcnc getcngcnc cgcncncc cccccc 697

<210> 18
 <211> 670
 <212> DNA
 <213> 人
 <220>
 <221> misc_feature
 <222> (1)...(670)
 <223> n = A,T,C or G

<400> 18
 ctctgtgtgaa ggggtgcagta cctaagccgg agcggggtag aggcggggcc gcacccccctt 60
 ctgacctcca gtgccgcccgg cctcaagatc agacatggcc cagaacttga acgacttggc 120
 gggacggctg cccgcccggc cccggggcat gggcacggcc ctgaagctgt tgctgggggc 180
 cggcgccgtg gcctacgggtg tgcgcgaatc tgtgttcacc gtggaaggcg ggncagagc 240
 catcttcttc aatcggatcg gtggagtgc caggacacta tcttggggcc anggccttca 300
 cttcaggatc cttgggttcca gtaccccanc atctatgaca ttccgggccag acctcgaaaa 360
 aatctcctcc ctacaggctc caaagacctc cagatgggtga atatctccct gcgagtgttg 420
 tctcgaccaa tgcctcangaa ctctcctaaca tgttccancg cctaagggtc ggactacnaa 480
 gaacgantgt tgccgtccat tgtcacgaag tgctcaagaa tttnggtggc caagtccaat 540
 gncctcacnn ctgatcncct agcggggcca agttanccct ggttgatccc cgggganctg 600
 acnnaaaagg gccaaaggact tccccctcct ctgggataatg tggcctcac aaagctcaac 660
 ttanccacc 670

<210> 19
 <211> 606
 <212> DNA
 <213> 人
 <220>
 <221> misc_feature
 <222> (1)...(606)
 <223> n = A,T,C or G


```

<400> 19
actagtgccca acctcagetc ccaggccagtt tctctgaatg tcgaggagtt ccaggatctc      60
tggcctcagtt tgtccttgggt tattgatggg ggacaaattg gggatggcca gagccccgag      120
tgtcgcccttg gctcaactgt ggttgatttg tctgtgcccg gaaagtttgg catcattcgt      180
ccaggctgtg ccctggaaag tactacagcc atcctccaac agaagtacgg actgctcccc      240
tcacatgctg cctacctgtg aaactctggg aagcaggaag gcccaagacc tgggtgctgga      300
tactatgtgt ctgtccactg acgactgtca aggcctcatt tgcagaggcc accggagcta      360
gggcaactagc ctgactttta aggcagtgtg tctttctgag cactgtagac caagcccttg      420
gagctgctgg ttttagccttg cacctgggga aaggatgtat ttatttqtat tttcataatat      480
cagccaaaag ctgaatggaa aagtttnagaa cattcctagg tggccttatt ctaataagtt      540
tcttctgtct gttttgtttt tcaattgaaa agttattaaa taacagattt agaattctagt      600
gagacc
606

```

```

<210> 20
<211> 449
<212> DNA
<213> 人

```

```

<400> 20
actagtaaac aacagcagca gaaacatcag tatcagcagc gtccgcaagca ggagaatatg      60
cagcgccaga gccgaggaga acccccgcctc cctgaggagg acctgtccaa actcttcaaa      120
ccaccacagc cgcctgccag gatggactcg ctgtcctatt caggccagat aaacacttac      180
tgccagaaca tcaaggagtt cactgcccac aacttaggca agctcttcac ggcccaggct      240
cttcaagaat accaacaacta agaaaaggaa gtttccagaa aagaagtaa catgaactct      300
tgaagtcaca ccaggggcaac tcttggaaga aatatatttg catattgaaa agcacagagg      360
atctcttttag tgtcattgcc gattttgggt ataacagtgt ctttctagcc ataataaat      420
aaaacaaaaat cttgactgct tgctcaaaa
449

```

```

<210> 21
<211> 409
<212> DNA
<213> 人

```

```

<400> 21
tatcaatcaa ctggtgaata attaaacaat gtgtggtgtg atcatacaaa gggtagcact      60
caatgataaa aggaacaagc tgcctatatg tggaaacaaca tggatgcatt tcagaaactt      120
tatgtttgagt gaaagaacaa acacggagaa catactatgt ggttctcttt atgtaacatt      180
acagaaataa aaacagaggg aaccaccttt gaggcagtat ggagtggagt agactggaaa      240
aaggaaaggaa ggaaactcta cgctgatgga aatgtctgtg tcttcatttg gtggtagtta      300
tgtggggata tacatttgtc aaattttatt gaactatata ctaaagaact ctgcatttta      360
ctgggatgta aataatacct caattaaaaa gacaaaaaaa aaaaaaaaaa      409

```

```

<210> 22
<211> 649
<212> DNA
<213> 人

```

```

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

```

```

<400> 22
acaatttttca ttatcttaag cacattgtac atttctacag aacctgtgat tattctcgca      60
tgataaggat ggtactttgca tatggtgaat tactactgtt gacagtttcc gcagaaatcc      120
tatttccagt gaccaacatt gtggcatggc agcaaatgcc aacattttgt ggaatagcag      180
caaatctaca agagaccctg gttgggtttt cgttttgttt tctttgtttt ttcccccttc      240
tcctgaatca gcagggatgg aangagggtta ggggaagttat gaattactcc ttccagtagt      300
agctctgaag tgtcacattt aatatcagtt ttttttaaac atgattctag ttnaatgtag      360
aagagagaaag aaagaggaag tgttcacttt ttttaatacac tgatttagaa atttgatgtc      420

```

```

ttatatcagt agttctgagg tattgatagc ttgcttttatt totgccttta cgttgacagt 480
gttgaagcag ggtgaataac taggggcata tatatttttt ttttttgtaa gctgtttcat 540
gatgttttct ttggaatttc cggataagtt caggaaaaca totgcatgtt gttatctagt 600
ctgaagtctc tatccatctc attacaacaa aaacnccccg aacggnttg 669

```

<210> 23

<211> 669

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 23

```

actagtgcgg tactggctga aatccctgca ggaccaggaa gagaaccagt tcagactttg 60
tactctcagt caccagctct ggaattagat aaattccttg aagatgtcag gaatgggac 120
tatcctctga cagccttttg gctgcctcgg cccagcagc cagagcagga ggaggtgaca 180
tcacctgtcg tgccccctc tgtcaagact ccgacacctg aaccagctga ggtggagact 240
cgcaagggtgg tgctgatgca gtgcaacatt gagtccggtg aggagggagt caaacaccac 300
ctgacacttc tgctgaagtt ggaggacaaa ctgaacoggc acctgagctg tgacctgatg 360
ccaaatgaga atatccccg gttggcggct gagctgggtg agctgggctt cattagtga 420
gctgaccaga gccgggttgac ttctctgcta gaagagactt gaacaagttc aattttgcca 480
ggaaacagtac cctcaactca gccgctgtca ccgtctctc ttagagctca ctcgggccag 540
gccctgatct gccgtgtggc tgtcctggac gtgctgcacc ctctgtcctt cccccagtc 600
agtattacct gtgaagccct tccctccttt attattccagg anggctgggg gggctccttg 660
nttctaacc 669

```

<210> 24

<211> 442

<212> DNA

<213> 人

<400> 24

```

actagtacca tcttgacaga ggatacatgc tcccaaaacg tttgttacca cacttaaaaa 60
tcactgccat cattaagcat cagtttcaaa attatagcca ttcatgattt actttttcca 120
gatgactatc attattctag tcocttgaat ttgtaagggg aaaaaaaaca aaaaCaaaaa 180
cttacgatgc acttttctoc agcacatcag atttcaattt gaaaattaaa gacatgctat 240
ggtaattgcac ttgctagtac tacacacttt ggtaCaacaa aaacagagg caagaaacaa 300
cggaagaga aaagccttcc tttgttgccc cttaactga gtcaagatct gaaatgtaga 360
gatgatctct gacgatacct gtatgttctt attgtgtaaa taaaattgct ggtatgaaat 420
gacctaaaaa aaaaaaaaaa aa 442

```

<210> 25

<211> 656

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 25

```

tgcaagtacc acacactgtt tgaattttgc acaaaaagtg actgtaggat caggtgatag 60
ccccggaatg tacagtgtct tgggtgcacca agatgccttc taaaggctga cataccttgg 120
accctaattg gccagagagt atagocctag cccagtggtg acatgaccac tccctttggg 180
aggcctgagg tagaggggag tggtatgtgt tttctcagtg gaagcagcac atgagtgggt 240
gacaggatgt tagataaagg ctctagttag ggtgtcattg tcatttgaga gactgacaca 300

```

```

ctcctagcag ctgggtaaagg ggtgctggan gccatggagg anctctagaa acattagcat 360
gggctgatct gattacttcc tggcatcccg ctcactttta tgggaagctc tattagangg 420
atgggacagt ttcccatatc cttgctgtgg agctctggaa cactctctaa atttccctct 480
attaaaaatc actgccctaa ctacaacttcc tccttgaagg aatagaaatg gaactttctc 540
tgacatannt cttggcatgg ggagccagcc acaaatgana atctgaacgt gtccaggttt 600
ctcctganac tcactctacat agaatttggt aaacctctcc ttggaataag gaaaaa 656

```

```

<210> 26
<211> 434
<212> DNA
<213> 人

```

```

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

```

```

<400> 26
actagttcag actgccagcc caacccccaga aaatacccca catgccagaa aagtgaagtc 60
ctaggtgttt ccactctatgt ttcaatctgt ccactctacca ggccctcgca taaaaacaaa 120
acaaaaaaac gctgccagggt tttagaagca gttctgtgtc caaaaccatc aggatcctgc 180
caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcactc 240
aataactgaa ttgtcaggct ttgattgata attgtagaaa taagtgcct tctgttgtgg 300
gaataagtta taatcagtat tcactctctt gttttttgtc actctttct ctctaattgt 360
gtcatttgta ctgtttgaaa aatatttctt ctatnaaatt aaactaacct gccttaaaaa 420
aaaaaaaaaa aaaa 434

```

```

<210> 27
<211> 654
<212> DNA
<213> 人

```

```

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

```

```

<400> 27
actagtccaa cacagtcaga aacattgttt tgaatcctct gtaaaccaag gcattaatct 60
taataaacca ggatccatct aggtaccact tgatataaaa aggatatcca taatgaatat 120
tttatactgc atccttttaca ttagccacta aatacgttat tgcttgatga agacctttca 180
cagaatccta tggattgcag catttcaact ggctacttca taccatgccc ttaaagaggg 240
gcagttttctc aaaagcagaa acatgcogcc agttctcaag ttttctctct aactccattt 300
gaatgtaagg gcagctggcc cccaatgtgg ggagggtccg acattttctg aattcccat 360
ttcttgttog cggctaaatg acagtttctg tcattactta gattccgac tttcccaag 420
gtgttgattt acaaagaggg cagctaatag cagaaatcat gacctgaaa gagagatgaa 480
attcaagctg tgagccaggg agganctcag tatggcaag gtcttgagaa tcngccattt 540
ggtacaaaaa aaatttttaa gcntttatgt tataccatgg aaccatagaa anggcaagg 600
aattgttaag aanaatttta agtgtccaga ccanaanga aaaaaaaaaa aaaa 654

```

```

<210> 28
<211> 670
<212> DNA
<213> 人

```

```

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

```

```

<400> 28
cgtgtgcaca tactgggagg atttccacag ctgcacggtc acagccctta cggattgcca      60
ggaaggggcg aaagatatgt gggataaact gagaaaagaa ndcaaaaacc tcaacatcca      120
aggcagctta ttcgaactct gcggcagcgg caacggggcg gcgggggtccc tgctcccggc      180
gttcccggtg ctccctgggtg ctctctcggc agcttttagcg acctgncttt ccttctgagc      240
gtggggccag ctccccccgc ggcgccacc cacnctcact ccattgctccc ggaatcgag      300
aggaagatca ttagttcttt ggggacgttn gtgattctct gtgatgctga      360
tatagggaat gtgggaaatc ctganctctt tnttatntcg tntgatttct tgtgttttat      420
ttgccaaaat gttaccaatc agtgaccaac cnagcacagc caaaaatcgg acntcngctt      480
tagtccgtct tcacacacag aataagaaaa cggcaaaccc accccaacttt tnantttnat      540
tattactaan ttttttctgt tgggcaaaag aatctcagga acngccctgg gccnccgta      600
ctanagttaa ccnagctagt tncatgaaaa atgatgggct cccnctcaat gggaaaagcca      660
agaaaaagnc                                         670

```

<210> 29

<211> 551

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

```

<400> 29
actagtcttc cacagcctgt gaatccccct agacctttca agcatagtga gcggagaaga      60
agatctcagc gtttagccac cttacccatg cctgatgatt ctgtagaaaa ggtttcttct      120
ccctctccag ccactgatgg gaaagtattc tccatcagtt ctcaaatca gcaagaatct      180
tcagtaccag aggtgcctga tgttgacatc ttgccacttg agaagctggg accctgtctc      240
cctcttgact taagtcgtgg ttcagaagtt acagcaccgg tagcctcaga ttcctcttac      300
cgtaatgaat gtcccagggc agaaaaagag gatacncaga tgcttccaaa tccttcttcc      360
aaagcaatag ctgatgggaa gaggagctcc agcagcagca ggaatatcga aaacagaaaa      420
aaaagtgaag ttgggaagac aaaaagctca cagcatttgg taaggagaaa aganaagatg      480
aggaaggaag agagaagaga gacnaagatc nctacggacc gnnhncggaag aagaagaagn      540
aaaaaanaaa a                                         551

```

<210> 30

<211> 684

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

```

<400> 30
actagttcta tctggaaaaa gcccgggttg gaagaagctg tggagagtgc gtgtgcaatg      60
cgagactcat ttcttggaaag catccctggc aaaaatgcag ctgagtacaa ggttatcact      120
gtgatagaac ctggactgct ttttgagata atagagatgc tgcagtctga agagacttcc      180
agcacctctc agttgaatga attaattgat gcttctgagt caactttact ggctcaggaa      240
ccacgagaga tgactgcaga tgtaatcgag cttaaaggga aattcctcat caacttagaa      300
ggtggtgata ttcgtgaaga gtcttcctat aaagtaattg tcatgccgac tacgaaagaa      360
aaatgcccc gttgttgga gttatcacgc ggagtcttca gatacactgt gtccctcgatg      420
tgcagaagtt gtcagtggga aaatagtatt aacagctcac tcgagcaaga accctcctga      480
cagtactggg ctagaagttt ggtatggatta tttacaatat aggaaagaaa gccaaagaatt      540
aggtnatgag tggatgagta aatgggtgaa gatggggaat tcaaatcaga attatggaag      600
aagttnttcc tgttactata gaaaggaaat atgtttattt acatgcagaa aatatanaatg      660
tgtggtgtgt accgtggatg gaan                                         684

```

<210> 31
 <211> 654
 <212> DNA
 <213> 人

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

<400> 31
 gccgcagaaaa ggaaccaata tttcagaaac aagcttaata ggaacagctg cctgtacatc 60
 aacatcttct cagaatgacc cagaagttat catcgtggga gctggcgtgc ttggctctgc 120
 tttggcagct gtgctttcca gagatggaag aaaggtgaca gtcattgaga gagacttaaa 180
 agagcctgac agaatagttg gagaattcct gcagccgggt ggttatcatg ttctcaaaga 240
 ccttggtctt ggagatacag tggaaaggtct tgatgccag gttgtaaag gttacatgat 300
 tcatgatcag ggaagcaaa tcagangttc agattcctta cctctgtca gaaaacaatc 360
 aagtgcagag tggaagagct ttccatcacg gaagattcat catgagtctc cggaagcag 420
 ctatggcaga gcccaatgca aagtttattg aaggtgttgt gttacagtta ttagaggaag 480
 atgatgttgt gatgggagtt cagtacaagg ataaagagac tgggagatat caaggaaactc 540
 catgctccac tgactgttgt tgcagatggg cttttctcca anttcaggaa aagcctggtc 600
 tcaataaagt ttctgtatca ctcatttggg ttgcttctta tgaagaatgc nccc 654

<210> 32
 <211> 673
 <212> DNA
 <213> 人

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

<400> 32
 actagtgaag aaaaagaaat tctgatacgg gacaasaatg ctcttcaaaa catcattctt 60
 tatcacctga caccaggagt tttcattgga aaaggatttg aacctgggtg tactaacatt 120
 ttaaagacca cacaaggaag caaaatcttt ctgaaagaag taatgatac acttctgggtg 180
 aatgaattga aatcaaaaaga atctgacatc atgacaacaa atgggtgtaat tcatgttgta 240
 gataaactcc tctatccagc agacacacct gttggnaatg atcaactgct ggaaatactt 300
 aataaattaa tcaaatatcat ccaaattaag tttgttcgtg gtgacacctt caaagaaatc 360
 cccgtgactg tctatnagcc aattattaaa aaatacacca aatcattga tgggagtggc 420
 tgtgggaact aactgaaaaa gagaccgaga agaaccgaatc 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> 人

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

<400> 33
 actagttatt tactttcttc cgcttcagaa ggtttttcag actgagagcc taagcatact 60
 ggatctgttg tttcttttgg gtctcacctc atcagtgtgc atagtggcag aaattataaa 120

```

gaaggttgaa aggagcaggg aaaagatcca gaagcatggt agttcgacat catcatcttt 180
tcttgaagta tgatgcatat tgcattatct tatttgcaaa ctaggaattg cagtctgagg 240
atcatttaga agggcaagtt caagaggata tgaagatttg agaacttttt aactattcat 300
tgactaaaaa tgaacattaa tgttnaagac ttaagacttt aacctgctgg cagtcocaaa 360
tgaaattatg caactttgat atcatattcc ttgatttaaa ttgggctttt gtgattgant 420
gaaactttat aaagcatatg gtcagttatt tnattaaaaa ggcaaacctt gaaccacctt 480
ctgcacttaa agaagtctaa cagtacaaat acctatctat cttagatgga tntatttntt 540
tntattttta aatattgtac tatttatggt nggtggggct ttcttactaa tacacaaatn 600
aatttatcat ttcaanggca ttctatttgg gtttagaagt tgattccaag nantgcatat 660
ttcgctactg tnt

```

```

<210> 34
<211> 684
<212> DNA
<213> 人

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

```

```

<400> 34
actagtttat tcaagaaaag aacttactga ttctctgtgt cctaaagcaa gagtggcagg 60
tgatcagggc tgggtgtagc tccggttcc ttagtgagc taactgcatt tgtcactgat 120
gaccaaggag gaaatcacta agacatttga gaagcagtg tatgaacgtt cttggacaag 180
ccacagttct gagecctaac cctgtagttt gcacacaaga acgagctcca cctccccctc 240
ttcaggagga atctgtgogg atagattggc tggacttttc aatggttctg ggttgcaagt 300
gggcactggt atggctgggt atggagcgga cagccccagg aatcagagcc tcagcccggc 360
tgccctggtg gaaggtacag gtgttcagca ccttcggaaa aagggcataa agtngtgggg 420
gacaattctc agtccaagaa gaatgcattg accattgctg gctatttgc tncctagtat 480
gaattggatn catttttgac cangatnntt ctncatgct tntttgcaat gaaatcaa 540
cccgcatat ctacaagtg tatgaagtc tgcnncccc agagaggctg ttcaggcnat 600
gtcttccaag ggcagggtgg gttacacat tttacctccc ctctcccccc agattatgna 660
cncagaagga atttntttcc tccc

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<210> 35
<211> 614
<212> DNA
<213> 人

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

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```

<400> 35
actagtccaa cgcgttngcn aatattcccc tggtagccta cttecttacc cccgaatatt 60
ggtaagatcg agcaatggct tcaggacatg ggttctcttc tctgtgatc attcaagtgc 120
tcactgcatg aagactggct tgtctcagtg tntcaacctc accagggctg tctcttggtc 180
cacacctgcg tccctgttag tgccgtatga cagcccccat canatgacct tggccaagtc 240
acggttttct tgtgggtcaat gttggtnggc tgattgggtg aaagtanggt ggaccaaagg 300
aagnencgtg agcagncanc nccagttctg caccagcagc gcctccgtcc tactnggggtg 360
ttccngtttc tcttgccct gngtgggcta nggcctgatt cgggaanatg cctttgcang 420
gaaggganga taantgggat ctaccaattg attctggcaa aacnatntct aagattnttn 480
tgctttatgt ggganacana tctanctctc atttntgtct gnanatnaca cctactcgt 540
gntcgancnc gtcttcgatt ttcgganaca cncantnaa tactggcggt ctggtgttaa 600
aaaaaaaaaa aaaa

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<210> 36
<211> 686

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<212> DNA

<213> 人

<220>

<221> misc feature

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

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

<400> 36

gtggetggcc	cggtttctccg	cttctcccca	ccccctaatt	tcctccctcc	ctccctttcc	60
ctccctcgtc	gactgttgct	tgctggctgc	agactccctg	acccctccct	caccctcccc	120
taacctcggt	gccaccggat	tgcccttctt	ttctgttgcc	ccagcccgag	cctagtgtca	180
gggcgggggc	ctggagcagc	ccgaggcact	gcagcagaag	ananaaaaga	cacgacnaac	240
ctcagctcgc	cagtccggtc	gctngettoc	cgcgcgatgg	caatnagaca	gacgcgcctc	300
acctgctctg	ggcacacggc	acccgtgggt	gatttggcct	tcagtggcat	cacccttatg	360
ggtatttctt	aatcagcgct	tgcaaagatg	gttaacctat	gtacgcccag	ggagatacag	420
gagactggat	tggaacattt	ttggggctta	aaggtctgtt	tggggtgcaa	cactgaataa	480
ggatgccacc	aaagcagcta	cagcagctgc	agatttcaca	goccaaagtg	gggatgctgt	540
ctcagganat	naattgataa	cctggctcat	aacacattgt	caagaatgtg	gatttcccca	600
ggatattatt	atttgtttac	cggggganag	gataactgtt	tmcntattt	taattgaaca	660
aactnaaca	aaanctaagg	aatcc				686

<210> 37

<211> 681

<212> DNA

<213> 人

<220>

<221> misc feature

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

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

<400> 37

gagacanaen	naacgtcang	agaanaaaaag	angcatggaa	cacaanccag	gcncgatggc	60
caccttccca	ccagcancca	gcgcccccca	gngccccca	ngncggang	accangactc	120
cancctgnat	caatctganc	tctattctctg	gcccattcct	acctcggagg	tggangccgn	180
aaaggtcgca	cnncagaga	agctgctgcc	ancaccancc	gccccnccc	tgncgggctn	240
nataggaaac	tggtgacenn	gctgcanaat	tcatacagga	gcacgcgang	ggcacnnnct	300
cacactgagt	tnnngatgan	gocnaccan	ggacctnccc	cagcnnattg	annacnggac	360
tgcgaggaa	ggaagacccc	gnaonggate	ctggccggcn	tgccaccccc	ccacccttag	420
gattatnccc	cttgactgag	tctctgaggg	gctaccggaa	cccgcctcca	ttccctacca	480
natnntgctc	nacgggact	gacangctgg	ggatnggagg	ggctatcccc	cancatcccc	540
tnanaccaac	agcnaacgan	natnggggct	ccccngggtc	ggngcaacnc	tcctncccc	600
cggcgcnggc	cttcggtgnt	gtctcctnc	aacnaattcc	naaanggcgg	gcccccnctg	660
ggactcctcn	ttgttccctc	c				681

<210> 38

<211> 687

<212> DNA

<213> 人

<220>

<221> misc feature

<222> (1)...(687)

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

<400> 38

canaaaaaaa	aaaacatggc	cgaaaccagn	aagctgcggc	atggcgccac	ggccccctctt	60
ctcccgccct	gtgtccggaa	ggtttccctc	cgaggcgccc	cggctccgc	aagcggagga	120
gagggcgggg	cntgcggggg	ccggagctca	naggccctgg	ggcgcctctg	ctctcccgcc	180

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atcgcaaggg cggcgctaac ctnaggcctc cccgcaaagg tccccnangc ggngggcggcg 240
gggggctgtg anaaccgcaa aaanaacgct gggcgcgcn ggaaccogtc ccccccgcg 300
aaggananac ttccacagan gcagcgtttc cacagccan agccaenttt ctaggggtgat 360
gcaccccagt aagttcctgn cggggaagct caccgctgtc aaaaaanctc ttcgctccac 420
cggcgcacna aggggangan ggcanangc tgcgcgccgc acaggtcate tgatcacgtc 480
gcccccccta ntctgctttt gtgaatctcc actttgttca accccacccg ccgttctctc 540
ctccttgccg ctctctctna ccttaanaac cagcttcttc taccnratng tanttntct 600
gcncnngtng aaattaatc ggtcnccgg aacctcttnc ctgtggcaac tgctnaaaga 660
aactgctgtt ctgnttactg cngtccc 687

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<210> 39
<211> 695
<212> DNA
<213> 人

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

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<400> 39
actagtctgg cctacaatat tgtgattcat gtaggacttc ttcatcaat tcaaaacccc 60
tagaaaaacg tatacagatt atataagtag ggataagatt tctaacattt ctgggctctc 120
tgacccctgc gctagactgt ggaaaggag tattattata gtatacaaca ctgctgttgc 180
cttattagtt ataacatgat aggtgctgaa ttgtgattca caatttaaaa acactgtaat 240
ccaaactttt ttttttaact gtagatcatg catgtgaatg ttaatgttaa tttgttcaan 300
gttggttatgg gtagaaaaaa ccacatgcct taaaatttta aaaagcaggg cccaaactta 360
ttagtttaaa attaggggta tgtttccagt ttgttattaa ntgggttatag ctctgtttag 420
aanaaatcna ngaacangat ttngaaantt aagntgacat tatttnccag tgacttgta 480
atttgaaate anacacggca ccttcogttt tggtnctatt ggnnttgaa tccaanengg 540
ntccaaatct tnttggaac ngtcnntta acttttttac nanatcttat ttttttattt 600
tggaatggcc ctatttaang ttaaaagggg ggggnnccac naccattcnt gaataaaact 660
naatatatat ccttggtccc ccaaaattta agng 695

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<210> 40
<211> 674
<212> DNA
<213> 人

<220>
<221> misc_feature
<222> (1)...(674)
<223> n = A,T,C or G

```

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<400> 40
actagtagtc agttgggagt ggttgctata ccttgacttc atttatatga atttccactt 60
tattaaataa tagaaaagaa aatcccggtg cttgcagtag agttatagga cattctatgc 120
ttacagaaaa tatagccatg attgaaatca aatagtaaag gctgttctgg ctttttatct 180
tcttagctca tottaataaa gtagtacact tgggatgcag tgcgtctgaa gtgctaata 240
gttgtaacaa tagcacaaat cgaacttagg atgtgtttct tctcttctgt gtttcgattt 300
tgatcaattc ttttaatttg ggaacctata atacagtttt cctattcttg gagataaaaa 360
ttaaatggat cactgatatt taagtcatte tgcttctcat ctnaatatc catattctgt 420
attagganaa antacctccc agcacagccc cctctcaaac cccacccaaa accaagcatt 480
tggaatgagt ctcttttatt tccgaantgt ggatgggtata acccatatcn ctccaatttc 540
tgnttggtt ggggtattaat ttgaactgtg catgaaaagn ggnaatcttt nctttgggtc 600
aaantttnc ggtaatttg nctngncaaa tccaatttnc ttttaagggtg tctttataaa 660
atttgcattt cngg 674

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<210> 41
<211> 657

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<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 41

gaaacatgca	agtaccacac	actgttttgaa	ttttgcacaa	aaagtgactg	tagggatcag	60
gtgatagccc	cggaatgtac	agtgtcttgg	tgcaccaaga	tgccttctaa	aggctgacat	120
accttggggac	cctaattgggg	cagagagtat	agccctagcc	cagtggtgac	atgaccactc	180
cctttggggag	gctgaagtta	aaggggaatgg	tatgtgtttt	ctcatggaag	cagcacatga	240
atnggttnaca	ngatgttaaa	ntaaggntct	antttgggtg	tcttgtcatt	tgaaaaantg	300
acacactcct	ancanctggg	aaaggggtgc	tggaagccat	ggaagaactc	taaaaacatt	360
agcatgggct	gatctgatta	cttctctggca	tcccgctcac	ttttatggga	agtcttatta	420
naaggatggg	ananttttcc	atatccttgc	tggttggaa	ctggaacact	ctctaaattt	480
ccctctatta	aaaatcactg	nccttactac	acttctctct	tganggaata	gaaatggacc	540
tttctctgac	ttagtctctg	gcatgggganc	cagcccaaat	taaaatctga	cttntccggg	600
ttctcngaa	ctcacctact	tgaattggta	aaacctcctt	tggaattagn	aaaaacc	657

<210> 42

<211> 389

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 42

actagtgtctg	aggaatgtaa	acaagtttgc	tgggccttgc	gagacttcac	caggttgttt	60
cgatagctca	cactcctgca	ctgtgcctgt	caccaggaa	tgtctttttt	aattagaaga	120
caggaagaaa	acaaaaacca	gactgtgtcc	cacaatcaga	aacctcogtt	gtggcagang	180
ggccttcacc	gccaccaggg	tgtcccgcca	gacagggaga	gactccagcc	ttctgaggcc	240
atcctgaaga	attcctgttt	gggggttgtg	aaggaaaatc	accoggattt	aaaaagatgc	300
tggtgcctgc	cgcgtnngtn	gggaaggagc	tggtttcctg	gtgaatttct	taaaagaaaa	360
atattttaag	ttaagaaaaa	aaaaaaaaaa				389

<210> 43

<211> 279

<212> DNA

<213> 人

<400> 43

actagtgaaca	agctcctggg	cttgagatgt	cttctcgtta	aggagatggg	ccttttggag	60
gtaaaggata	aaatgaatga	gttctgtcat	gattcactat	tctagaactt	gcatgacctt	120
tactgtgtta	gctctttgaa	tgctcttgaa	atttttagact	ttctttgtaa	acaaataata	180
tgctccttacc	attgtataaa	agctgttatg	tgcaacagtg	tggagatcct	tgtctgattt	240
aataaaatac	ttaaactctg	aaaaaaaaaa	aaaaaaaaaa			279

<210> 44

<211> 449

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 44

actagtagca	tcttttctac	aacgttaaaa	ttgcagaagt	agcttatcat	taaaaaacia	60
caacaacaac	aataacaata	aatcctaagt	gtaaatcagt	tattctaccc	cctaccaagg	120
atatcagcct	gttttttccc	ttttttctcc	tgggaataat	tgtgggcttc	ttcccaaatt	180
tctacagcct	ctttcctctt	ctcatgcttg	agcttccctg	tttgcaagca	tgcggtgtgc	240
aagantgggc	tgtttngctt	ggantnccgt	ccnagtggaa	ncatgctttc	ccttggtact	300
gttggaagaa	actcaaacct	tcnanccta	ggtgttncca	ttttgtcaag	tcatactgt	360
atTTTTgtac	tggcattaac	aaaaaaagaa	atnaaatatt	gttccattaa	actttaataa	420
aacttttaaaa	gggaaaaaaa	aaaaaaaaa				449

<210> 45

<211> 559

<212> DNA

<213> 人

<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	tgcctgtcat	tcaaacagat	gaaggcaaga	gtattgctat	tcgactaatt	240
ggtgaagctc	ttggaaaaaa	ttnactagaa	tactttttgt	gttaagttaa	ttacataagt	300
tgtattttgt	taactttatc	tttctacact	acaattatgc	ttttgtatat	atattttgta	360
tgatggatat	ctataattgt	agattttgtt	tttacaagct	aatactgaag	actcgactga	420
aatattatgt	atctagccca	tagtattgta	cttaactttt	acagggtgaa	aaaaaaattc	480
tgtgtttgca	ttgattatga	tattctgaat	aaatatggga	atatatttta	atgtgggtaa	540
aaaaaaaaaa	aaaaaggaa					559

<210> 46

<211> 731

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 46

actagttcta	gtaccatggc	tgtcatagat	gcaaccatta	tattccattt	agtttcttcc	60
tcaggttccc	taacaattgt	ttgaaactga	atatatatgt	ttatgtatgt	gtgtgtgttc	120
actgtcatgt	atatgggtga	tatgggatgt	gtgcagtttt	cagttatata	tatattcata	180
tatacatatg	catatatatg	tataatatac	atatatacat	gcatacactt	gtataatata	240
catatatata	cacatatatg	cacacatatn	atcactgagt	tccaaagtga	gtctttattt	300
ggggcaattg	tattctctcc	ctctgtctgc	tactggggcc	tttgcaagac	atagcaattg	360
cttgatttcc	tttggataag	agtcttatct	tcggcactct	tgactctagc	cttaacttta	420
gattttctatt	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	atagtttaatt	720
taggnntggg	c					731

<210> 47

<211> 640
 <212> DNA
 <213> 人
 <220>
 <221> misc_feature
 <222> (1)...(640)
 <223> n = A,T,C or G

<400> 47
 tgcgngccgg tttggccctt ctttgtanga cactttcacc cgccctgaaa tcttcccgat 60
 cgtaataaac tcttcagggt cctgcctgca caggggtttt tcttantttg ttgcctaaca 120
 gtacacaaaa tgtgacatcc ttccaccaat atngatttct tcataccaca tcttcnatgg 180
 anaagactnc aacaattttt tgatnaccn aaanactggg ggctnnaana agtacantct 240
 ggagcagcat ggacctgtcn gcnactaang gaacaanagt nntgaacatt tacacaacct 300
 ttggtatgtc ttactgaaag anagaaacat gcttctnncc ctagaccacg aggncaaccg 360
 caganattgc caatgccaag tccgagcggg tagatcagggt aatacattcc atggatgcat 420
 tacatacntt gtccccgaaa nanaagatgc cctaanggct tcttcanact ggctcngaaa 480
 acanctacac ctgggtgcttg ganaacanac tctttggaag atcatctggc acaagttccc 540
 cccagtgggt tttnccttgg cacttanctt accanactna ttcggaancc attctttgac 600
 ntggcnttnt ntggggacca ntcttctcac aactgnaccc 640

<210> 48
 <211> 257
 <212> DNA
 <213> 人

<400> 48
 actagtatat gaaaatgtaa atatcacttg tgtactcaaa caaaagtgtg tcttaagctt 60
 ccaccttgag cagccttgga aacctaacct gcctctttta gcataatcac attttctaaa 120
 tgattttctt tggctcctgaa aaagtgtatt gtattagttt tacatttgtt ttttggaaga 180
 ttatatttgt atatgtatca tcataaaata tttaaataaa aagtatcttt agagtgaana 240
 aaaaaaaaaa aaaaaaa 257

<210> 49
 <211> 652
 <212> DNA
 <213> 人

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

<400> 49
 actagttcag atgagtggct gctgaagggg ccccttctgc 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 attagactg 300
 ttttcaaagc tttcttcaca tttttaaggt gtgattttcc ttttaataata catatttatt 360
 ttcttttaaag cagctatata ccaacccatg actttggaga tatacctatn aaaccaatat 420
 aacagcangg ttattgaagc agctttctca aatgttgctt cagatgtgca agttgcaaat 480
 ttatttgtat ttgtanaata caatttttgt tttaaactgt atttcaatct atttctccaa 540
 gatgcttttc atatagagtg aaatatccca ngataactgc ttctgtgtcg togcatttga 600
 cgcataactg cacaaatgaa cagtgtatac ctcttggttg tgcattnacc cc 652

<210> 50
 <211> 650
 <212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(650)

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

<400> 50

ttgcgctttg	atTTTTtttag	ggcttTgtgcc	ctgttttcaact	tatagggtct	agaatgcttg	60
tgTTgagtaa	aaaggagatg	cccaattatc	aaagctgcta	aatgtttctct	ttgccataaa	120
gactccgtgt	aactgtgtga	acacttggga	tttttctctct	ctgtcccgag	gtcgtcgtct	180
gctttctttt	ttgggttctt	tctagaagat	tgagaaatgc	atatgacagg	ctgagancac	240
ctccccaaac	acacaagctc	tcagccacan	gcagcttctc	cacagcccca	gcttcgcaca	300
ggctcctgga	nggctgcctg	ggggaggcag	acatgggagt	gccaaagggtg	ccagatgggt	360
ccaggactac	aatgtcttta	tttttaactg	tttgccactg	ctgccctcac	ccctgcccgg	420
ctctggagta	cogtctgccc	canacaagtg	ggantgaaat	gggggtgggg	gggaacactg	480
attcccantt	aggggtgccc	taactgaaca	gtagggtatan	aagggtgtgaa	cctgngaant	540
gcttttataa	attatnttcc	ttgttanatt	tatttttttaa	tttaattctct	gttnaactgc	600
ccngggaaaa	ggggaaaaaa	aaaaaaaaat	tctnttttaa	cacatgaaca		650

<210> 51

<211> 545

<212> DNA

<213> 人

<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	cagtcttTgt	acgtggcaca	gggcaaacct	120
gactcccttt	gggcctcagt	ttccctctcc	cttcatgana	tgaaaagaat	actacttttt	180
cttgTttggtc	taacnttTgt	ggacncaaag	Tgtngtcatt	attgtttgtat	tgggtgatgt	240
gtncaaaact	gcagaagctc	actgcctatg	agaggaanta	agagagatag	tggatganag	300
ggacanaagg	agtcattatt	tggatatagat	ccaccntcc	caacctttct	ctcctcagtc	360
cctgcncctc	atgtntctgg	tntggTgagt	cctttTgtgcc	accanccatc	atgctttTgca	420
ttgctgccat	cctgggaagg	gggtgnatog	tctcacaact	Tgtttgtcatc	gtttganatg	480
catgctttct	tnatnaaaca	aanaaanna	Tgtttgacag	ngtttaaaat	aaaaaanaaa	540
caaaa						545

<210> 52

<211> 678

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(678)

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

<400> 52

actagtagaa	gaactttTgcc	gctttttTgtgc	ctctcacagg	cgcttaaagt	cattgccatg	60
ggaggaagac	gatttggggg	gggagggggg	gggggcanng	tccgtggggc	tttccctant	120
ntatctccat	ntccantggn	cnntgtcgcc	tcttccctcg	tccattnga	anttantccc	180
tggneccenn	neccctctccn	ncctnccct	ccccctccg	nccctccnn	ctttttntan	240
nettcgccat	ctccntcccc	cctnaanngtc	ccaacnccgn	cagcaatnnc	ncacttnctc	300
netccnccncc	tcennccggt	cttctntttct	cnactntnnc	nccnntnccn	tgcnnntnaa	360
annctctccc	cnctgcaanc	gattctctcc	ctccnccnna	ctntccactc	cntncttctc	420

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nencgctcct nttctcnncc ccacctctcn ccttcgncce cantacnctc nccncccttn 480
cgnntctntn nnttcctcnn accncccncc tcccttcncc cctctttctc ccggtntntc 540
tctctccncc nncnncncc cncnccncc nngcgncnt ttccgccccn cncnccntt 600
ccttctcnc cantccatcn cntntnccat nctnccncc nctcncncc gctnccccn 660
ntctctttca cactgtcc 678

```

```

<210> 53
<211> 502
<212> DNA
<213> 人

<220>
<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 ttgcatttt 120
tgacctgggg cggaaaaang caaaantgga tgagtctccg ctttgtggcc acatgggtgc 180
agatcaatat gagcagctgt cctctgaagc cctgnanget gcccgaaatt gtgccaataa 240
gtacatggta aaaagtngtg gcaagatgc ttccatatcc ggggtgggnt ccaccccttc 300
cacgtcatcc gcatcaacaa gatgttgtcc tgtgctgggg ctgacaggct cccaacaggc 360
atgcgaagtg cctttggaaa acccanggca ctgtggccag ggttcacatt gggccaattn 420
atcatgttca tccgcaccaa ctgcagaaca angaaentgt naattnaagc cctgccccagg 480
gncaanttca aatttcccgg cc 502

```

```

<210> 54
<211> 494
<212> DNA
<213> 人

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

```

```

<400> 54
actagtccaa gaaaaaatatg cttaatgtat attacaaagg ctttgtatat gttaacctgt 60
tttaagtcca aaagtgtgct ttgtccacaa ttctcctaag acctcttcag aaagggattt 120
gtttgcctta atgaatactg ttgggaaaaa acacagtata atgagtgaag agggcagaag 180
caagaaattt ctacatctta gcgactccaa gaagaatgag tatccacatt tagatggcac 240
attatgagga ctttaatctt tccttaaaac caataatgtt ttcttttttc ttttattcac 300
atgattttta agtatatttt tcatgcagga cagtttttca accttgatgt acagtgactg 360
tgttaaattt ttctttcagt ggcaacctct ataatcttta aaatatgggt agcatcttgt 420
ctgttttgaa ngggatatga cnatnaatct atcagatggg aaatcctgtt tccaagttag 480
aaaaaaaaaa aaaa 494

```

```

<210> 55
<211> 606
<212> DNA
<213> 人

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

```

```

<400> 55
actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataatgaaat 60

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gatgttaagc	tttttgaaaa	gtttagggtta	aacctactgt	tgtttagatta	atgtatttgt	120
tgcttccctt	tatctggaat	gtggcattag	ctttttttatt	ttaaccctct	ttaattctta	180
ttcaattcca	tgacttaagg	ttgggagagct	aaacactggg	atttttggat	aacagactga	240
cagttttgca	taattataat	cggcatttga	catagaaagg	atatggctac	cttttggtta	300
atctgcactt	tctaaatata	aaaaaaggga	aatgaagtat	aaatcaattt	ttgtataatc	360
tgtttgaaac	atgantttta	tttgcttaat	attanggctt	tgcccttttc	tgttagtctc	420
ttgggatcct	gtgtaaaact	gttctcatta	aacaccaaac	agttaagtcc	attctctggt	480
actagctaca	aattccgttt	catattctac	ntaacaattt	aaattaactg	aaatatttct	540
anatggtcta	cttctgtcnt	ataaaaacna	aacttgantt	nccaaaaaaa	aaaaaaaaaa	600
aaaaaa						606

<210> 56
 <211> 183
 <212> DNA
 <213> 人

<400> 56						
actagtatat	ttaaaacttac	aggettattt	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> 人

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

<400> 57						
actagtcaact	actgtcttct	ccttgtagct	aatcaatcaa	tattcttccc	ttgcctgtgg	60
gcagtggaga	gtgctgctgg	gtgtacgctg	caacctgcca	ctgagttggg	gaaagaggat	120
aatcagtgag	cactgttctg	ctcagagctc	ctgatctacc	ccacccctta	ggatccagga	180
ctgggtcaaa	gctgcatgaa	accaggccct	ggcagcaacc	tgggaaatggc	tgagggtggg	240
agagaacctg	acttctcttt	ccctctccct	cctccaacat	tactggaact	ctatcctggt	300
agggatcttc	tgagcttggt	tccctgctgg	gtgggacaga	agacaaagga	gaagggangg	360
tctacaanaa	gcagcccttc	tttgtcctct	ggggttaatg	agcttgacct	ananttcatg	420
gaganaccan	aagcctctga	tttttaattt	ccntnaaatg	tttgaagtnt	atatntacat	480
atatatat	ctttnaatnt	ttgagtcttt	gatatgtctt	aaaatccant	ccctctgccn	540
gaaacctgaa	ttaaaaccat	gaanaaaaat	gtttncctta	aagatgttan	taattaattg	600
aaacttgaaa	aaaaaaaaaa	aa				622

<210> 58
 <211> 433
 <212> DNA
 <213> 人

<400> 58						
gaacaaattc	tgattgggtta	tgtaccgtca	aaagacttga	agaaatttca	tgattttgca	60
gtgtggaagc	gttgaaaatt	gaaagttact	gcttttccac	ttgctcatat	agtaaagggg	120
tccttttcagc	tgccagtgtt	gaataatgta	tcattccagag	tgatgttatc	tgtagacgtc	180
accagcttta	agctgaacca	ttttatgaat	accaaataaa	tagacctctt	gtactgaaaa	240
catattttgtg	actttaatcg	tgctgcttgg	atagaaatat	ttttactggg	tcttctgaat	300
tgacagtaaa	cctgtccatt	atgaatggcc	tactgttcta	ttatttgttt	tgacttgaat	360
ttatccacca	aagacttcat	ttgtgtatca	tcaataaagt	tgtatgtttc	aactgaaaaa	420
aaaaaaaaaa	aaa					433

<210> 59
 <211> 649
 <212> DNA
 <213> 人

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

<400> 59
 actagttatt atctgacttt cngggtataa tcattctaata gagtgtgaag tagcctctgg 60
 tgtcatttgg atttgcattt ctctgatgag tgatgctatc aagcaccttt gctgggtgctg 120
 ttggccatat gtgtatgttc cctggagaag tgtctgtgct gagccttggc ccacttttta 180
 attagcgctn tgtcttttta ttactgagtt gtaaganttc tttatatatt ctggattcta 240
 gacccttata agatacatgg tttgcaaata tttctccca ttctgtgggt tgtgttttca 300
 ctttatcgat aatgtcctta gacatataat aaatttgtat tttaaaagtg acttgatttg 360
 ggctgtgcaa ggtgggctca cgcttgtaat cccagcactt tgggagactg aggtgggtgg 420
 atcatatgan gangctagga gtctgaggtc agcctggcca gcatagcgaa aacttgtctc 480
 tacnaaaaaat acaaaaatta gtcaggcatg gtggtgcacg tctgtaatac cagcttctca 540
 ggangctgan gcacaaggat cacttgaacc ccagaangaa gangttgcag tganctgaag 600
 atcatgccag ggcaacaaaa atgagaactt gtttaaaaaa aaaaaaaaaa 649

<210> 60
 <211> 423
 <212> DNA
 <213> 人

<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 ttttttttcc cattagtana acacaagact cngattcagc cgaattgtgg 240
 tgtcttacaa ggcagggtct tctacaggg ggtgganaaa acagccttcc ttccttgggt 300
 aggaattggc tgagttggcg ttgtgggcag gctactgggt tgtatgatgt attagtagag 360
 caaccatta atcttttgta gtttgatna aacttganct gagaccttaa acaaaaaaaaaa 420
 aaa 423

<210> 61
 <211> 423
 <212> DNA
 <213> 人

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

<400> 61
 cgggactgga atgtaaagtg aagttcggag ctctgagcac gggtctctcc cgccgggtcc 60
 tccctcccca gacccagag ggagaggccc acccgcacca gccccgcccc agccctgct 120
 caggtctgag tatggctggg agtcgggggc cacaggcctc tagctgtgct gctcaagaag 180
 actggtacag ggtanctaca agtggcggg ccttgccctt gggattctac cctgttccta 240
 atttgggtgtt ggggtgcggt gtcctggcc ccttttccca cactnccctc ctccngacag 300
 caacctccct tggggcaatt gggcctggnt ctccncccnh tgttgcnaac ctttgttgggt 360

ttaaggnctt taaaaatggt annttttccc ntgccnggggt taaaaaagga aaaaactnaa 420
aaa 423

<210> 62
<211> 683
<212> DNA
<213> 人

<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 gggaaatggt cctgccttca ggaaagtgaa agacgcttag 120
gctgtcaaca cttaaaggaa gtcccccctga agcccagagt ggacagacta gacccattga 180
tgggggccact ggccatggtc cgtggacaag acattccngt gggccatggc acaccggggg 240
ggatcaaaat gtgtacttgt ggggtctcgc cccttgccaa aaacaaacca ntcccactcc 300
tgtcnttggg ctttcttccc attccctcct ccccaaatgc acttccccctc ctccctctgc 360
ccctcctgtg tttttggaat tctgtttccc tcaaaattgt taatttttta nttttngacc 420
atgaacttat gtttggggtc nangttcccc ttnccaatgc atactaatat attaattggt 480
atattttttt gaaatatttt ttaatgaact tggaaaaaat tnntggaatt tccttncttc 540
cntttntttt ggggggggtg gggggntggg ttaaaatttt tttggaancc cnatnggaaa 600
ttnttacttg gggcccccct naaaaaantn anttccaatt cttnnatngc ccctnttccn 660
ctaaaaaaa ananannaaa aan 683

<210> 63
<211> 731
<212> DNA
<213> 人

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

<400> 63
actagtcata aagggtgtgc gcgtcttcga cgtggcggtc ttggcgccac tgetgcgaga 60
cccggccctg gacctcaagg tcatccactt ggtgcgtgat ccccgcgcgg tggcgagttc 120
acggatccgc tcgcgccacg gcctcatccg tgagagccta cagggtggtg gcagccgaga 180
ccgcgagctc accgcatgcc cttcttggag gccgcgggcc acaagcttgg cgcccahaaa 240
gaaggcgtng ggggcccga aantaccacg ctctggcgcg tatggaangt cctcttgcaa 300
taatattggt tnaaaanctg canaanagcc cctgcanccc cctgaactgg gntgcagggc 360
cncttacctn gtttggntgc ggttacaaag aacctgtttn ggaaaaccct nccnaaaacc 420
ttccgggaaa attntncaaa ttttnttgg ggaattnttg ggtaaaccct ccnaaaatgg 480
gaaacntttt tgccctnnaa antaaaccat tnggttccgg gggccccccc ncaaaaccct 540
ttttntttt tttntgcccc cantnncccc ccggggcccc ttttttngg ggaaaanccc 600
ccccctncc nanantttta aaagggnggg anaatttttn nttnecccc gggncecccn 660
ggngntaaaa nggtttcncc ccccgaggg gnggggnhnc ctennaacc cntntcnna 720
cncnttttn n 731

<210> 64
<211> 313
<212> DNA
<213> 人

<220>
<221> misc_feature
<222> (1)...(313)

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

<400> 64

actagttgtg	caaaccacga	ctgaagaaa	acgaaaagt	ggaaataact	tgcaacgtct	60
gtagagatg	gttgctacac	atgttgggtc	tgtagagaaa	catcttgagg	agcagattgc	120
taaagttgat	agagaatatg	aagaatgcat	gtcagaagat	ctctcggaan	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> 人

<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	tccttccctg	120
tctgggaggt	tggagggaag	aatctaggcc	ttagcttgcc	ctctgccac	ccttcccctt	180
gtagatactg	ccttaacact	cctctctctc	tcagctgtgg	ctgccacca	agccagggtt	240
ctccgtgtct	actaatttat	ttccaggaaa	gggtgtgtga	agacatgagc	cgtgtataat	300
atttgtttta	acattttcat	tgcaagtatt	gaccatcatc	cttggttgtg	tatcgttgta	360
acacaaatta	atgatattaa	aaagcatcca	aacaaagccn	annnnnaana	nnannngaaa	420

<210> 66

<211> 676

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(676)

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

<400> 66

actagtttcc	tatgatcatt	aaactcattc	tcagggttaa	gaaaggaatg	taaattttctg	60
cctcaatttg	tacttcatca	ataagttttt	gaagagtcca	gattttttagt	caggtcttaa	120
aaataaaact	acaaatctgg	atgcatttct	aaattctgca	aatgtttcct	ggggtgactt	180
aacaaggaat	aatcccacaa	tatacctagc	tacctaatac	atggagctgg	ggctcaacct	240
actgttttta	aggattttcg	cttacttgtg	gctgaggaaa	aataagtagt	tcogagggaa	300
gtagttttta	aatgtgagct	tatagatngg	aaacagaata	tcaacttaat	tatggaaatt	360
gttagaaacc	tgttctcttg	ttatctgaat	cttgattgca	attactattg	tactggatag	420
actccagccc	attgcaaagt	ctcagatata	ttanctgtgt	agttgaattc	cttggaaatt	480
ctttttaaga	aaaaattgga	gttttaaaaga	aataaaacccc	tttgttaaat	gaagcttggc	540
tttttggtga	aaaanaatca	tccccagggg	cttattgttt	aaaaanggaa	ttttaagcct	600
ccctggaaaa	anttgttaat	taaatgggga	aaatgntggg	naaaaattat	ccgttagggg	660
ttaaagggaa	aactta					676

<210> 67

<211> 620

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(620)

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

<400> 67

caccattaaa	gctgcttacc	aagaacttcc	ccagcatttt	gacttccttg	tttgatagct	60
gaattgtgag	caggtgatag	aagagccttt	ctagttgaac	atacagataa	tttgctgaat	120
acattccatt	taatgaagg	gttacatctg	ttacgaagct	actaagaagg	agcaagagca	180
taggggaaaa	aaatctgac	agaacgcac	aaactcacat	gtgccccctc	tactacaaac	240
agattgtagt	gctgtggtgg	tttattccgt	tgtgcagaac	ttgcaagctg	agtcactaaa	300
cccaaagaga	ggaaattata	ggttagttaa	acattgtaat	cccaggaact	aagtttaatt	360
cacttttgaa	gtgttttgtt	ttttattttt	ggtttgtctg	atttactttg	ggggaaaang	420
ctaaaaaaa	agggatatca	atctctaatt	cagtgcacac	taaaagtgtg	ccctaaaag	480
tctttactgg	aanttatggg	actttttaag	ctccaggtnt	tttggtcctc	caaattaacc	540
ttgcatgggc	cccttaaaat	tgttgaangg	catttcctgcc	tctaagtttg	gggaaaattc	600
ccccnttttn	aaaatttgga					620

<210> 68

<211> 551

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 68

actagtagct	ggtacataat	cactgaggag	ctatttctta	acatgctttt	atagaccatg	60
ctaattgctag	accagtattt	aagggtcaat	ctcacacctc	cttagctgta	agagtctggc	120
ttagaacaga	cctctctgtg	caataacttg	tggccactgg	aaatccctgg	gccggcattt	180
gtattggggg	tgcantgact	cccaagggcc	aaaagagtta	aaggcacgac	tgggatttct	240
tctgagactg	tgggtgaaact	ccttccaagg	ctgagggggg	cagtangtgc	tctgggaggg	300
actcggcacc	actttgatat	tcaacaagcc	acttgaaagg	caattatana	attgttattt	360
tacagctgat	ggaactcaat	ttgaaccttc	aaaactttgt	tagtttatcc	tatttatattg	420
ttaaacctaa	ttacattttg	ctagcattgg	atttggttcc	tgtngcatat	gtttttttcn	480
cctatgtgct	cccccccc	nnatcttaat	ttaaaccnca	attttgcnat	tcnccnnnnn	540
nannnannna	a					551

<210> 69

<211> 396

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(396)

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

<400> 69

cagaaatgga	aagcagagtt	ttcattttctg	tttataaacy	tctccaaaca	aaaatggaaa	60
gcagagtttt	cattaaatcc	ttttaccttt	tttttttctt	ggtaatcccc	tcaaatmaca	120
gtatgtggga	tattgaatgt	taaagggata	tttttttcta	ttatttttat	aattgtacaa	180
aattaagcaa	atgttaaaag	ttttatatgc	ttttattaatg	ttttcaaaag	gtatnataca	240
tgtgatacat	tttttaagct	tcagttgctt	gtcttctggt	actttctggt	atgggctttt	300
ggggagccan	aaaccaatct	acnatctctt	tttgtttgcc	aggacatgca	ataaaattta	360
aaaaataaat	aaaaactatt	nagaatttga	aaaaaa			396

<210> 70

<211> 536

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(536)

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

<400> 70

actagtgc	aaagcaaatat	aaacatcgaa	aaggcggttc	tcacgttagc	tgaagatata	60
cttcgaaaga	ccctgtataa	agagcccaac	agtgaataatg	tagatatcag	cagtggagga	120
ggcgtgacag	gctggaagag	caaatgctgc	tgagcattct	cctgttccat	cagttgccat	180
ccactacccc	gttttctctt	cttgctgcaa	aataaaccac	tctgtccatt	tttaactcta	240
aacagatatt	tttgtttctc	atcttaacta	tccaagccac	ctatttttatt	tgttctttca	300
tctgtgactg	cttgctgact	ttatcataat	tttcttcaaa	caaaaaaatg	tatagaaaaa	360
tcagtgtctg	gacttcattt	ttaatgnta	cttgctcagc	tcaactgcat	ttcagttggt	420
ttatagtcca	gttcttatca	acattnaaac	ctatngcaat	catttcaaat	ctattctgca	480
aattgtataa	gaataaaaagt	tagaatttaa	caattaaaaa	aaaaaaaaaa	aaaaaa	536

<210> 71

<211> 865

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(865)

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

<400> 71

gacaaagcgt	taggagaaga	anagaggcag	ggaanactnc	ccaggcacga	tgggcncctt	60
cccaccagca	accagcgccc	cccaccagcc	cccaggcccc	gacgacgaag	actccatcct	120
ggattaatct	nacctctntc	gcctgnccca	ttcctacctc	ggagggtggag	gccggaaagg	180
toncaccaag	aganaanctg	ctgccaaacac	caaccgcccc	agtcctggcg	ggcacganag	240
gaaactgggtg	accaatctgc	agaattctna	gaggaanaag	cnagggggccc	cgcgctnaga	300
cagagctgga	tatgangcca	gaccatggac	ntacncccn	ncaatncana	cgggactgcg	360
gaagatggan	gaccnncgac	nngatcaggc	cngctnncca	nccccccacc	cctatgaatt	420
attcccgcgtg	aangaatctc	tgannggctt	ccannaaagc	gcctccccnc	cnaacgnaan	480
tncaacatng	ggattanang	ctgggaactg	naaggggcaa	ancctnnaat	atccccagaa	540
acaanctctc	ccnaanaaac	tggggcncct	catnggtggn	accaactatt	aactaaaccg	600
cacgccaaagn	aantataaaa	ggggggcccc	tcnccggnng	accccccttt	gtcccttaat	660
ganggttata	cnccttggtt	accatggtnc	ccnnttctgt	ntgmatgttt	ccnctcccct	720
ccncetatnt	cnagccgaac	tcnnatttnc	ccgggggtgc	natcnantng	tncccttttn	780
ttngttgncc	cngcccttcc	cgnccggaacn	cgtttccccc	ttantaacgg	caccgggggn	840
aagggtgntt	ggccccctcc	ctccc				865

<210> 72

<211> 560

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 72

cctggacttg	tcttggttcc	agaacotgac	gacccggcga	cggcgacgtc	tcttttgact	60
aaaagacagt	gtccagtgtc	ccagcctagg	agtctacggg	gacccgctcc	cgcgcgcgca	120
ccatgcccaa	cttctctggc	aactggaaaa	tcattccgatc	ggaaaaacttc	gangaattgc	180
tcaantgtct	gggggtgaat	gtgatgctna	ngaanattgc	tgtggctgca	gcgtccaagc	240

cagcagtgga	gatcnaacag	gagggagaca	ctttctacat	caaaacctcc	accaccgtgc	300
gcaccacaaa	gattaacttc	nnngttgggg	aggantttga	ggancaaact	gtggatngga	360
ngcctgtnaa	aacctggtga	aatgggagaa	tganaataaa	atgggtctgt	ancanaaact	420
cctgaaagga	gaaggccccc	anaactcctg	gaccngaaaa	actgaccnc	cnatngggga	480
actgatnctt	gaaccctgaa	cgggcgggat	ganccttttt	tnttgccncc	naanggggtc	540
tttcnntttc	cccaaaaaaa					560

<210> 73

<211> 379

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 73

ctggggancc	ggcggtnggc	nccatntcnn	gncgcgaagg	tggtcaataaa	aancnctga	60
aaccgcncaa	naaacatgcc	naagatatgg	acgagggaaga	tnngctttc	nngnacaaac	120
gnanngagga	acanaacaaa	ctcnangagc	tctcaagcta	atgccgcggg	gaagggggccc	180
ttggccacnn	gtggaattaa	gaaatctggc	aaanngtann	tggtccttgt	gcctnangag	240
ataagnagcc	ctttatttca	tctgtattta	aacctctctn	ttccctgnca	taacttcttt	300
tnccacgtan	agntggaant	anttgttgtc	ttggactggt	gtncatttta	gannaaactt	360
ttgttcaaaa	aaaaaataa					379

<210> 74

<211> 437

<212> DNA

<213> 人

<220>

<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	ggcctcgca	taaaaaacaaa	120
acaaaaaaaa	gctgccaggt	tttanaagca	gttctggtct	caaaaccatc	aggatcctgc	180
caccagggtt	cttttgaaat	agtaccacat	gtaaaaggga	atttggcttt	cacttcatct	240
aatcactgaa	ttgtcaggct	ttgattgata	attgtagaaa	taagtagcct	tctgttgtgg	300
gaataagtta	taatcagtat	tcatctcttt	gttttttgtc	actcttttct	ctctnattgt	360
gtcatttcta	ctgtttgaaa	aatatttctt	ctataaaatt	aaactaacct	gccttaaaaa	420
aaaaaaaaaa	aaaaaaa					437

<210> 75

<211> 579

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1) ... (579)

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

<400> 75

ctccgtcgcc	gccaaagatga	tgtgcggggc	gcctccggcc	acgcagccgg	ccaccgcoga	60
gaccagcac	atgcgcgacc	aggtgaggtc	ccagcttgaa	gagaagaaa	acaagaagtt	120
ccctgtgttt	aaggccgtgt	cattcaagag	ccaggtggtc	gcggggacaa	actacttcat	180

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caaggtgcac gtcggcgacg aggaacttcgt acacctgcga gtgttccaat ctctccctca 240
tgaaaacaag cccttgacct tatctaacta ccagaccaac aaagccaagc atgatgagct 300
gacctatttc tgatcctgac tttggacaag gcccttcagc cagaagactg acaaagtcac 360
cctccgtcta ccagagcgtg cacttgtgat cctaaaataa gcttcacatc cgggctgtgc 420
ccttgggggtg gaagggggcan gatctgcact gcttttgcac ttctcttcct aaatttcatt 480
gtgttgattc tttccttcca ataggtgatc ttnattactt tcagaatatt ttccaaatna 540
gatatatatt naaatcctt aaaaaaaaaa aaaaaaaaaa 579

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<210> 76

<211> 666

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(666)

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

<400> 76

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gtttatccta tctctccaac cagattgtca gctccttgag ggcaagagcc acagtatatt 60
tccctgtttc ttccacagtg cctaataata ctgtggaact aggttttaac aattttttta 120
ttgatgttgt tatgggcagg atggcaacca gaccattgtc tcagagcagg tgctggctct 180
ttcctgggta ctccatgttg gctagcctct ggtaacctct tacttattat cttcaggaca 240
ctcactacag ggaccagggg tgatgcaaca tccctgtcct tttatgacag gatgtttgct 300
cagcttctcc aacaataaaa agcacgtggt aaaacacttg cggatattct ggactgtttt 360
taaaaaatat acagttttacc gaaatcata ttatcttaca atgaaaagga ntttatagat 420
cagccagtgga acaacctttt cccaccatac aaaaattcct tttcccgaan gaaaanggct 480
ttctcaataa ncctcacttt cttaanactc tacaagatag ccccganac ttatcgaaac 540
tcatttttagg caaatatgan ttttattgtc cgttacttgt ttcaaaattt ggtattgtga 600
atatcaatta ccaccccatc ctcccatgaa anaaanggga aanggtgaan ttcntaancg 660
cttaaa 666

```

<210> 77

<211> 396

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(396)

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

<400> 77

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ctgcagcccg ggggatccac taatctacca nggttatttg gcagctaatt ctanatttgg 60
atcattgccc aaagttagcac ttgctgggtc cttgggattt ggccttggaa aggtatcata 120
catanganta tgccanaata aattccattt ttttgaaat canctccttg gggctggttt 180
tggtccacag cataacangc actgcctcct tacctgtgag gaatgcaaaa taaagcatgg 240
attaagttag aagggagact ctcagccttc agcttcctaa attctgtgtc tgtgactttc 300
gaagtttttt aaacctctga atttgtacac atttaaaatt tcaagtgtac tttaaaataa 360
aatacttcta atgggaacaa aaaaaaaaaa aaaaaa 396

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<210> 78

<211> 793

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(793)

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

<400> 78
gcacccctagc cgcccgactca cacaaggcag gtgggtgagg aaatccagag ttgccatgga 60
gaaaaattcca gtgtcagcat tcttgctcct tgtggccctc tctacactc tggccagaga 120
taccacagtc aaacctggag ccaaaaagga cacaaggac tctcgacca aactgcccc 180
gaccctctcc agagggttggg gtgaccaact catctggact cagacatatg aagaagctct 240
atataaatcc aagacaagca acaaacccctt gatgattatt catcacttgg atgagtgc 300
acacagtcna gctttaaaga aagtgtttgc tgaataaaa gaaatccaga aattggcaga 360
gcagtttgc ctcctcaatc tggtttatga aacaactgac aaacaccttt ctctgatgg 420
ccagtatgtc ccaggattat gtttgttgac ccctctctga cagttgaagc cgtatcctg 480
ggaagatatt cnaaccgtct ctatgcttac aaactgcaga tacgctctgt tgcttgacac 540
atgaaaaagc tctcaagttg ctnaaatga attgtaagaa aaaaaatctc cagccttctg 600
tctgtcggct tgaataatga aaccagaaaa atgtgaaaaa tggctattgt ggaacanatn 660
gacacctgat taggttttgg ttatgttcac cactattttt aaaaaaaaaa nttttaaaaa 720
ttggttcaat tntctttttn aaacaatntg tttctacntt gnganctgat ttctaaaaaa 780
aataatnttt ggc 793

<210> 79

<211> 456

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 79
actagtatgg ggtgggaggc cccacccttc tcccctaggc gctgttcttg ctccaaaggg 60
ctccgtggag agggactggc agagctgang ccacctgggg ctggggatcc cactcttctt 120
gcagctgttg agcgaccta accactggtc atgccccac cctgctctc cgcaccgct 180
tctcccgac cccangacca ggctacttct cccctctctc tgcctccctc ctgcccctgc 240
tgctctgat cgtangaatt gangantgtc cdgecttgtg gctganaatg gacagtggca 300
ggggctggaa atgggtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt gcnccccccc 360
tgcaagaccg agattgaggg aaancatgtc tgctgggtgt gaccatgttt cctctccata 420
aantncccc ctgtacnctca naaaaaaaaa aaaaaa 456

<210> 80

<211> 284

<212> DNA

<213> 人

<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 acttttagca cacatactaa aattggaacc atactgagaa 120
gaatagcatg acctccgtgc aaacaggaca agcaaatgtg tgatgtgttg attaaaaaga 180
aataaataaa tgtgtatatg tgttaactgt atgtttatgt ggaatacaga ttgggaataa 240
aaatgtattt cttactgtga aaaaaaaaaa aaaaaaaaaa aana 284

<210> 81

<211> 671

<212> DNA

<213> 人

<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 ctatctgcca agagtagaaa 120
 gaaaggctgg ggatatttgg gttggcttgg ttttgatttt ttgcttggtt gtttgttttg 180
 tactaaaaca gtattatctt ttgaatatcg tagggacata agtatataca tgttatccaa 240
 tcaagatggc tagaatgggt cctttctgag tgtctaaaac ttgacacccc tggtaaattct 300
 ttcaacacac ttccactgcc tgcgtaatga agttttgatt catttttaac cactggaatt 360
 tttcaatgcc gtcattttca gttagatnat ttgcacttt gagattaaaa tgccatgtct 420
 atttgattag tcttattttt ttatttttac aggccttatca gtctcactgt tggctgtcat 480
 tgtgacaaag tcaataaac cccnaggac aacacacagt atgggatcac atattgtttg 540
 acattaagct ttggccaaaa aatgttgcac gtgttttacc tcgacttgc aaatcaatan 600
 canaaaggct ggctnataat gttggtgggt aaataattaa tnantaacca aaaaaaaaaa 660
 aaaaaaaaaa a 671

<210> 82
 <211> 217
 <212> DNA
 <213> 人

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

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

<210> 83
 <211> 460
 <212> DNA
 <213> 人

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

<400> 83
 cgcgagtggg agcaccagga tctcgggctc ggaacgagac tgacaggatt gttttaagaa 60
 aatggcagac aaaccagaca tgggggaaat cgccagcttc gatnaggcca agctgaanaa 120
 aacggagacg caggagaaga acacctgcc gaccaaagag accattgagc angagaagcg 180
 gagtgaaatt tcctaagatc ctggaggatt tectacccc gtectcttcg agacccagct 240
 cgtgatgtgg aggaagagcc acctgcaaga tggacacgag ccacaagctg cactgtgaac 300
 ctgggcactc cgcgccgatg ccaccggcct gtgggtctct gaagggaccc cccccaatcg 360
 gactgccaaa ttctccggtt tgcccgggga tattatacaa nattatttgt atgaataatg 420
 annataaaac acacctcgtg gcancaaaaa aaaaaaaaaa 460

<210> 84
 <211> 323
 <212> DNA
 <213> 人

<220>

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

<400> 84
 tgggtggatct tggctctgtg gagctgctgg gacgggatct aaaagactat tctggaagct 60
 gtgggtccaan gcatttttgc ggcttaacgg gtcccggaac aaaggacacc agctctctaa 120
 aattgaagtt taccgganac aacaatcttt tgggcagaga tgectatctt aacaaacncc 180
 gtccctgcgc aacaacnaac aatctctggg aaataccggc catgaacntg ctgtctcaat 240
 cnancatctc tctagctgac cgatcatatc gtcccagatt actacanatc ataataattg 300
 atttctgtga naaaaaaaaa aaa 323

<210> 85
 <211> 771
 <212> DNA
 <213> 人

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

<400> 85
 aaactgggta ctcaacactg agcagatctg ttctttgagc taaaaacccat gtgctgtacc 60
 aanagtttgc tccctggctgc tttgatgtca gtgctgctac tccacctctg cggcgaatca 120
 gaagcaagca actttgactg ctgtcttgga tacacagacc gtattcttca tcctaaattt 180
 attgtgggct tcacacggca gctggccaat gaaggctgtg acatcaatgc tatcatcttt 240
 cacacaanga aaaagtgtgc tgtgtgcgca aatccaaaac agacttgggt gaaatatatt 300
 gtgcgtctcc tcagtaaaaa agtcaagaac atgtaaaaac tgtggctttt ctggaatgga 360
 attggacata gcccaagaac agaaagaact tgctggggtt ggagggtttca cttgcacatc 420
 atgganggtt tagtgcttat cttattttgt cctcctggac ttgtccaatt natgaagtta 480
 atcatattgc atcatanttt gctttgttta acatcacatt naaattaaac tgtattttat 540
 gttattttata gctntaggtt ttctgtgttt aactttttat acnaantttc cttaaactatt 600
 ttggtnant gcaanttaa aattatattt ggggggggaa taatatattg antttctgca 660
 gccacaagct ttttttaaaa aaccantaca nccnngttaa atggtnngtc ccaatgggtt 720
 tttgcttttn antagaaat ttnttagaac natttgaaaa aaaaaaaaa a 771

<210> 86
 <211> 628
 <212> DNA
 <213> 人

<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 gtgaccttc ttgtcataag 120
 attatcttaa agctgaagcc aaaatatgct tcaaaagaaa angactttat tgttcattgt 180
 agttcatata ttcaaaagcat ctgaactgta gtttctatag caagccaatt acatccataa 240
 gtggagaaang aaatagatta atgtcnaagt atgattgggt gagggagcaa ggttgaagat 300
 aatctgggggt tgaaattttc tagttttcat tctgtacatt tttagttnga catcagattt 360
 gaaatattaa tgtttacctt tcaatgtgtg gtatcagctg gaetcantaa cacccttttc 420
 ttccctnnggg gatggggaat ggattattgg aaaatggaaa gaaaaaagta cttaaagcct 480
 tcccttcnca gtttctggct cctaccctac tgatttancc agaataagaa aacattttat 540
 catcntctgc tttattccca ttaatnaant tttgatgaat aaatctgctt ttatgcnnac 600
 ccaaggaatt nagtggnttc ntcnttgt 628

<210> 87
 <211> 518
 <212> DNA
 <213> 人

<220>
 <221> misc feature
 <222> (1)...(518)
 <223> n = A,T,C or G

<400> 87
 tttttttattt ttttttagaga gtagttcagc tttttatttat aaattttattg cctgtttttat 60
 tataacaaca ttatactgtt tatggtttaa tacatatggt tcaaaatgta taatacatca 120
 agtagtacag tttttaaatt ttatgcttaa aacaagtttt gtgtaaaaaa tgcagataca 180
 ttttacatgg caaatcaatt ttttaagtcac cctaaaaattt gattttttttt tgaaatttaa 240
 aaacacattt aattttcaatt tctctcttat ataaccctta ttactatagc atgggtttcca 300
 ctacagttaa acaatgcagc aaaattccca tttcacggtt aattgggttt taagcggcaa 360
 ggtaaattg ctttgaggat cctnaatacc ctttgaactt caaatgaagg ttatgggtgt 420
 naatttaacc ctcatgccat aagcagagca acaagtttag ctgcattttg ctctaaactg 480
 taaaancgag cccccgttg aaaaagcaaa agggaccac 518

<210> 88
 <211> 1844
 <212> DNA
 <213> 人

<400> 88
 gagacagtga atcctagtat caaaggattt ttggcctcag aaaaagtgtg tgattattttt 60
 tatttttattt tatttttctga gactccgtct caaaaaaa aaiaaaaaaa agaatcacaa 120
 ggtattttgct aaagcatttt gagctgcttg gaaaaagggg agtagttgca gtagagtttc 180
 ttccatcttc ttgggtgctgg gaagccatat atgtgtcttt tactcaagct aaggggtata 240
 agcttatgtg ttgaattttgc tacatctata tttcacatat tctcacaata agagaatttt 300
 gaaatagaaa tatcatagaa catttaagaa agtttagtat aaataatatt ttgtgtgttt 360
 taateccctt gaagggatct atccaaagaa aatattttac actgagctcc ttctacacg 420
 tctcagtaac agatccgtg ttagtctttg aaatatagctc atttttttaa tgcagtgag 480
 tagatgtagc atacatatga tgtataatga cgtgtattat gttacaatg tctgcagatt 540
 ttgtaggaa acaaaaacatg gcctttttta taagcaaaac gggccaatga ctagaataac 600
 acatagggca atctgtgaat atgtattata agcagcattc cagaaaaagta gttgggtgaa 660
 taattttcaa gtcaaaaagg gatattgaaa ggaattatg agtaacctct atttttttaag 720
 ccttgctttt aaatttaaag ctacagccat ttaagccttg aggataataa agcttgagag 780
 taataatgtt aggttagcaa aggttttagat gtatcacttc atgcatgcta ccatgatagt 840
 aatgcagctc ttcgagtcac ttctggtcac tcaagatatt cacccttttg cccatagaaa 900
 gcacctacc tcacctgctt actgacattg tcttagctga tcacaagatc attatcagcc 960
 tccattattc cttactgtat atnaaataca gagttttata ttttcctttc ttogtttttc 1020
 accatattca aaacctaaat ttgtttttgc agatggaaatg caaagtaatc aagtgttcgt 1080
 gctttcacct agaaggggtg ggtcctgaag gaaagaggtc cctaaatata cccaccctg 1140
 ggtgctcttc ctccctgggt accctgacta ccagaagtca ggtgctagag cagctggaga 1200
 agtgcagcag cctgtgcttc cacagatggg ggtgctgctg caacaaggct ttcaatgtgc 1260
 ccatcttagg gggagaagct agatccgttg cagcagcctg gtaagtccctg aggaggttcc 1320
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 catgtagcta acttgtgctt ctgcttatgc atgagggtta aattaacaac cataaccttc 1440
 atttgaagggt caaagggtgta ttcaggatcc tcaaaagcatt ttaaccttgc cgcttaaaac 1500
 ccaatttacc gtgaattggg aattttgtct cattgttaaa ctgtagtga aacctagcta 1560
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 aaaatcaatc tttaggatga cttaaaaatt gatttgccat gtaaaatgta tctgcatttt 1680
 ttacacaaaa cttgttttaa gcataaaatt ttaaaactgt actacttgat gtattatata 1740
 ttttgaaoca tatgtattaa accataaaaa gtataatgtt gttataataa aacaggcant 1800
 aaattttata ataaaagctg aaaaaaaaaa aaaaaaaaaa aaaa 1844

<210> 89

<211> 523

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 89

tttttttttt	tttttttttagt	caatccacat	ttattgatca	cttattatgt	accaggcact	60
gggataaaga	tgactgttag	tcactcacag	taaggaaaga	aactagcaaa	taagacgatt	120
acaatatgat	gtagaaaatg	ctaagccaga	gatatagaaa	ggtcctattg	ggtccttctg	180
tcaccttgtc	tttccacatc	cctacccttc	acaggccttc	cctccagctt	cctgcccccg	240
ctccccactg	cagatccccc	gggattttgc	ctagagctaa	acgagganac	gggccccctg	300
gccttgcat	gaactgaacc	caaccacaga	ctgggaagg	gagcctttcg	anagtggatc	360
actttgatna	gaaaacacat	aggggaattga	agagaaantc	cccaaattgc	cacccgtgct	420
ggtgctcaag	aaaagtttgc	agaattggata	aattgaaggat	caagggaatt	aatanatgaa	480
taattgaatg	gtggctcaat	aagaatgact	ncnttgaatg	acc		523

<210> 90

<211> 604

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 90

ccagtgtggt	ggaatgcaaa	gattaccccg	gaagctttcg	agaagctggg	attccctgca	60
gcaaaggaaa	tagccaatat	gtgtcggttc	tatgaantga	agccagaccg	agatgtcaat	120
ctcaccacc	aactaaatcc	caaagtcaaa	agcttcagcc	agtttatctc	agagaaccag	180
gggagccttc	aaggggcatgt	agaaaatcag	ctgttcagat	aggcctctgc	accacacagc	240
ctctttcctc	tctgatcctt	ttcctcttta	cggcacaaaca	ttcatgtttg	acagaacatg	300
ctggaatgca	attgttttgc	acaccgaagg	atttcctgcg	gtcgcctctt	cagtaggaag	360
cactgcattg	gtgataggac	acggtaattt	gattcacatt	taacttgcta	gttagtgata	420
aggggtggta	cacctgtttg	gtaaaatgag	aagcctcgga	aacttgggag	cttctctcct	480
accactaatg	gggagggcag	attattactg	ggatttctcc	tgggggtgaat	taatttcgaag	540
cactaatg	tgaaattccc	ctnggcaggc	tccagttttc	tcaactgcat	tgcaaaattc	600
cccc						604

<210> 91

<211> 858

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 91

tttttttttt	tttttttttta	tgattattat	tttttttatt	gatctttaca	tcctcagtgt	60
tggcagagtt	tctgatgctt	aataaacatt	tgttctgac	agataagtgg	aaaaaattgt	120
catttcctta	ttcaagccat	gcttttctgt	gatattctga	tcctagtgtg	acatacagaa	180
ataaatgtct	aaaacagcac	ctogattctc	gtctataaca	ggactaagtt	cactgtgatc	240
ttaastaagc	ttggctaaaa	tgggacatga	gtggaggtag	tcacacttca	gcgaagaaag	300
agaatctcct	gtataatctc	accaggagat	tcaacgaatt	ccaccacact	ggactagtgg	360

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atcccccggtg ctgcaggaat tcgatatcaa gcttatcgat accgtcgacc tcgagggggg 420
gcccggtacc caattcgccc tatagtgagt cgtattacgc gcgctcactg gccgtcgttt 480
tacaacgtcg tgactgggaa aaccctggcg ttacccaact taatcgctt gcagcacatc 540
cccttttcgc cagctggcgt aatagcgaan agcccgacc gatcgccctt ncaacagttg 600
cgacgctga atggcgaatg ggacgcgcc cgtacgctt tgtagcgcg cattaaagcg cggcngggtg 660
tgngngntcc cccacgtgac cgtacactt ggcagcgct taecgcggtc ntctgctttc 720
ttcccttctt ttctcgacc gttcgccggg tttccccgnn agctnttaat cgggggntct 780
cctttanggg tncnaattaa nggnttacng gaccttngan cccaaaaact ttgattaggg 840
ggaaggtccc cgaagggg 858

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<210> 92

<211> 585

<212> DNA

<213> 人

<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 gccaaagotta ttttaagatca cagtgaactt agtcctgtta 120
tagacgagaa tcgaggtgct gtttttagaca tttattttctg tatgttcaac taggatcaga 180
atatcacaga aaagcatggc ttgaataagg aatgacaat tttttccact tatctgatca 240
gaacaaatgt ttatttaagca tcagaaactc tgccaacact gaggatgtaa agatcaataa 300
aaaaataat aatcatnann naanannann nngaaggcg gccgccaccg cgggtggagct 360
ccagcttttg ttccctttag tgagggttaa ttgcgcgctt ggggttaatc atgggtcatag 420
ctgtttcctg tgtgaaattg ttatccggct cacaattccn cncacatac gagccgggaa 480
gcntnangtg taaaagcctg ggggtgcta attgagttag ctactcaca ttaattgngt 540
tgcgctccac ttgcccgctt ttccantccg ggaacacctg tcgnc 585

```

<210> 93

<211> 567

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 93

```

cggcagtggt gctgtctgcg tgtccacctt ggaatctggc tgaactggct gggaggacca 60
agactcgggc tgggggtggc angsaaggga accgggggct gctgtgaagg atcttggaac 120
ttccctgtac ccaccttccc cttgcttcat gtttgtnag gaaccttggt ccggccaagc 180
ccagtttctt tgtgtgatac actaatgtat ttgctttttt tgggaaatan anaaaaatca 240
attaaattgc tantgtttct ttgaannnnn nnnnnnnnnn nnnnnnnggg ggggncgccc 300
ccnccgngga aacnccccct tttgttccct ttaattgaaa ggttaattng cncnctggc 360
gttaancnt ggccaaanc tngtttcccg tgntgaaatt gttnatcccc tcccaaattc 420
cccccncc ttccaaaccc ggaanccctn annntgttna ancccggggg gttgcctaan 480
ngnaattnaa ccnaaccccc nttaaatng nntttgcn cnccnngccc cnccttccca 540
nttcggggaa aacctntcc gtgccca 567

```

<210> 94

<211> 620

<212> DNA

<213> 人

<220>

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

<400> 94
 actagtcaaa aatgctaana taatttggga gaaaatattt ttttaagtagt gttatagttt 60
 catgtttatc ttttattatg ttttgtgaag ttgtgtcttt tcactaatta cctatactat 120
 gccaatattt ccttatatct atccataaca tttatactac atttgtaana naatatgcac 180
 gtgaaactta acactttata aggtaaaaat gaggtttcca anatttaata atctgatcaa 240
 gttcttgtaa tttccaaata gaatggactt ggtctgttaa gggctaagga gaagaggaag 300
 ataagggttaa aagttgttaa tgaccaaaaca ttctaaaaga aatgcaaaaa aaaagtttat 360
 tttcaagcct tcgaactatt taaggaaagc aaatcattt cctaaatgca tatcatttgt 420
 gagaatttct cattaatatc ctgaatcatt catttcaacta aggcctcatgt tnactccgat 480
 atgtctctaa gaaagtacta tttcatggtc caaacctggt tgccatantt gggtaaaggc 540
 tttcccttaa gtgtgaaant atttaaaatg aaattttcct ctttttaaaa attctttana 600
 agggttaagg gtgttgggga 620

<210> 95
 <211> 470
 <212> DNA
 <213> 人

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

<400> 95
 ctgcaccttc tctgcacagc ggatgaaccc tgagcagctg aagaccagaa aagccactat 60
 nactttntgc ttaattcang agcttacang attcttcaaa gagtnggtcc agcatccttt 120
 gaaacatgag ttcttaccag cagaagcaga cctttacccc accacctcag ctccaacagc 180
 agcaggtgaa acaacccatc cagcctccac ctnaggaat atttgttccc acaaccaagg 240
 agccatgcca ctcaaagggt ccacaacctg naaacacaaa nattccagag ccaggctgta 300
 ccaaggtccc tgagccaggg ctgtaccaan gtccctgagc caggttgtag caangtcctt 360
 gagccaggat gtaccaaggc cctgancca ggtgttccaa ggtccctgag ccaggctaca 420
 ccaagggcct gngccaggca gcacaaagt cctgaccaa ggcttatcaa 470

<210> 96
 <211> 660
 <212> DNA
 <213> 人

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

<400> 96
 tttttttttt tttttttttt ggaattaaaa gcaatttaat gagggcagag caggaaacat 60
 gcatttcttt tcattcgaat cttcagatga accctgagca gccgaagacc agaaaagcca 120
 tgaagacttt ctgcttaatt caggggctta caggattett cagagtgtgt gtgaacaaaa 180
 gctttatagt acgtattttt aggtatacaa taagagagag actatggctt ggggtgagaa 240
 tgtactgatt caaaggctta cagacaatta agacacagaa acagatggga agaggggtgnc 300
 cagcatctgg nggttggtt ctcaagggct tgtctgtgca ccaaaattact tctgcttggn 360
 cttctgctga gctgggcctg gagtgaacct tgaaggacat ggtctggtta cctttgtgta 420
 gcctgncaca ggaacttttg tgtatccttg ctcaggaaact ttgatggcac ctggctcagg 480
 aaacttgatg aagccttggt caagggaacct tgatgcttgc tggctcaggg accttggn 540
 ancctgggct cagggaacct tgnncnaacc ttggcttcaa gggacccttg gnacatcctg 600
 gcnnaggagac ccttgggncc aacctggggt ttnaggagacc ctttggntnc nanccttggc 660

<210> 97
 <211> 441
 <212> DNA
 <213> 人

<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 tgcateccac cccctcagct tcagcagcag cagggtgaaac      120
agccttgcca gcctccacct caggaaccat gcatecccaa aaccaaggag ccctgccacc      180
ccaagggtgcc tgagccctgc cccccaaaag tgctgagcc ctgccagccc aagggtccag      240
agccatgcca cccaagggtg cctgagccct gcccttcaat agtcactcca gcaccagccc      300
agcagaanac caagcagaag taatgtgtgt cacagccatg cccttgagga gccggccacc      360
agatgtgtaa tcccctatcc cattctgtgt atgagtccca tttgccttgc aattagcatt      420
ctgtctcccc caaaaaaaaaa a                                     441
```

<210> 98
 <211> 600
 <212> DNA
 <213> 人

<220>
 <221> misc_feature
 <222> (1)...(600)
 <223> n = A,T,C or G

```
<400> 98
gtattcctct cttcacacca ggaccagcca ctgttgagc atgagttccc agcagcagaa      60
gcagccctgc atcccccccc ctcagcttca gcagcagcag gtgaaacagc cttgccagcc      120
tccacctcag gaacctatga tccccaaac caaggagccc tgccacccca aggtgcctga      180
gccctgccac cccaagtgc ctgagccctg ccagcccaag gtccagagc catgccaccc      240
caagggtgct gagccctgcc cttcaatagt cactccagca ccagcccagc agaanaacca      300
gcagaaagtaa tgtgtgtcac agccatgccc ttgaggagcc ggccaccana tgctgaatcc      360
cctatcccat tctgtgtatg agtcccattt gccttgcaat tagcattctg tctcccccaa      420
aaaagaatgt gctatgaagc tttctttect acacactctg agtctctgaa tgaagctgaa      480
ggtcttaant acagantctag ttttcagctg ctcaagaattc tctgaagaaa agatttaaga      540
tgaaaaggcaa atgattcagc tccttattac cccattaat tcnctttcaa ttccaaaaaa      600
```

<210> 99
 <211> 667
 <212> DNA
 <213> 人

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

```
<400> 99
actagtgact gagttcctgg caaagaaatt tgacctggac cagttgataa ctcatgtttt      60
accattttaa aaantcagtg aaggatttga gctgctcaat tcaggacaaa gcattcgaac      120
ggtcctgacg ttttgagatc caaagtggca ggaggtctgt gttgtcatgg tgaactggag      180
tttctcttgt gagagttccc tcatctgaaa tcatgtatct gtctcacaaa tacaagcata      240
agtagaagat ttgttgaaag catagaaccc ttataaagaa ttattaacct ttataaacat      300
ttaaagtctt gtgagcacct gggnaattag ataataacaa tgttnatatt tttgatttac      360
attttgttaag gctataattg tatcttttaa gaaaacatac ctgggatttc tatgttgaaa      420
```

tggagatttt	taagagtttt	aaccagctgc	tgacagatata	ttactcaaaa	cagatatagc	480
gtataaagat	atagtaaagt	catctcctag	agtaatatct	acttaacaca	ttggaaacta	540
ttattttttt	gatttgaata	tnaatgttat	tttttaaaaa	cttggttatga	gttacttggg	600
attacatttt	gaaatcagtt	cattccatga	tgcanattac	tggtgattaga	ttaagaaaga	660
cggaataa						667

<210> 100

<211> 583

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(583)

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

<400> 100

gttttgtttg	taagatgatc	acagtcattg	tacactgatc	taaaggacat	atatataacc	60
cttttaaaaa	aaaatcactg	cctcattctt	atttcaagat	gaatttctat	acagactaga	120
tggtttttctg	aagatcaatt	agacattttg	aaaatgattt	aaagtgtttt	ccttaattgtt	180
ctctgaaaac	aagtttcttt	tgtagtttta	acaaaaaag	tgcccttttt	gtcactggat	240
tctcctagca	ttcatgattt	ttttttcata	caatgaattt	aaaattgcta	aaatcatgga	300
ctggcctttct	ggttggattt	caggttaagat	gtgttttaagg	ccagagcttt	tctcagttat	360
tgattttttt	ccccaattatt	tgatttttta	aaaatatata	catnggtgct	gcatttatat	420
ctgctgggtt	aaaattctgt	catattttcac	ttctagcctt	ttagtatttg	caaatcatat	480
tttactttta	cttaaaagcat	ttggttnattt	ggantatctg	gttctannct	aaaaaaanta	540
attctatnaa	ttgaantttt	ggtactcnnc	catattttgga	tcc		583

<210> 101

<211> 592

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(592)

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

<400> 101

gtggagacgt	acaaagagca	gccgctcaag	acacctggga	agaaaaagaa	aggcaagccc	60
gggaacacga	aggagcagga	aaagaaaaaa	cggcgaactc	gctctgcctg	gttagactct	120
ggagtgaactg	ggagtgggct	agaaggggac	cacctgtctg	acacctccac	aacgtcgctg	180
gagctcgatt	cacggaggca	ttgaattttt	cagcaganac	cttccaagga	catattgcag	240
gattctgtaa	tagtgaacat	atggaagta	ttagaatat	ttattgtctg	taaataactgt	300
aaatgcattg	gaataaaact	gtctcccca	ttgctctatg	aaactgcaca	ttgggtcattg	360
tgaatatttt	tttttttgcc	aaggctaato	caattattat	tatcacattt	accataattt	420
attttgtcca	ttgatgtatt	tattttgtaa	atgtatcttg	gtgctgctga	atttctatat	480
tttttgtaca	taatgcnttt	anatatacct	atcaagtttg	ttgataaatg	acncaatgaa	540
gtgnncnncn	ttggnggttg	aatttaattga	atgcctaatt	ttattatccc	aa	592

<210> 102

<211> 587

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(587)

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

```

<400> 102
cgtcctaagc acttagacta catcagggaa gaacacagac cacatccctg tcctcatgcg      60
gcttatgttt tctggaagaa agtggagacc nagtccttgg ctttaggggt ccccggtgg      120
gggctgtgca ntccggtcag ggcgggaagg gaaatgcacc gctgcatgtg aacttacagc      180
ccaggcggat gcccttccc ttagcactac ctggcctcct gcatccctc gcctcatgtt      240
cctccacact tcaanaaatg aanaacccca tgggcccagc cccttgccct ggggaacca      300
ggcagccttc caaaactcag gggctgaagc anactattag ggcaggggct gactttgggt      360
gacactgccc attccctctc agggcagctc angtcacccn ggnctcttga acccagcctg      420
ttcctttgaa aaagggcaaa actgaanaag gcttttctta nanaaagaaa aaccagggaa      480
ctttgccagg gcttcnntnt taccasaaen ncttctcnng gatttttaat tccccattng      540
gcctccactt accnggggcn atgccccaaa attaanaatt tcccatc      587

```

<210> 103

<211> 496

<212> DNA

<213> 人

<220>

<221> misc feature

<222> (1)... (496)

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

```

<400> 103
anaggactgg ccctaentgc tctctctcgt cctacctatc aatgcccac atggcagaac      60
ctgcancctt tggncactgc anaggaac ctctcagtgt ctgacatca ccctaccnt      120
gcgggtgggtc tccaccacaa ccactttgac tetgtgttcc ctgnanggtg gnttctctg      180
actggcagga tggacettan ccnacctatc cctctgttcc ctctgctnag anaaagaatt      240
cccttaacat gatataatcc acccatgcaa ntngctactg gccagctac catttaccat      300
ttgcctacag aatttcattc agtctacaet ttggcattct ctctggcgat agagtgtggc      360
tgggctgacc gcaaaaggtg ccttacacac tggccccac cctcaaccgt tgacncatca      420
gangettgcc tctccttctt gattncccc catgttggat atcaggggtg tcnagggatt      480
ggaaaagaaa caaac      496

```

<210> 104

<211> 575

<212> DNA

<213> 人

<220>

<221> misc feature

<222> (1)... (575)

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

```

<400> 104
gcacctgctc tcaatecnnc tctcaccatg atcctccgcc tgcanaaact cctctgccaa      60
ctatggangt ggtttcnggg gtggtctctt ccaactggga agaagccgtg gtgtctctac      120
ctgttcaact cngtttgtgt ctgggggata aactnggggc tatggaagcg gctnaactgt      180
tgttttgggt gaagggctgg taattggctt tgggaagtng cttatngaag ttggcctngg      240
gaagttgcta ttgaaagtng ccttggaagt ngmtttgggt gggggttttg ctggtggcct      300
ttgttnaatt tgggtgcttt gtnaatggcg gcccctcnc ctgggcaatg aaaaaaatca      360
ccnatgcngn aaacctcnac nnaacagect gggcttccct cacctcgaaa aaagtgtgctc      420
ccccccaaa aaaggncaan cccctcaann tgggaangtg aaaaaatcct cgaatgggga      480
nccnaaaac aaaaacccc ccttttcccn gnaangggg aaataccncc ccccaactta      540
cnaaaacctt tntaaaaaac cccccgggaa aaaaa      575

```

<210> 105

<211> 619

<212> DNA

<213> 人

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

<400> 105
 cactagtagg atagaacac tgtgtcccg gagtaaggag agaagctact attgattaga 60
 gcctaaccce ggtaactgc aagaagaggc gggatacttt cagctttcca tgtaactgta 120
 tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaact gaatcccact 180
 tcaatacaca ctcatgaact cctgatgga caataacagg cccaagcctg tggatatgatg 240
 tgcacacttg ctgactcan aaaaaatact actctcataa atgggtggga gtattttggt 300
 gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg 360
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgcact cttgtgtata 420
 tttccaaatt tttgtacagt cgctgcacat atttgaatc atatattaag acttccaaaa 480
 aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcncct ctggttggta 540
 cttaaacat ctactattn gtttnatga aattcctttt cccncctcc cgaaaaana 600
 aagtgggtgg gaaaaaaa 619

<210> 106
 <211> 506
 <212> DNA
 <213> 人

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

<400> 106
 cattggtnct ttcatttget ntggaggtgt nnatctctaa cagtggacaa agttcccngt 60
 gccttaaaact ctgtnacact tttgggaant gaaaanttng tantatgata ggttattctg 120
 angtanagat gttctggata ccattanatn tgccccnng gtcagaggct catattgtgt 180
 tatgtaaatg gtatntcatt cgtactatn antcaattng aaatanggtc tttgggttat 240
 gaatanntng cagcncanct nanangctgt ctgtngtatt cattgtggtc atagcacctc 300
 acancattgt aacctcnatc nagtgagaca nactagnaah ttectagtga tggtcanga 360
 ttccaaatgg nctcatntcn aatgtttaaa agttanttaa gtgtaagaa tacagactgg 420
 atgttccacc aactagtacc tgtaatgach ggcctgtccc aacacatctc ccttttccat 480
 gactgtggta ncccgcatcg gaaaaa 506

<210> 107
 <211> 452
 <212> DNA
 <213> 人

<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 attgttttgt aaatgtttct tttgttttgt aaatgtttct 120
 ttaaaagacc ctctattct ataaaaactc gcatgtagag gcttgtttac ctttctctct 180
 ctaagggtta caataggagt ggtgatttga aaaaataaaa attatgagat tggttttcct 240
 gtggcataaa ttgcatcact gtatcatttt cttttttaac cggtaagant ttcagtttgt 300
 tggaaagtaa ctgtganaac ccagtttccc gtccatctcc cttagggact acccatagaa 360
 catgaaaagg tccccacnga agcaagaaga taagtctttc atggctgctg gttgcttaaa 420
 ccactttaaa accaaaaant tcccccttga aa 452

<210> 108

<211> 502

<212> DNA

<213> 人

<220>

<221> misc feature

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

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

<400> 108

atcttcttcc	cttaattagt	tnttatttat	ntattaaatt	ttattgcatg	tcctggcaaa	60
caaaaagaga	ttgtagattg	gcttctggct	ccccaaaagc	ccataacaga	aagtaccaca	120
agaccncaac	tgaagcttaa	aaaatctatc	acatgtataa	taaccttnga	agaacattaa	180
tanagcatat	aaaactttta	acatntgott	aatgttgtnc	aattataaaa	ntaatngaaa	240
aaaatgtccc	tttaacatnc	aatatcccac	atagtgttat	ttuaggggat	taccnngnaa	300
naaaaaaagg	gtagaaggga	tttaantgaa	actctgcttn	ccattttctgt	ttanaaacgt	360
ctccagaaca	aaaacttntc	aantctttca	gctaaacgca	tttgagctna	ggccactcaa	420
aaactccatt	agnccactt	tctaanggtc	tctanagctt	actaancctt	ttgacccctt	480
accctggnta	ctctgacct	ca				502

<210> 109

<211> 1308

<212> DNA

<213> 人

<400> 109

acccgaggtc	tcgctaaaat	catcatggat	tcacttggcg	ccgtcagcac	tcgacttggg	60
tttgatcttt	tcaaagagct	gaagaaaaca	aatgatggca	acatcttctt	ttcccttctg	120
ggcatcttga	ctgcaattgg	catggtcttc	ctggggaccc	gaggagccac	cgttcccag	180
ttggaggagg	tgtttcactc	tgaaaaagag	acgaagagct	caagaataaa	ggctgaagaa	240
aaagagggtga	ttgagaacac	agaagcagta	catcaacaat	tccaaaaagt	tttgactgaa	300
ataagcaaac	tcactaantga	ttatgaactg	aacataacca	acaggctgtt	tggagaaaaa	360
acatacctct	tccttcaaaa	atacttagat	tatgttgaaa	aatattatca	tgcactctctg	420
gaacctgttg	atthttgtana	tgcagccgat	gaagtgcgaa	agaagattaa	ttctggggtt	480
gaaagcaaaa	caaatgaaaa	aatcaaggac	ttgttcccag	atggctctat	tagtagctct	540
accaagctgg	tgctggtgaa	catggtttat	tttaaaagggc	aatgggacag	ggagttaaag	600
aaagaaaata	ctaagggaaga	gaatttttgg	atgaataaga	gcacaagtaa	atctgtacag	660
atgatgacac	agagccattc	ctttagcttc	actttcctgg	aggacttgca	ggccaaaatt	720
ctagggtattc	catataaaaa	caacgaccta	agcatgtttg	tgettctgcc	caacgacatc	780
gatggcctgg	agaagataat	agataaanta	agtcctgaga	aattggtaga	gtggactagt	840
ccaggggcata	tgggaagaaag	aaagggtgaat	ctgcacttgc	cccggtttga	ggtggaggac	900
agttacgatc	tagaggcggt	cctggctgcc	atggggatgg	gcgatgcctt	cagttagcac	960
aaagccgact	actcggaat	gtcgtcagyc	tcggggttgt	acgcccagaa	gttcctgcac	1020
agttcccttg	tggcagtaac	tgagggaagyc	accgaggetg	caqctgccac	tggcataggc	1080
tttactgtca	catecgcccc	aggtcatgaa	aatgttcaact	gcaatcatcc	cttcctgttc	1140
ttcatcaggc	acaatgaatc	caacagcatc	ctcttcttcg	gcagattttc	ttctccttaa	1200
gatgatcggt	gccatggcat	tgctgctttt	agcaaaaaaac	aactaccagt	gttactcata	1260
tgattatgaa	aatcgtccat	tcttttaaat	ggtggctcac	ttgcattt		1308

<210> 110

<211> 391

<212> PRT

<213> 人

<400> 110

Met	Asp	Ser	Leu	Gly	Ala	Val	Ser	Thr	Arg	Leu	Gly	Phe	Asp	Leu	Phe
1				5					10					15	
Lys	Glu	Leu	Lys	Lys	Thr	Asn	Asp	Gly	Asn	Ile	Phe	Phe	Ser	Pro	Val
			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
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		
100	105	110
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		
145	150	155
Lys Asp Leu Phe Pro Asp Gly Ser Ile Ser Ser Ser Thr Lys Leu Val		
165	170	175
Leu Val Asn Met Val Tyr Phe Lys Gly Gln Trp Asp Arg Glu Phe Lys		
180	185	190
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
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
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 Ala Thr Gly Ile Gly		
340	345	350
Phe Thr Val Thr Ser Ala Pro Gly His Glu Asn Val His Cys Asn His		
355	360	365
Pro Phe Leu Phe Phe Ile Arg His Asn Glu Ser Asn Ser Ile Leu Phe		
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Phe Gly Arg Phe Ser Ser Pro		
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<210> 111

<211> 1419

<212> DNA

<213> 人

<400> 111

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<210> 112

<211> 400

<212> PRT

<213> 人

<400> 112

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Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
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Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
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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
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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
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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
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<210> 113

<211> 957

<212> DNA

<213> 人

<400> 113

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<210> 114

<211> 161

<212> PRT

<213> 人

<400> 114

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			20					25					30		
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
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Gly	Cys	Thr	Lys	Val	Pro	Glu	Pro	Gly	Cys	Thr	Lys	Val	Pro	Glu	Pro
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	130				135					140					
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Lys

150

155

160

<210> 115
 <211> 506
 <212> DNA
 <213> 人

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 <212> DNA
 <213> 人

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<211> 6921

<212> DNA

<213> 人

<400> 117

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ggcactag                                     8948

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<210> 120
<211> 587
<212> DNA
<213> 人

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

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<400> 120
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cctccacct tcaanaaatg aanaacocca tgggcccagc ccttgccct ggggaaccaa 300
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ctttgccagg gcttcnntnt taccaaaacn ncttctcnng gatttttaat tccccattng 540
gctccactt accnggggcn atgccccaaa attaanaatt tcccatc 587

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<210> 121
<211> 619
<212> DNA
<213> 人

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

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<400> 121
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tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaact gaatccact 180
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aatgaagtcc	ctgggttttc	atggcaactt	gatcagtaaa	ggattcncct	ctgtttggta	540
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aagtgggtgg	gaaaaaaaa					619

<210> 122
 <211> 1475
 <212> DNA
 <213> 人

<400> 122						
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<210> 123
 <211> 2294
 <212> DNA
 <213> 人

<400> 123						
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<210> 124

<211> 956

<212> DNA

<213> 人

<400> 124

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cgcagccgcc	ccatctgccc	cacagtctcc	ggcctctcca	gcctcagccc	cctgcttcag	900
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<210> 125

<211> 486

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 125

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agcgcagggt	ttggatacta	gagaaagtca	tttgcttgta	ctattgccat	tttagaaagc	420
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<210> 126

<211> 3552

<212> DNA

<213> 人

<400> 126

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<210> 127

<211> 754

<212> DNA

<213> 人

<400> 127

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<210> 128

<211> 374

<212> DNA

<213> 人

<400> 128

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<210> 129

<211> 546

<212> DNA

<213> 人

<400> 129

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 <213> 人

<400> 130						
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<210> 131

<211> 671

<212> DNA

<213> 人

<400> 131

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<210> 132

<211> 590

<212> DNA

<213> 人

<400> 132

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<210> 133

<211> 581

<212> DNA

<213> 人

<400> 133

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<210> 134

<211> 4797

<212> DNA

<213> 人

<220>

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<400> 134

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4797

<210> 135

<211> 2856

<212> DNA

<213> 人

<400> 135

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<210> 136

<211> 356

<212> DNA

<213> 人

<400> 136

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

<211> 356

<212> DNA

<213> 人

<220>

<221> misc_feature

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

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

<400> 137

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cctttttctc	aaagacatcg	gcgaggtaat	ttgtgccctt	tttacctcgg	cccgcgacca	240
cgctaaggcc	aaanttcag	acaaayggcc	gggcccgtnc	nataggggan	cccaacttgg	300
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<210> 138

<211> 353

<212> DNA

<213> 人

<400> 138

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tacattgatg	tggaatttgc	tgctgctaoc	accacctcct	gaagaggctt	ccctgatgcc	180
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<210> 139

<211> 371

<212> DNA

<213> 人

<400> 139

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<210> 140

<211> 370

<212> DNA

<213> 人

<400> 140
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aggagctgcc tgagtgtac 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> 人

<400> 141
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aaggagcttc agggtcctgg tactcctcca cagaatactc ggagtattca gactactcat 180
catcctcagg gggtagccgc tcttctctct ctgcatgaga gacggggagc acaggcacag 240
catggagctg ggagccggca gtgtctgcag cataactagg gaggggctcg gatccagatg 300
cgatgaactg gccctggcag gcacagtgtc gactcatctc ttggcgacct gcccgggcgg 360
ccgctcgaaag c 371

<210> 142
<211> 343
<212> DNA
<213> 人

<400> 142
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aacacccttt ttgtagaatc tacagggtgga catttagagt gct 343

<210> 143
<211> 354
<212> DNA
<213> 人

<400> 143
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<210> 144
<211> 353
<212> DNA
<213> 人

<400> 144
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agggtttgcct gataccagac ctgtggcccc acctcccatg caggtctctg tgg 353

<210> 145
<211> 371
<212> DNA
<213> 人

<400> 145
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tggaatttgg ggtgtcctta taggaccaga ggttgtgttt gctccacctt cttgactccc 300
atgtgagacc tcggccgcga ccacgctaag ccgaattcca gcacactggc ggcccgttac 360
tagtggatcc g 371

<210> 146
<211> 355
<212> DNA
<213> 人

<400> 146
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<210> 147
<211> 355
<212> DNA
<213> 人

<400> 147
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acatttggtat tatcttcatt ctttgaaaca caatctatcc ttggcactcc ttcag 355

<210> 148
<211> 369
<212> DNA
<213> 人

<400> 148
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agggagtgtg ccgagggtt ctgagaaggc ttctctcaca tctagaaaga agcgcttaag 180
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acttcttca 369

<210> 149
<211> 620
<212> DNA
<213> 人

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

<400> 149
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 gccaatattt ccttatatct atccataaca tttatactac atttgaana naatatgcac 180
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 agggttaagg gtgttgggga 620

<210> 150
 <211> 371
 <212> DNA
 <213> 人

<400> 150
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<210> 151
 <211> 4655
 <212> DNA
 <213> 人

<400> 151
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<210> 152

<211> 586

<212> PRT

<213> 人

<400> 152

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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	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	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	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	240
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Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp	260	265	270	
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His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp	290	295	300	
Glu	Leu	Val	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu	305	310	315	320
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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	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
 465 470 475 480
 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
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 565 570 575
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
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<210> 153

<211> 2007

<212> DNA

<213> 人

<400> 153

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<210> 154

<211> 2148

<212> DNA

<213> 人

<400> 154

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<210> 155

<211> 153

<212> PRT

<213> 人

<400> 155

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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
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 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

<210> 156

<211> 128

<212> PRT

<213> 人

<400> 156

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

<210> 157

<211> 424

<212> DNA

<213> 人

<220>

<221> misc feature

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

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

<400> 157

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 aattcagtca ccactgttat attaccttct ccaggaaacc tccagtgggg aaggctgcga 180
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 agaggaagga gaaactgca tcataacttt acagaattga atctagagtc ttccccgaaa 300
 agcccagaaa cttctctgcn gnattctggt tgtccatctg gtctaagggt gctgcttctt 360
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 tgct 424

<210> 158

<211> 2099

<212> DNA

<213> 人

<400> 158

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<210> 159

<211> 291

<212> PRT

<213> 人

<400> 159

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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
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Glu	Asp	Phe	Val	Cys	Asn	Thr	Leu	Gln	Pro	Gly	Cys	Lys	Asn	Val	Cys
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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
		100						105					110		
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

	180		185		190
Ile Phe Met	Ile Ser Ala Ser Val Ile Cys Met	Leu Leu Asn Val Ala			
	195	200		205	
Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe	Arg Arg Ser Lys Arg				
	210	215		220	
Ala Gln Thr Gln Lys Asn His Pro Asn His Ala	Leu Lys Glu Ser Lys				
	225	230		235	240
Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser	Gly Gln Asn Ala Ile				
	245	250		255	
Thr Gly Ser Gln Ala Lys His Phe Lys Val Lys	Cys Ser Cys Val Ile				
	260	265		270	
Arg Arg Leu Leu Ser Ser Pro Glu Gly Asn Thr	Asn Leu Lys Val Pro				
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Ser Val Ala					
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<210> 160

<211> 3951

<212> DNA

<213> 人

<400> 160

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<210> 161

<211> 943

<212> PRT

<213> 人

<400> 161

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			20					25					30		
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				
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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															
				275					280						285
Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu															
				290					295						300
Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser															
305				310					315						320
Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu															
				325					330						335
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
Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe															
465				470					475						480
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 Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val															
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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															
545				550					555						560
Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr															
				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
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															
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Ser Arg Tyr Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys															
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Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile															
				690					695						700

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 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 Lys Val Glu Glu Glu Leu Thr Leu Ser
 770 775 780
 Trp Thr Ala Pro Gly Glu Asp Phe Asp Gln Gly Gln Ala Thr Ser Tyr
 785 790 795 800
 Glu Ile Arg Met Ser Lys Ser Leu Gln Asn Ile Gln Asp Asp Phe Asn
 805 810 815
 Asn Ala Ile Leu Val Asn Thr Ser Lys Arg Asn Pro Gln Gln Ala Gly
 820 825 830
 Ile Arg Glu Ile Phe Thr Phe Ser Pro Gln Ile Ser Thr Asn Gly Pro
 835 840 845
 Glu His Gln Pro Asn Gly Glu Thr His Glu Ser His Arg Ile Tyr Val
 850 855 860
 Ala Ile Arg Ala Met Asp Arg Asn Ser Leu Gln Ser Ala Val Ser Asn
 865 870 875 880
 Ile Ala Gln Ala Pro Leu Phe Ile Pro Pro Asn Ser Asp Pro Val Pro
 885 890 895
 Ala Arg Asp Tyr Leu Ile Leu Lys Gly Val Leu Thr Ala Met Gly Leu
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<210> 162
 <211> 498
 <212> DNA
 <213> 人

<400> 162
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<210> 164

<211> 1310

<212> DNA

<213> 人

<400> 164

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<210> 165

<211> 177

<212> PRT

<213> 人

<400> 165

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			20				25						30		
Arg	Leu	Lys	Arg	Ala	Val	Ser	Glu	His	Gln	Leu	Leu	His	Asp	Lys	Gly
		35				40						45			
Lys	Ser	Ile	Gln	Asp	Leu	Arg	Arg	Phe	Phe	Leu	His	His	Leu	Ile	
	50				55			60							
Ala	Glu	Ile	His	Thr	Ala	Glu	Ile	Arg	Ala	Thr	Ser	Glu	Val	Ser	Pro
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Asn	Ser	Lys	Pro	Ser	Pro	Asn	Thr	Lys	Asn	His	Pro	Val	Arg	Phe	Gly
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Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
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 Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Gly
 115 120 125
 Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
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 165 170 175
 His

<210> 166
 <211> 177
 <212> PRT
 <213> 人

<400> 166
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 35 40 45
 Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile
 50 55 60
 Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro
 65 70 75 80
 Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
 85 90 95
 Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
 100 105 110
 Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Gly
 115 120 125
 Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
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 165 170 175
 His

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<400> 167
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 aatgataact gaagcttcat tttaacctatt taatgctacc aagagaagag tatttttcag 300
 aaatataaag attttaatac ctgccacatg gaaagctaata aataacagca aaataaaaca 360
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<210> 168
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 <212> DNA
 <213> 人

<400> 168						
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<210> 169

<211> 592

<212> PRT

<213> 人

<400> 169

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			20					25					30		
Val	Gln	Leu	Gln	Asp	Asn	Gly	Tyr	Asn	Gly	Leu	Leu	Ile	Ala	Ile	Asn
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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
						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
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01.10.31

Val	Thr	Asp	Trp	Tyr	Gly	Ala	His	Gly	Asp	Asp	Pro	Tyr	Thr	Leu	Gln
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Tyr	Arg	Gly	Cys	Gly	Lys	Glu	Gly	Lys	Tyr	Ile	His	Phe	Thr	Pro	Asn
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Phe	Leu	Leu	Asn	Asp	Asn	Leu	Thr	Ala	Gly	Tyr	Gly	Ser	Arg	Gly	Arg
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Val	Phe	Val	His	Glu	Trp	Ala	His	Leu	Arg	Trp	Gly	Val	Phe	Asp	Glu
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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
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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
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Met	Phe	Met	Gln	Ser	Leu	Ser	Ser	Val	Val	Glu	Phe	Cys	Asn	Ala	Ser
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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
		275					280					285			
Phe	Pro	Met	Asn	Gly	Thr	Glu	Leu	Pro	Pro	Pro	Pro	Thr	Phe	Ser	Leu
	290					295					300				
Val	Glu	Ala	Gly	Asp	Lys	Val	Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser
305					310					315					320
Lys	Met	Ala	Glu	Ala	Asp	Arg	Leu	Leu	Gln	Leu	Gln	Gln	Ala	Ala	Glu
			325						330					335	
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				
Phe	Phe	Val	Pro	Asp	Ile	Ser	Asn	Ser	Asn	Ser	Met	Ile	Asp	Ala	Phe
465					470					475					480
Ser	Arg	Ile	Ser	Ser	Gly	Thr	Gly	Asp	Ile	Phe	Gln	Gln	His	Ile	Gln
				485					490					495	
Leu	Glu	Ser	Thr	Gly	Glu	Asn	Val	Lys	Pro	His	His	Gln	Leu	Lys	Asn
			500					505					510		
Thr	Val	Thr	Val	Asp	Asn	Thr	Val	Gly	Asn	Asp	Thr	Met	Phe	Leu	Val
		515					520					525			
Thr	Trp	Gln	Ala	Ser	Gly	Pro	Pro	Glu	Ile	Ile	Leu	Phe	Asp	Pro	Asp
	530					535					540				
Gly	Arg	Lys	Tyr	Tyr	Thr	Asn	Asn	Phe	Ile	Thr	Asn	Leu	Thr	Phe	Arg
545					550					555					560
Thr	Ala	Ser	Leu	Trp	Ile	Pro	Gly	Thr	Ala	Lys	Pro	Gly	His	Trp	Thr
				565					570					575	
Tyr	Thr	Leu	Met	Cys	Phe	His	His	Ala	Lys	Leu	Leu	Thr	Trp	Lys	Leu
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01.10.31

<210> 170
<211> 791
<212> PRT
<213> 人

<400> 170
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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
Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser
275 280 285
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Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu
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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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385 390 395 400
Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
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Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr
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Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser

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Thr	Val	Thr	Val	Asp	Asn	Thr	Val	Gly	Asn	Asp	Thr	Met	Phe	Leu	Val
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Thr	Ala	Ser	Leu	Trp	Ile	Pro	Gly	Thr	Ala	Lys	Pro	Gly	His	Trp	Thr
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Tyr	Thr	Leu	Asn	Asn	Thr	His	His	Ser	Leu	Gln	Ala	Leu	Lys	Val	Thr
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Ser	Arg	Tyr	Phe	Phe	Ser	Phe	Ala	Ala	Asn	Gly	Arg	Tyr	Ser	Leu	Lys
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Ile	Gln	Met	Asn	Ala	Pro	Arg	Lys	Ser	Val	Gly	Arg	Asn	Glu	Glu	Glu
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Arg	Lys	Trp	Gly	Phe	Ser	Arg	Val	Ser	Ser	Gly	Gly	Ser	Phe	Ser	Val
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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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<211> 364

<212> PRT

<213> 人

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Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His
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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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Gly Ser Val Lys Arg Glu Asp Ile Phe Tyr Thr Ser Lys Leu Trp Ser
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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
165 170 175
Lys Ile Leu Phe Asp Thr Val Asp Leu Cys Ala Thr Trp Glu Ala Met
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Glu Lys Cys Lys Asp Ala Gly Leu Ala Lys Ser Ile Gly Val Ser Asn
195 200 205
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
245 250 255
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
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His Lys Arg Thr Pro Ala Leu Ile Ala Leu Arg Tyr Gln Leu Gln Arg
290 295 300

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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
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<212> PRT

<213> 人

<400> 176

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 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
 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

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> 人

<400> 177

atgccccgta aatgtcttca gtgttcttca gggtagttgg gatctcaaaa gatttggttc 60
agatccaaac aaatacacat tctgtgtttt agctcagtgt tttctaaaaa aagaaactgc 120
cacacagcaa aaaattgttt actttgttgg acaaaacaaa tcagttctca aaaaatgaac 180
ggtgcttata aaaagtata aatatacagt agctctaaaa caaaccaact gaccagagg 240
gaagtgaagt tgtgcttagt atttacattg gatgccagtt ttgtaatcac tgacttatgt 300
gcaaaactggt gcagaaattc tataaactct ttgctgtttt tgataacctgc tttttgtttc 360

attttgtttt gttttgtaaa aatgataaaa cttcagaaaa t

401

<210> 178

<211> 561

<212> DNA

<213> 人

<400> 178

```
acgcctttca aggggtgtacg caaagcactc attgataccc ttttggatgg ctatgaaaca 60
gccgcgtatg ggacaggggt ctttggccag aatgagtacc tacgctatca ggaggccctg 120
agttagctgg ccactgcggt taaagcaaga attgggagct ctcagcgaca tcaccagtca 180
gcagccaaag acctaaactca gtcccttgag gtctcccaa caaccatcca ggtgacatac 240
ctccctcca gtcagaagag taacagtgc aagcacttcc ttgaattgaa gagctttaag 300
gataactata acacattgga gactactctg tgacggagct gaaggactct tgccgtagat 360
taagccagtc agttgcaatg tgcaagacag gctgcttgcc gggccgacct cggaacatct 420
ggccagcag gccagactg tatccatcca agttcccggt gtatccagag ttcttagagc 480
ttgtgtctaa agggtaattc cccaacctt ccttatgagc atttttagaa cattggctaa 540
gactattttc cccagtagc g
```

561

<210> 179

<211> 521

<212> DNA

<213> 人

<400> 179

```
cccaacgcgt ttgcaaatat tccctggta gcctacttcc ttacccccga atattggtaa 60
gatcgagcaa tggcttcagg acatgggttc tcttctcctg tgatcattca agtgctcact 120
gcatgaagac tggcttgtct cagtgtttca acctcaccag ggctgtctct tgggccacac 180
ctcgctccct gttagtgcgg tatgacagcc cccatcaaat gaccttggcc aagtacgggt 240
ttctctgtgg tcaagggttg ttggctgatt ggtggaaagt aggggtggacc aaaggaggcc 300
acgtgagcag tcagcaccag ttctgcacca gcagcgctc cgtcttagtg ggtgttcctg 360
tttctcctgg cctgggttg gctagggcct gattcgggaa gatgcctttg cagggagggg 420
aggataagtg ggatctacca attgattctg gcaaaacaat ttctaagatt tttttgcttt 480
atgtgggaaa cagatctaaa tctcatttta tgctgtattt t
```

521

<210> 180

<211> 417

<212> DNA

<213> 人

<400> 180

```
ggtggaattc gccgaagatg gcggaggtgc aggtcctggt gcttgatggt cgaggccatc 60
tcctgggccc cctggcggcc atcgtggcta aacagggtact gctgggcccg aagggtggtg 120
tcgtacgctg tgaaggcatc aacatttctg gcaatttcta cagaacaag ttgaagtacc 180
tggttttctt ccgcaagcgg atgaacacca acccttcccg aggcacctac cacttccggg 240
ccccagccc catcttcttg cggaccgtgc gaggtatgct gccccacaaa accaagcgag 300
gccaggccc tctggaccgt ctcaagggtg ttgacggcat cccaccgccc tacgacaga 360
aaaagcggat ggtggttctt gctgcctca aggtcgtgcg tctgaagcct acaagaa 417
```

<210> 181

<211> 283

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (35)

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

<400> 181

```

gattttcttct aaataggatg taaaacttct ttcanattac tcttcctcag tcttgcttgc 60
caagaactca agtgtaactg tgataaaata acctttccca ggtatattgg caggtatgtg 120
tgtaatctca gaatacacag gtgacataga tatgatatga caactggtaa tgggtggattc 180
atttacattg tttacacttc tatgaccagg ccttaaggga aggtcagttt tttaaaaaac 240
caagtagtgt cttcctacct atctccagat acatgtcaaa aaa 283

```

<210> 182

<211> 401

<212> DNA

<213> 人

<400> 182

```

atattcttgc tgcttatgca gctgacattg ttgcccctccc taaagcaacc aagtagcctt 60
tatttcccac agtgaagaa aacgctggcc tatcagttac attacaaaag gcagatttca 120
agaggattga gtaagtagtt ggatggcttt cataaaaaaca agaattcaag aagaggattc 180
atgctttaag aaacatttgt tatacattcc tcacaaatta tacctgggat aaaaactatg 240
tagcagggcag tgtgttttcc ttocatgtct ctctgcacta cctgcagtgt gtccctctgag 300
gctgcaagtc tgtcctatct gaattcccag cagaagcact aagaagctcc accctatcac 360
ctagcagata aaactatggg gaaaacttaa atctgtgcat a 401

```

<210> 183

<211> 366

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (325)

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

<400> 183

```

accgtgtcca agtttttaga acccttggtt gccagaccga ggtgtcctgg tcaccgtttc 60
accatcatgc tttgatgttc cctgtcttt ctctctcttg ctctcaagag caaagggttaa 120
tttaaggaca aagatgaagt cactgttaac taatctgtca ttgtttttac cttccttttc 180
tttttcagtg cagaaattaa aagtaagtat aaagcacctg gattgggagt gtttttgcgt 240
gtgtcggaat cactggtaaa tgttggctga gaacaatccc tccccttgca cttgtgaaaa 300
cactttgagc gctttaagag attanctga gaataatta aatatctttt ctcttcaaaa 360
aaaaaa 366

```

<210> 184

<211> 370

<212> DNA

<213> 人

<400> 184

```

tcttacttca aaagaaaaat aaacataaaa aataagttgc tggttcctaa caggaaaaat 60
tttaataatt gtactgagag aaactgctta cgtacacatt gcagatcaaa tatttggagt 120
taaaaatgta gtctacatag atgggtgatt gtaactttat tgccattaaa agatttcaaa 180
ttgcattcat gcttctgtgt acacataatg aaaaatgggc aaataatgaa gatctctcct 240
tcagtctgct ctgttttaatt ctgctgtctg ctctctctta atgctgcgtc cctaattgta 300
cacagtttag tgatatctag gagtataaag ttgtcgccca tcaataaaaa tcacaaagtt 360
ggtttaaaaa 370

```

<210> 185

<211> 107

<212> DNA

<213> 人

<400> 185

```

ctcatattat tttccttttg agaaattgga aactctttct gttgctatta tattaataaa 60

```

gttgggtgttt attttctggt agtcaccttc cccatttaaa aaaaaaa 107

<210> 186

<211> 309

<212> DNA

<213> 人

<400> 186

gaaaggatgg	ctctggttgc	cacagagctg	ggacttcatg	ttcttctaga	gagggccaca	60
agagggccac	aggggtggcc	gggagtgttc	agctgatgcc	tgctgagagg	caggaattgt	120
gccagtga	gacagtcatg	agggagtgtc	tcttcttggg	gaggaagaa	ggtagagcct	180
ttctgtctga	atgaaaggcc	aaggctacag	tacagggccc	cgccccagcc	aggggtgtta	240
tgcccacgta	gtggaggcct	ctggcagatc	ctgcattcca	aggtcactgg	actgtacgtt	300
tttatgggtt						309

<210> 187

<211> 477

<212> DNA

<213> 人

<400> 187

ttcagtccta	gcaagaagcg	agaattctga	gatcctccag	aaagtcgagc	agcaccacc	60
tccaacctcg	ggccagtgtc	ttcaggcttt	actggggacc	tgcgagctgg	cctaattgtg	120
tggcctgcaa	gccaggccat	ccctgggggc	cacagacgag	ctcogagcca	ggtcaggctt	180
cggaggccac	aagctcagcc	tcaggccccag	gcactgattg	tggcagaggg	gccactacc	240
aaggtctagc	taggccaag	acctagttag	ccagacagtg	agaagcccct	ggaaggcaga	300
aaagttggga	gcatggcaga	cagggaaagg	aaacattttc	agggaaaaga	catgtatcac	360
atgtcttcag	aagcaagtca	ggtttcatgt	aaccgagtg	cctcttgctg	gtccaaaagt	420
agcccagggc	tgtagcacag	gcttcacagt	gattttgtgt	tcagccgtga	gtcacac	477

<210> 188

<211> 220

<212> DNA

<213> 人

<400> 188

taaatatgg	agatatatt	attcctctta	gatgaccagt	gattccaatt	gtcccaagtt	60
ttaaataagt	accctgtgag	tatgagata	attagtga	atcagaacaa	gtttcagtat	120
cagatgttca	agaggaaagt	gctattgcat	tgattttaat	atttgtacat	aaacactgat	180
ttttttgagc	attattttgt	atttgttcta	ctttaatacc			220

<210> 189

<211> 417

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (76)

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

<221> 不确定

<222> (77)

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

<400> 189

accatcttga	cagaggatac	atgctcccaa	aacgtttgtt	accacactta	aaaatcactg	60
ccatcattaa	gcattcattt	caaaattata	gccattcatg	atttactttt	tccagatgac	120
tatcattatt	ctagtccctt	gaatttctaa	ggggaaaaaa	aacaaaaaca	aaaacttacy	180
atgcactttt	ctccagcaca	tcagattcca	attgaaaat	taaagacatg	ctatggtaat	240
gcacttgcta	gtactacaca	ctttgtacaa	caaaaaacag	aggcaagaaa	caacgggaag	300

agaaaagcct tcccttgttg gcccttaaac tgagtcaaga tctgaaatgt agagatgatc 360
tctgacgata cctgtatgtt cttattgtgt aaataaaatt gctgggtatga aatgaca 417

<210> 190

<211> 497

<212> DNA

<213> 人

<400> 190

gcactgcggc gctctcccggt cccgcgggtg ttgctgctgc tgccgctgct gctgggcctg 60
aacgcaggag ctgtcattga ctggccacac gaggagggca aggaagtatg ggattatgtg 120
acggtcgcga aggatgccta catgttcttg tggctctatt atgcaccaa ctctgcaag 180
aacttctcag aactgcccct ggtcatgttg cttcagggcg gtccaggcgg ttctagcact 240
ggatttgga aacttgagga aattggggcc cttgacagt atctcaaacc acggaaaacc 300
acctggctcc aggctgccag tctctatatt gtggataatc ccgtgggcac tgggttcagt 360
tatgtgaatg gtagtggtgc ctatgccaa gacctggcta tgggtggctt agacatgatg 420
gttctcctga agaccttctt cagtggccac aaagaattcc agacagttcc attctacatt 480
ttctcagagt cctatgg 497

<210> 191

<211> 175

<212> DNA

<213> 人

<400> 191

atgttgaata ttttgcttat taactttgtt tattgtcttc tccctcgatt agaataattag 60
ctacttgagt acaaggattt gagcctgtta cattcactgc tgaatttttag gctcctggaa 120
gatccccagc attcaataga gaccacacaa taaatatatg tcaataaaaa aaaaa 175

<210> 192

<211> 526

<212> DNA

<213> 人

<400> 192

agtaaacatt attatttttt ttatatattgc aaaggaaaca tatctaatacc ttcttataga 60
aagaacagta ttgctgtaat tccctttctt ttcttctca tttctctgc cccttaaaag 120
attgaagaaa gagaacttg tcaactcata tccacgttat ctacgaaagt acataagaat 180
ctatcactaa gtaatgtatc ctccagatg tgttggttta ccagtgcac ccataattca 240
tcacaaaatt aaagcaagaa gtccatagta atttatattgc taatagtggg tttttaatgc 300
tcagagtttc tgaggtcaaa ttttatcttt tcaacttaca gctctatgat cttaaataat 360
ttacttaatg tatttttggtg tattttcctc aaattaatat tgggtgtcaa gactatatct 420
aattcctctg atcactttga gaacaaact tttattaaat gtaaggcact tttctatgaa 480
ttttaaatat aaaaaataat attgttctga ttattactga aaaaaa 526

<210> 193

<211> 553

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (290)

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

<221> 不确定

<222> (300)

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

<221> 不确定

<222> (411)

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

<221> 不确定

<222> (441)

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

<400> 193

```
tccattgtgg tggaaattcgc tctctggtaa aggcgtgcag gtgttgcccg cggcctctga 60
gctgggatga gccgtgctcc cgggtggaagc aagggagccc agcgggagcc atggccagta 120
cagtggtagc agttggactg accattgctg ctgcaggatt tgcaggccgt tacgttttgc 180
aagccatgaa gcatatggag cctcaagtaa aacaagtttt tcaagccta ccaaaatctg 240
ccttcagtgg tggctattat agagggtgggt ttgaacccaa aatgacaaan cgggaagcan 300
cattaatact aggtgtaagc cctactgccca ataaagggaa aataagagat gctcatcgac 360
gaattatgct tttaaatcat cctgacaaag gaggatctcc ttatatagca nccaaaatca 420
atgaagctaa agatttacta naagggtcaag ctaaaaaatg aagtaaattgt atgatgaatt 480
ttaagttcgt attagtttat gtatatgagt actaagtttt tataataaaa tgcctcagag 540
ctacaattttt aaa 553
```

<210> 194

<211> 320

<212> DNA

<213> 人

<400> 194

```
cccttcccaa tccatcagta aagaccccat ctgccttgtc catgccgttt cccaacaggg 60
atgtcacttg atatgagaat ctcaaatctc aatgccttat aagcattcct tcctgtgtcc 120
attaagactc tgataattgt ctccoctcca taggaatttc tcccaggaaa gaaatataatc 180
cccatctccg tttcatatca gaactaccgt ccccgatatt cccttcagag agattaaaga 240
ccagaaaaaa gtgagcctct tcactctgac ctgtaatagt ttcagttcct attttcttcc 300
attgacccat atttatacct 320
```

<210> 195

<211> 320

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (203)

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

<221> 不确定

<222> (218)

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

<400> 195

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aagcatgacc tggggaaatg gtcagacctt gtattgtgtt tttggccttg aaagtagcaa 60
gtgaccagaa tctgccatgg caacaggctt taaaaagac ccttaaaaag acactgtctc 120
aactgtgtgtg ttagcaccag ccagctctct gtacatttgc tagctttag ttttctaaga 180
ctgagtaaac ttcttatttt taaaaagggg aggcctggnnt gtaactttcc ttgtacttaa 240
ttgggtaaaa gtctttttcca caaaccacca tctattttgt gaactttgtt agtcatcttt 300
tatttggtaa attatgaact 320
```

<210> 196

<211> 357

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (36)

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

<400> 196

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atataaaaata atacgaaaact ttaaaaaagca ttggantgtc agtatgttga atcagtagtt 60
tcactttaac tgtaaacaaat ttcttaggac accatttggg ctagtttctg tgtaagtgtg 120
aatactacaa aaacttattt atactgttct tatgtcattt gttatattca tagatttata 180
tgatgatatg acatctggct aaaaagaant tattgcaaaa ctaaccacta tgtacttttt 240
tataaatact gtatggacaa aaatggcat tttttatatt aaattgttta gctctggcaa 300
aaaaaaaaa ttttaagagc tggactaat aaaggattat tatgactgtt aaaaaaa 357
```

<210> 197

<211> 565

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (27)

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

<400> 197

```
tcagctgagt accatcagga tatttanccc ttttaagtgtc gttttgggag tagaaaacta 60
aagcaacaat acttctctt gacagctttg attggaatgg ggthattaga tcattcacct 120
tggtcctaca ctttttagga tgcttgggtga acataacacc acttataatg aacatccctg 180
gttcttatat tttgggctat gtgggttagga attgttactt gttactgcag cagcagccct 240
agaaagtaag cccagggctt cagatctaag ttagtcctaaa agctaaatga tttaaagtca 300
agttgtaatg ctaggcataa gcactctata atacattaaa ttataggccg agcaattagg 360
gaatgtttct gaaacattaa acttgtattt atgtcactaa aattctaacn caaacttaaa 420
aatgtgtct catcacatag ctgtactagg cttcatcatg cttttctaaa tttgtgtatg 480
atttgaatat atgaaagaat ttatacaaga gtgttattta aaattattaa aaataaatgt 540
atataatttg tacctattgt aaaaa 565
```

<210> 198

<211> 484

<212> DNA

<213> 人

<400> 198

```
tatgtaagta ttggtgtctg ctttaaaaaa ggagaccag acttcacctg tccttttttaa 60
acatttgaga acagtgttac tctgagcagt tgggcccact tcaccttato cgacagctga 120
ctgttggatg tgtccattgt cgccagtttg gctgttgccc ggacaggaca ggacctccat 180
tgggcgcagc agcaggtggc aggggtgttg cttgaggtgg gtggcagcgt ctggctctcc 240
tctctgggtg tttctgagag ggtctctaaa gcagagtgtg gttggcctgg ggggaaggcag 300
agcacgtatt tctccctct agtacctctg catttgtgag tgttccctct ggctttctga 360
agggcagcag actcttgagt atactgcaga ggacatgctt tatcagtagg tcctgagggc 420
tccaggggct caactgacca agtaacacag aagttggggt atgtggccta tttgggtcgg 480
aaac
```

<210> 199

<211> 429

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (77)

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

<221> 不确定

<222> (88)

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

<221> 不确定
 <222> (134)
 <223> n=A,T,C or G
 <221> 不确定
 <222> (151)
 <223> n=A,T,C or G
 <221> 不确定
 <222> (189)
 <223> n=A,T,C or G
 <221> 不确定
 <222> (227)
 <223> n=A,T,C or G
 <221> 不确定
 <222> (274)
 <223> n=A,T,C or G
 <221> 不确定
 <222> (319)
 <223> n=A,T,C or G

<400> 199
 gcttatgttt tttgttttaa cttttgtttt ttaacattta gaatattaca ttttgtatta 60
 tacagtacct ttctcanaca ttttgtanaa ttcatttcgg cagotcacta ggattttgct 120
 gaacattaaa aagngtgata gcgatattag ngccaatcaa atggaaaaaa ggtagtctta 180
 ataaacaana cacaacgttt ttatacaaca tacttttaaaa tattaanaaa actccttaat 240
 attgtttcct attaatgatt attctttggg caanattttc tgatgotttt gattttctct 300
 caatttagca tttgctttng gtttttttct ctatttagca ttctgttaag gcacaaaaac 360
 tatgtactgt atgggaaatg ttgtaaatat taccttttcc acatttttaa cagacaactt 420
 tgaatccaa 429

<210> 200
 <211> 279
 <212> DNA
 <213> 人

<400> 200
 gcttttttga ggaattacag ggaagctcct ggaattgtac atggatatct ttatccctag 60
 ggggaaatca aggagctggg caccctaat tctttatgga agtgtttaaa actattttta 120
 ttttattaca agtattacta gagtagtggt tctactctaa gattttcaaaa gtgcatttaa 180
 aatcatacat gttcccgctt gcaaatatat tgttattttg gtggagaaaa aaatagtata 240
 ttctacataa aaaattaaag atattaacta agaaaaaaa 279

<210> 201
 <211> 569
 <212> DNA
 <213> 人

<400> 201
 taggtcagta tttttagaaa ctcttaatat ctcatactct tgataccaaa agcagccctg 60
 attgttaaag cacacacctg cacaagaagc agtgatgggt gcattttacat ttctggggtg 120
 cacaaaaaaa aattctcaaa aagcaaggac ttacgctttt tgcaaagcct ttgagaagtt 180
 actggatcat aggaagctta taacaagaat ggaagattct taaataactc actttctttg 240
 gtatccagta acagtagatg ttcaaaatat gtagctgatt aataccagca ttgtgaacgc 300
 tgtacaacct tgtggttatt actaagcaag ttactactag cttctgaaaa gtagcttcat 360
 aattaatggt atttatacac tgccttccat gacttttact ttgcctaag ctaatctcca 420
 aaatctgaaa tgctactcca atatcagaaa aaaaggggga ggtggaatta tatttctctg 480
 gattttaaga gtacagagaa tcatgcacat ctctgattag ttcatatatg tctagtgtgt 540
 aataaaagtc aaagatgaac tctcaaaaa 569

<210> 202

<211> 501
 <212> DNA
 <213> 人

<400> 202
 attaataaggc ttaataattg ttggcaagga tccttttgct ttcttttgca tgcaagctcc 60
 tagcatctgg cagtggggcc aagaaaataa gggttatgca tgtatgatgg ttttcttctt 120
 gagcaacatg attgagaacc agtgtatgtc aacagggtgca tttgagataa ctttaaatga 180
 tgtacctgtg tggctctaagc tgggaatctgg tcaccttcca tccatgcaac aacttggttca 240
 aattcttgac aatgaaatga agctcaatgt gcatatggat tcaatccac accatcgatc 300
 atagcaccac ctatcagcac tgaanaactct tttgcattaa gggatcattg caagagcagc 360
 gtgactgaca ttatgaaggc ctgtactgaa gacagcaagc tgtagtagta gaccagatgc 420
 tttcttggca ggctcgttgt acctcttggg aaacctcaat gcaagatagt gtttcagtgc 480
 tggcatatct tgggaattctg c 501

<210> 203
 <211> 261
 <212> DNA
 <213> 人

<220>
 <221> 不确定
 <222> (36)
 <223> n=A,T,C or G
 <221> 不确定
 <222> (96)
 <223> n=A,T,C or G

<400> 203
 gacaagctcc tggctcttgag atgtcttctc gtttaangaga tgggcctttt ggaggtaaag 60
 gataaaatga atgagttctg tcatgattca ctattntata acttgcatga cctttactgt 120
 gttagctctt tgaatgttct tgaattttta gactttcttt gtaaacaaat gatatgtcct 180
 tatcattgta taaaagctgt tatgtgcaac agtgtggaga ttcttctgtct gatttaataa 240
 aatacttaaa cactgaaaaa a 261

<210> 204
 <211> 421
 <212> DNA
 <213> 人

<400> 204
 agcatctttt ctacaacggt aaaattgcag aagtagctta tcattaaaaa acaacaacaa 60
 caacaataac aataaatcct aagtgttaant cagttattct acccctacc aaggatatca 120
 gectgttttt tccctttttt ctectgggaa taattgtggg ctctcttcca aattttctaca 180
 gectctttcc tcttctcatg cttgagcttc cctgtttgca cgcattgctg tgcaggactg 240
 gcttggtgtg ttggactcgg ctccaggtgg aagcatgctt tcccttggtta ctgttggaga 300
 aactcaaac ttcaagccct aggtgttagc attttgtcaa gtcattcaact gtatttttgt 360
 actggcatta acaaaaaaag aagataaaat attgtaccat taactttta taaaacttta 420
 a 421

<210> 205
 <211> 460
 <212> DNA
 <213> 人

<400> 205
 tactctcaca atgaaggacc tggaaatgaa aatctgtgtc taaacaagtc ctcttttagat 60
 tttagtgcac atccagagcc aggttgggtt gcctcgagta attctttcat gggtaacctt 120
 ggaaaagctc tcaggagacc tcccttagat gcctattcaa gctttggaca gccatcagat 180
 tgtcagccaa gagcctttta tttgaaagct cattcttccc cagacttggg ctctgggtca 240


```

gaggaagatg ggaaagaaag gacagatttt caggaagaaa atcacatttg taccttttaa 300
cagacttttag aaaactacag gactccaaat tttcagtctt atgacttgga cacatagact 360
gaatgagacc aaaggaaaag cttaacatac tacctcaagg tgaactttta tttaaaagag 420
agagaatctt atgtttttta aatggagtta tgaattttta 460

```

<210> 206
 <211> 481
 <212> DNA
 <213> 人

```

<400> 206
tgtggtggaa ttcgggacgc cccagacccc tgactttttc ctgcgtgggc cgtctcctcc 60
tgcggaagca gtgacctctg acccctgggt accttcgctt tgagtgcctt ttgaacgctg 120
gtcccgcggg acttggtttt ctcaagctct gtctgtccaa agacgctccg gtcgaggtcc 180
cgctgcctt ggggtggatac ttgaacccca gacgcccctc tgtgctgctg tgtccggagg 240
cgcccttccc atctgcctgc ccaccggag ctctttccgc cggcgcaggg tcccaagccc 300
acctcccgc ctcagtcctg cgggtgtgct ctgggcacgt cctgcacaca caatgcaagt 360
cctggcctcc gcgcccgcgc gccacgcga gccgtaccgc ccgcacaactc tgttatttat 420
ggtgtgaccc cctggaggtg cctcggccc accggggcta tttattgttt aatttatttg 480
t 481

```

<210> 207
 <211> 605
 <212> DNA
 <213> 人

```

<400> 207
accctttttg gattcagggc tcttcacaat taaaatgagt gtaatgaaac aagggtgaaaa 60
tatagaagca tcccttttga tactgttttg ctacttacag tgtacttggc attgctttat 120
ctcactggat tctcacggta ggattttctga gatcttaatc taagctccaa agttgtctac 180
ttttttgato ctagggtgct ccttttgttt tacagagcag ggtcacttga tttgctagct 240
ggtggcagaa ttggcaccat taccaggtc tgactgacca ccagtccagag gcactttatt 300
tgtatcatga aatgatttga aatcatttga aagcagcgaa gtctgataat gaatgccagc 360
tttccttgct ctttgataac aaagactcca aatattctgg agaaccctga taaaagtttg 420
aagggtctaga ttgggatttg aagacaaat tgtaggaaat cttacatttt tgcaataaca 480
aacattaatg aaagcaaac attataaaag taattttaat tcaccacata cttatcaatt 540
tcttgatgct tccaaatgac atctaccaga tatggttttg tggacatctt tttctgttta 600
cataa 605

```

<210> 208
 <211> 655
 <212> DNA
 <213> 人

```

<400> 208
ggcgttgctt tggattcccg tcgtaactta aagggaact ttcacaaatgt ccggagccct 60
tgatgtcctg caaatgaagg aggaggatgt ccttaagtcc cttgcagcag gaaccacttt 120
agggtggacc aatcttgact tccagatgga acagtacatc tataaaagga aaagtgatgg 180
catctatata ataaatctca agaggacctg ggagaagctt ctgctggcag ctctgcaat 240
tgttgccatt gaaaaccctg ctgatgtcag tgttatatcc tccaggaata ctggccagag 300
ggctgtgctg aagtttgctg ctgccactgg agccactcca attgctggcc gcttcaactcc 360
tggaaccttc actaaccaga tccaggcagc cttccgggag ccacggcttc ttgtggttac 420
tgaccccagg gctgaccacc agcctctcac ggaggcatct tatgttaacc tacctaccat 480
tgcgctgtgt aacacagatt ctctctgctg ctatgtggac attgccatcc catgcaacaa 540
caaggagct cactcagtgg gtttgatgtg gtggatgctg gctcgggaag ttctgcgcat 600
gcgtggcacc atttccctg aacacccatg ggaggtcatg cctgatctgt acttc 655

```

<210> 209
 <211> 621
 <212> DNA

<213> 人

<400> 209

```

catttagaac atggttatca tccaagacta ctctaccctg caacattgaa ctcccaagag 60
caaateccaca ttctctttga gttctgcagc ttctgtgtaa atagggcagc tgtcgtctat 120
gccgtagaat cacatgatct gaggaccatt catggaagct gctaaatagc ctagtctggg 180
gagtcttcca taaagttttg catggagcaa acaaacagga ttaaaactagg tttgggttct 240
tcagccctct aaaagcatag ggcttagcct gcaggcttcc ttgggcttcc tctgtgtgtg 300
tagttttgta aacactatag catctgttaa gatccagtgt ccatggaaac cttccacat 360
gccgtgactc tggactatat cagtttttgg aaagcagggg tctctgct gctaacaagc 420
ccacgtggac cagtctgaat gtcttttctt tacacctatg tttttaataa gtcaaacttc 480
aagaaacaat ctaaacaagt ttctgttgca tatgtgtttg tgaacttgta tttgtattta 540
gtaggcttct atattgcatt taacttgatt ttgttaactcc tgattcttcc ttttcggata 600
ctattgatga ataaagaaat t                                     621

```

<210> 210

<211> 533

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (20)

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

<221> 不确定

<222> (21)

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

<221> 不确定

<222> (61)

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

<400> 210

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cgccttgggg agccggcggn ngagtccggg acgtggagac ccgggggtccc ggcagccggg 60
nggcccgcgg gcccagggtg gggatgcacc gccgcggggt gggagctggc gccatcgcca 120
agaagaaact tgcagaggcc aagtataagg agcgagggac ggtcttggct gaggaccagc 180
tagcccagat gtcaaaagcag ttggacatgt tcaagaccaa cctggaggaa tttgccagca 240
aacacaagca ggagatccgg aagaatcctg agttccgtgt gcagttccag gacatgtgtg 300
caaccattgg cgtggatccg ctggcctctg gaaaaggatt ttggtctgag atgctgggcg 360
tgggggactt ctattacgaa ctagggtgtcc aaattatcga agtgtgctg gcgctgaagc 420
atcggaatgg aggtctgata actttggagg aactacatca acagggtgtt aagggaaagg 480
gcaagttcgc ccaggatgtc agtcaagatg acctgatcag agcdatcaag aaa 533

```

<210> 211

<211> 451

<212> DNA

<213> 人

<400> 211

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ttagcttgag ccgagaacga ggcgagaaag ctggagaccg aggagaccgc ctagagcggg 60
gtgaacgggg aggggaccgt ggggaccggc ttgatcgtgc gccgacacct gctaccaagc 120
ggagcttcag caagggaagt gaggagcggg gtagagaaag gccctcccag cctgaggggc 180
tgcgcaaggc agctagcctc acggaggatc gggaccgtgg gcgggatgcc gtgaagcgag 240
aagctgcctt acccccagtg agccccctga aggcggctct ctctgaggag gaggtagaga 300
agaaatccaa ggctatcatt gaggaatata tccatctcaa tgacatgaa gaggcagtc 360
agtgcgtgca ggagctggcc tcacctcctt tgctcttcat ctttgtacgg catggtgtcg 420
agtctacgct ggagcgcagt gccattgctc g                                     451

```

<210> 212

<211> 471

<212> DNA

<213> 人

<220>

<221> 不确定

<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 ttgggttac tcatgttaag ggattccttg ttgttgtgtt 180
gagatccagt gcagtgtga tttctgtgga tccagcttg gttccaggaa ttttgtgtga 240
ttggcttana tccagttttc aatcctcgac agctgggctg gaaagtgaac tcagtagctg 300
aacctgtctg acccggtcac gttottggat cctcagaact ctttgcctct gtcgggtgg 360
gggtgggaac tcacgtgggg agcgtggct gagaaatgt aaggattctg gaatacatat 420
tccatgggac tttccttccc tctcctgctt cctcttttcc tgctccctaa c 471
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<210> 213

<211> 511

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (27)

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

<221> 不确定

<222> (63)

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

<221> 不确定

<222> (337)

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

<221> 不确定

<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 agagttagtg taattaaact 180
atctcagccg tttccctgct ttcccttctg ctccatatgc ctcatgttcc ttccaggag 240
ctcttttaat cttaaagttc tacatttcat gctcttagtc aaattctgtt accttttta 300
taactcttcc cactgcatac ttccatcttg aattggnggt tctaaattct gaaactgtag 360
ttgagataca gctatttaac atttctggga gatgtgcac cctcttcttt gtggttgccc 420
aaggttgttt tgcgtaactg anactccttg atatgcttca gagaatttag gcaaacactg 480
gccatggccg tgggagtact gggagtaaaa t 511
```

<210> 214

<211> 521

<212> DNA

<213> 人

<400> 214

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agcattgcca aataatccct aattttccac taaaaatata atgaaatgat gttaaagcttt 60
ttgaaaagtt taggttaaac ctactgttgt tagattaatg tatttgttgc ttccctttat 120
ctggaatgtg gcattagctt ttttatttta accctcttta attcttattc aattccatga 180
cttaaggttg gagagctaaa cactgggatt tttggataac agactgacag ttttgcataa 240
ttataatcgg cattgtacat agaaaggata tggctacctt ttgttaaatc tgcactttct 300
aaatatcaaa aaagggaaat gaagtataaa tcaatttttg tataatctgt ttgaacatg 360
```

```

agttttatatt gcttaatatatt agggcttttc cctttttctg taagtctctt gggatcctgt 420
gtagaagctg ttctcattaa acaccaaaaca gttaagtcca ttctctggtta ctagctacaa 480
attcgggttc atattctact taacaattta aataaactga a 521

```

<210> 215

<211> 381

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (17)

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

<221> 不确定

<222> (20)

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

<221> 不确定

<222> (60)

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

<221> 不确定

<222> (61)

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

<221> 不确定

<222> (365)

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

<400> 215

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gagcggagag cggacnngtn agagccctga gcagccccac cgcgcgcgcc ggcctagttn 60
ncatcacacc ccgggagagag ccgcagctgc ccgcagccggc cccagtcacc atcacccgcaa 120
ccatgagcag cgagggccgag acccagcagc cgcgcgcgcc cccccccgcc gccccccgcc 180
tcagcgcgcc cgacaccaag cccggcacta cgggcagcgg cgaggggagc ggtggccggg 240
gcggcctcac atcggcggcg cctgccggcg gggacaagaa ggtcatcgca acgaagggtt 300
tgggaaacagt aaaatgggtc aatgtaaggga acggatatgg tttcatcaac aggaatgaca 360
ccaangaaga tgtatttgta c 381

```

<210> 216

<211> 425

<212> DNA

<213> 人

<400> 216

```

ttactaacta ggtcattcaa ggaagtcaag ttaacttaaa catgtcacct aaatgcactt 60
gatgggtgttg aaatgtccac cttctttaat ttttaagatg aacttagttc taaagaagat 120
aacaggccaa tcttgaaagt actccctgtt tgctgcagaa tgtcagatat tttggatgtt 180
gcataagagt cctatttgcc ccagtttaatt caacttttgt ctgcctgttt tgtggactgg 240
ctggctctgt tagaactctg tccaaaaagt gcatggaata taacttgtaa agcttcccac 300
aattgacaat atatatgcat gtgttttaaac caaatccaga aagcttaaac aatagagctg 360
cataatagta tttatttaag aatcacaaact gtaaacatga gaataactta aggattctag 420
ttag 425

```

<210> 217

<211> 181

<212> DNA

<213> 人

<400> 217

```

gagaaaccaa atgataggtt gtagagcctg atgactccaa acaaagccat caccgcgcat 60
cttctcctt cttctgggtg taagctcca agggcccttc accttcattg ctgaatatga 120
actttggctt tttcagtggg agaatatggt gaaggtttca ttttgttcta gaaaaaaaaa 180

```

a

181

<210> 218

<211> 405

<212> DNA

<213> 人

<400> 218

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caggccttcc agttcactga caaacatggg gaagtgtgcc cagctggctg gaaacctggc 60
agtgatacca tcaagcctga tgtccaaag agcaagaat atttctccaa gcagaagtga 120
gcgctgggct gtttttagtgc caggctgcgg tgggcagcca tgagaacaaa acctcttctg 180
tatttttttt ttccattagt aaaacacaag acttcagatt cagccgaatt gtggtgtctt 240
acaaggcagg cctttcctac agggggtgga gagaccagcc tttcttcctt tggtaggaat 300
ggcctgagtt ggcgttggtg gcaggctact ggtttgtatg atgtattagt agagcaaccc 360
attaatcttt tgtagtttgt attaaacttg aactgagaaa aaaaaa 405

```

<210> 219

<211> 216

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (207)

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

<221> 不确定

<222> (210)

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

<400> 219

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actccaagag ttagggcagc agagtggagc gatttagaaa gaacatttta aaacaatcag 60
ttaatttacc atgtaaaatt gctgtaatg ataattgtga cagattttct gttcaaatat 120
tcaattgtaa acttcttggt aagactgtta cgtttctatt gcttttgtat gggatattgc 180
aaaaataaaa aggaaagaac cctcttnaan aaaaaa 216

```

<210> 220

<211> 380

<212> DNA

<213> 人

<400> 220

```

cttacaaatt gcccccatgt gtaggggaca cagaaccctt tgagaaaact tagatttttg 60
tctgtacaaa gtctttgcct ttttccttct tcattttttt ccagtacatt aaatttgtca 120
atttcattctt tgagggaanc tgattagatg ggttgtgttt gtgttctgat ggagaaaaca 180
gcaccccaag gactcagaag atgattttta cagttcagaa cagatgtgtg caatattggg 240
gcatgtaata atgttgagtg gcagtcaaaa gtcattgatt ttatcttagt tcttcattac 300
tgcatgaaa aggaaaacct gtctgagaaa atgcctgaca gtttaattta aaactatggg 360
gtaagtcttt gacaaaaaaa

```

<210> 221

<211> 398

<212> DNA

<213> 人

<400> 221

```

ggttagtaag ctgtcgactt tgtaaaaaag ttaaaaatga aaaaaaagg aaaaatgaat 60
tgtatatatta atgaatgaac atgtacaaatt tgccactggg aggaggttcc tttttgttgg 120
gtgagtctgc aagtgaattt cactgatgtt gatattcatt gtgtgtagtt ttatttcggg 180
cccagccccg ttttccttta ttttggagct aatgccagct gcgtgtctag ttttgagtgc 240
agtaaaatag aatcagcaaa tcactcttat ttttcactct tttccgggat tttttggggt 300

```

gtttctgttg gagcagtgt caccactct tctgtatat tgcctttttg ctggaaaatg 360
 ttgtatgttg aataaaattt tctataaaaa ttaaaaaa 398

<210> 222

<211> 301

<212> DNA

<213> 人

<220>

<221> 不确定

<222> (49)

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

<221> 不确定

<222> (64)

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

<400> 222

ttcgataatt gatctcatgg gctttccctg gaggaaggt tttttttgnt gtttattttt 60
 taanaacttg aaacttgtaa actgagatgt ctgtagcttt tttgcccac tgtagtgtat 120
 gtgaagattt caaaacctga gagcactttt tctttgttta gaattatgag aaaggcacta 180
 gatgacttta ggattttgcat ttttcccttt attgcctcat ttcttgtgac gccttggttg 240
 ggagggaaat ctgtttattt tttcctacaa ataaaaagct aagattctat atcgcaaaaa 300
 a 301

<210> 223

<211> 200

<212> DNA

<213> 人

<400> 223

gtaagtgtt aggaagaaac tttgcaaca tttaatgagg atacactgtt catttttaaa 60
 attccttcac actgttaattt aatgtgtttt atattctttt gtagtaaaac aacataactc 120
 agattttctac aggagacagt ggttttattt ggattgtctt ctgtaaatagg tttcaataaa 180
 gctggatgaa cttaaaaaaa 200

<210> 224

<211> 385

<212> DNA

<213> 人

<400> 224

gaaaggtttg atccggactc aaagaaagca aaggagtgtg agccgccatc tgctggagca 60
 gctgtaactg caagacctgg acaagagatt cytcagcgaa ctgcagctca aagaaacctt 120
 tctccaacac cagcaagccc taaccagggc cctcctceac aagttccagt atctcctgga 180
 ccaccaagg acagttctgc ccctggtgga cccccagaaa ggactgttac tccagcccta 240
 tcatcaaagtg tgttaccaag acatcttggg tccccgcta cttcagtgcc tggaatgggt 300
 aaacagagca cttaatgtta tttacagttt atattgtttt ctctgggttac caataaaacg 360
 ggccattttc aggtggttaa aaaaa 385

<210> 225

<211> 560

<212> PRT

<213> 人

<400> 225

Met	Glu	Cys	Leu	Tyr	Tyr	Phe	Leu	Gly	Phe	Leu	Leu	Leu	Ala	Ala	Arg
1				5				10					15		
Leu	Pro	Leu	Asp	Ala	Ala	Lys	Arg	Phe	His	Asp	Val	Leu	Gly	Asn	Glu
			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
	210					215					220				
Gln	Val	Lys	Asp	Val	Tyr	Val	Val	Thr	Asp	Gln	Ile	Pro	Val	Phe	Val
225					230					235					240
Thr	Met	Phe	Gln	Lys	Asn	Asp	Arg	Asn	Ser	Ser	Asp	Glu	Thr	Phe	Leu
				245					250					255	
Lys	Asp	Leu	Pro	Ile	Met	Phe	Asp	Val	Leu	Ile	His	Asp	Pro	Ser	His
			260					265					270		
Phe	Leu	Asn	Tyr	Ser	Thr	Ile	Asn	Tyr	Lys	Trp	Ser	Phe	Gly	Asp	Asn
		275					280					285			
Thr	Gly	Leu	Phe	Val	Ser	Thr	Asn	His	Thr	Val	Asn	His	Thr	Tyr	Val
	290					295					300				
Leu	Asn	Gly	Thr	Phe	Ser	Leu	Asn	Leu	Thr	Val	Lys	Ala	Ala	Ala	Pro
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tgactttaac aatgctattt tagtaaatc atcaaaagcga aatctcagc aagctggcat 7500
cagggagata tttaagttct caccccaat tccacgaat ggaacctgaac atcagccaaa 7560
tgagaaaca catgaaagcc acagaattta tgttgcaata cgaagcaatg ataggaaactc 7620
cttacagtct gctgtatcta acattgcccc ggccctctg tttattcccc ccaattctga 7680
tcctgtacct gccagagatt atcttatatt gaaaggagtt ttaacagcaa tgggtttgat 7740
aggaatcatt tgccttatta tagttgtgac acatcatact ttaagcagga aaaagagagc 7800
agacaagaaa gagaatggaa caaattatt ataatgaatt ctgcagatat ccatcacact 7860
ggcgccgct cgagcaccac caccaccacc actgagatcc ggctgctaac aaagcccga 7920
aggaagctga gttggctgct gccaccgctg agcaataact agcataacc cttggggcct 7980
ctaaacgggt cttgaggggt tttttgctga aaggaggaac tatatccgga t 8031

```

<210> 255

<211> 401

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(401)

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

<400> 255

```

gtggccagng actagaaggc gaggcggcgc gggaccatgg cggcgccggc ggacgagcgg 60
agtccanagg acggagaaga cgaggaagag gaggagcagt tggttctggt ggaattatca 120
ggaattattg attcagactt cctctcaaaa tgtgaaata aatgcaaggt tttgggcatt 180
gacactgaga ggccattctt gcaagtggac agctgtgtct ttgctgggga gtatgaagac 240
actctangga cctgtgttat atttgaaaga aatgntnaac atgctgatac agaaggcaat 300
aataaaacag tgctaaaata taaatgccat acaatgaaga agctcagcat gacaagaact 360
ctcctgacag agaagaagga aggagaagaa aacatangtg g 401

```

<210> 256

<211> 401

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(401)

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

<400> 256

```

tgggtgncct gggagtggga accgcggtgg cttccngnga ggtttcggca ntggcatccg 60
gggccgggggt cgcggccgng gacggggccg gggccnangc cgnnganctc gcggangcaa 120
ggccgaggat aaggagtgga tgcccgtcac caacttgggc cgcttgacca aggacatgaa 180
nancaagccc ctgnaggaga tctatntctt ctccctgcc ccattaagga atcaagagat 240
catttgattt ctccctgggg gectctctca aggatnagg ttttgaagat tatgccagtg 300
canaaannan accccgttgc ccngtccatc tncacccaac ncttocaagg gcnatttttg 360
tttaggcctc attncngggg ggaaccttaa cccaatttgg g 401

```


<210> 257

<211> 401

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(401)

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

<400> 257

atgtatgtaa	aacacttcac	aaaatgtaaa	gggctataac	aaatatgtta	taaagtgttt	60
ctctcagccc	tgaggtatag	agaatcattt	gcctcagact	gctgttggat	tttaaaattt	120
ttaaaatata	tgctaagtaa	tttgctatgt	cttctccac	actatcaata	tgctgtcttc	180
taacaggctc	cccactttct	tttaantgtc	tgttatgagc	tttggacatg	agataaccgt	240
gcctgttcag	agtgtctaca	gtaagagctg	gacaaaactct	ggagggacac	agtctttgag	300
acagctcttt	tggttgcttt	ccacttttct	gaaagggtca	cagtaacctt	ctagataata	360
gaaactccca	gttaaagcct	angctancaa	ttttttttag	t		401

<210> 258

<211> 401

<212> DNA

<213> 人

<400> 258

ggagcgctag	gtcgggtgtac	gaccgagatt	aggggtgcgtg	ccagctccgg	gaggccgcgg	60
tgagggggccg	ggcccaagct	gccgaccga	gccgatcgtc	aggggtcgcca	gcgcctcagc	120
tctgtggagg	agcagcagta	gtcggagggt	gcaggatatt	agaaatggct	actccccagt	180
caattttcat	ctttgcnaatc	tgcatttttaa	tgataacaga	attaattctg	gcctcaaaaa	240
gtactatga	tatcttaggt	gtgccaaaat	cggcatcaga	gcgccaaatc	aagaaggcct	300
ttcacaaagt	ggccatgaag	taccacctg	acaaaaataa	gaccagatg	ctgaagcaaa	360
attcagagag	attgcagaag	catatgaanc	actctcagat	g		401

<210> 259

<211> 401

<212> DNA

<213> 人

<400> 259

attgggtttg	gagggaggat	gatgacagag	gaatgccctt	tggccatcac	ggtttttgatt	60
ctccagaata	ttgtgggttt	gatcatcaat	gcagtcattg	taggctgcat	tttcatgaaa	120
acagctcagg	ctcacagaag	ggcagaaact	ttgattttca	gcgcctatgc	tgtgattgcc	180
gtccgaaatg	gcaagctgtg	cttcattgtc	cgagtgggtg	acctgaggaa	aagcatgatc	240
attagtgcct	ctgtgcgcac	ccaggtgggtc	aagaaaacaa	ctacacctga	aggggagggtg	300
gttccatttc	accaactgga	cattccctgt	gataacccaa	tcgagagcaa	taacattttt	360
ctgggtggccc	ctttgatcat	ctgccacgtg	attgacaagc	g		401

<210> 260

<211> 363

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(363)

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

<400> 260

aggaganang	gagggggana	tgaatagga	tggagagga	natagtggat	gagcagggca	60

```

canggagagg aancagaaag gagaggcaag acagggagac acacancaca nangangana      120
caggtggggg ctgggggtggg gcatggagag ccttttnangt cncccaggcc acctgtctct      180
cgctggngctg ttgaaaccca ctccatggct tcctgccact gcagttgggc ccagggctgg      240
cttattnctg gaatgcaagt ggctgtggct tggagcctcc cctctggnnn anggaaannn      300
attgctccct tatctgcttg gaatatctga gtttttccan ccoggaaata aaacacacac      360
aca                                                                    363

```

```

<210> 261
<211> 401
<212> DNA
<213> 人

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

```

```

<400> 261
cggtctctccg ccgtctctccc ggggttttcgg ggcacttggg tcccacagtc tggctctgct      60
tcaccttccc ctgaacctgag tagtcgccat ggcacagggt ctcagaggca ctgngactga      120
cttccctgga tttgatgagc gggctgatgc anaaactott cggagggcta tgaaggctt      180
gggcacagat gaggagagca tcctgactct gttgacatcc cgaagtaatg ctcagcgcca      240
ggaaatctct gcagctttta agactctgtt tggcagggat cttctggatg acctgaaatc      300
agaactaact ggaaaatttg aaaaattaat tgtggctctg atgaaacctt ctgggcttta      360
tgatgcttat gaactgaaac atgccttgaa gggagctgga a                                                                    401

```

```

<210> 262
<211> 401
<212> DNA
<213> 人

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

```

```

<400> 262
agtctanaac atttctaata ttttngtctt tcatatatca aaggagatta tgtgaaacta      60
tttttaataa ctgtaagtg acatatagtt ataagatata tttctgtaca gtagagaaag      120
agtttataac atgaagata ttgtaccatt atacattttc attctcgatc tcataagaaa      180
ttcaaaagaa taatgataga ggtgaaaata tgtttacttt ctctaaatca agcctagtgtg      240
tcaactcaaa aattatgntg catagtttta ttttgaatth aggttttggg actacttttt      300
tccancttca atgagaaaat aaatcttaca actcaggagt tactacagaa gttctaanta      360
tttttttgct aannagcnaa aaatataaac atatgaaaat g                                                                    401

```

```

<210> 263
<211> 401
<212> DNA
<213> 人

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

```

```

<400> 263
ctgtccgacc aagagaggcc ggcagagccc gaggcttggg cttttgcttt ctggcggagg      60
gatctgcggc ggtttaggag ggggtgctga tcctgggagg aagaggcagc tacggcggcg      120
gcggcggttg cggctaggc ggggtgaaat aaaggggccc ccgcccgggtg atgcccgtgac      180
cactgcggca ggcacaggag ctgagctggc cccggccctc agcccgtccc gncgggacccg      240

```

```

ctttcctcaa ctctccatct tctcctgccg accgagatcg ccgaggcggn ctcaggctcc 300
ctanccctt ccccgctcct tcccccccc cgtccccgcc ccggggggcg ccgccaccg 360
cctccacca tggtctgaa ganaatccac saggaattga a 401

```

```

<210> 264
<211> 401
<212> DNA
<213> 人

```

```

<400> 264
aacaccagcc actccaggac cctgaaggc ctctaccagg tcaccagtgt tctgcgcta 60
aagccacccc ctggcagaaa cttcagctgt gtgttctgga atactcacgt gagggaaactt 120
actttggcca gcattgaact tcaagtcag atggaaccca ggaccatcc aacttggtg 180
cttcacattt tcatccctc ctgcacatt gctttcattt tcatagccac agtgatagcc 240
ctaaganaac aactctgtca aaagctgtat tcttcaaaag acacaacaaa aagacctgtc 300
accacaacaa agagggaagt gaacagtgt gtgaatctga acctgtggtc ttgggagcca 360
gggtgacctg atatgacatc taaagaagct tctggactct g 401

```

```

<210> 265
<211> 271
<212> DNA
<213> 人

```

```

<220>
<221> misc_feature
<222> (1)...(271)
<223> n = A,T,C or G

```

```

<400> 265
gccacttctt gtggacatgg gcagagcgt gctgccagtt cctggtagcc ttgaccacna 60
cgctgggggg tctttgtgat ggtcatgggt ctcatcttga cttgggggtg tgggattcaa 120
gttagaagtt tctagatctg gccggcgcca gtggctcaca cctgtaatcc cagcacttta 180
ggaggctgag gcaggcggt catgaggtca ggagatcgag accgtcctgg ctaacacagt 240
gaaacccctt ctctactaaa aatacaaaaa a 401

```

```

<210> 266
<211> 401
<212> DNA
<213> 人

```

```

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

```

```

<400> 266
attcataaat ttagctgaaa gatactgatt caatttgtat acagngaata taaatgagac 60
gacagcaaaa ttttcatgaa atgtaaaata tttttatagt ttgttcatac tatatgaggt 120
tctattttta atgactttct ggatttttaa aaatttcttt aaatacaatc atttttgtaa 180
tattttattt atgcttatga tctagataat tgcagaatat cattttatct gactctgtct 240
tcataagaga gctgtggcgg 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> 人

```

```

<220>

```

<221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 267
 gaagaggcat cacttgatcc cggagacctt tggagttaag aggcggcgga agcgagggcc 60
 tgtggagtcg gatcctcttc ggggtgagcc agggtcggcg cgcgcggctg tctcanaact 120
 catgcagctg ttcccgcgag gcctgtttga ggacgcgctg ccgcccacgc tgctgaggag 180
 ccaggtgtac agccttgtgc ctgacaggac cgtggccgac cggcagctga aggagcttca 240
 agagcanggg gagacaaaat cgtccagctg ggcttchact tggatgcca tggaaanttat 300
 tctttcnctt ganggactta cnngggacoc aagaanccct tncaaggggc ccttngtgga 360
 tgggncccg aaccccnnta tttgcccttg ggggggncca a 401

<210> 268
 <211> 223
 <212> DNA
 <213> 人

<400> 268
 tcgccatggt ggccaggctg gtcttgaact cctgacttta agtgatccac ccgcctcaac 60
 ctcccaaagt gctgggatta caggtgtgag ccaccgcgcc tggcctgata catactttta 120
 gaatcaagta gtcaagcact tttctctgtc atttttctaa aaagtaaata tacaaatggt 180
 ttgttttttg ttttttttgt ttgtttgttt ctgttttttt ttt 223

<210> 269
 <211> 401
 <212> DNA
 <213> 人

<400> 269
 actatgtaaa ccacattgta ctttttttta ctttggcaac aaatatttat acatacaaga 60
 tgctagtcca tttgaatatt tctcccaact tatccaagga tctccagctc taacaaaatg 120
 gtttattttt atttaaatgt caatagtgtt tttttaaaat ccaaatacaga ggtgcaggcc 180
 accagttaaa tgccgtctat cagggtttgt gccttaagag actacagagt caaagctcat 240
 ttttaaagga gtaggacaaa gttgtcacag gtttttgttg ttgtttttat tgcccccaaa 300
 attacatggt aatttccatt tatatcaggg attctattta cttgaagact gtgaagttgc 360
 cattttgtct cattgttttc tttgacataa ctaggatcca t 401

<210> 270
 <211> 401
 <212> DNA
 <213> 人

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 270
 tggctgttga ttcacctcag cactgcttgg tatctgcacc ctacctctct ttagaggctg 60
 ccttgtcaac tgaaaaatgc acctgacttc gagcaagact ctctccttag gttctggatc 120
 tgtttgagcc ccatggcact gagctggaat ctgagggtct tgttccaagg atgtgatgat 180
 gtgggagaat gttctttgaa agagcagaaa tccagtctgc atggaaacag cctgtagagn 240
 agaagtttcc agtgataagt gttcactgtt ctaaggaggt acaccacagc tacctgaatt 300
 ttcccaaaat gagtgettct gtgcgttaca actggccttt gtacttgact gtgatgactt 360
 tgttttttct tttcaattct anataacat gggaaaaaat g 401

<210> 271
 <211> 329
 <212> DNA

<213> 人

<400> 271

ccacagcctc	caagtcaggt	ggggtggagt	cccagagctg	cacagggttt	ggcccaagtt	60
tctaagggag	gcatttcctc	ccctcgccca	tcagtgccag	ccctgctgg	ctggtgctg	120
agccctcag	acagccccct	gccccgcagg	cctgccttct	cagggacttc	tgoggggct	180
gaggcaagcc	atggagtgg	acccaggagc	cggacacttc	tcaggaaatg	gcttttccca	240
acccccagcc	cccacccggt	ggttcttctc	gttctgtgac	tgtgtatagt	gccaccacag	300
cttatggcat	ctcattgagg	acaaaaaaaa				329

<210> 272

<211> 401

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(401)

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

<400> 272

nggctgntaa	cntcggaggt	nacttcctgg	actatcctgg	agacccccctc	cgcttccacg	60
nncatnatat	cncctcatngc	tgggccentn	angacacnat	ccactccaa	cacctgngng	120
atgctggncn	cctnggaacc	ancntcagaa	ngacccctgnt	cntntgtnnt	cgcgaanctg	180
aagnnaangc	gggntacacc	tnctntgeant	ggncacnct	gcnggggaact	ntacacacct	240
acgggatgtg	gctgcgccan	gagccaagag	cntttctgga	tgattcccca	gcctcttgnn	300
agggantcta	caacattgct	nnntaccttt	ntccnnncgc	nnntnntgga	ntacaggngn	360
tnntaacact	acatcttttt	tactgcncn	tncttggtgg	g		401

<210> 273

<211> 401

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(401)

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

<400> 273

cagcaccatg	aagatcaaga	tcctgcacc	cccagagcgc	aagtactcgg	tgtggatcgg	60
tggtccatc	ctggcctcac	tgccacett	ccagcagatg	tggtattagca	agcaggagta	120
cgacgagtcg	ggcccccca	tcgtccaccg	caaagtcttc	taaaccgact	cagcagatgc	180
gtagcatttg	ctgcatgggt	taattgagaa	tagaaatttg	cccttgga	atgcacacac	240
ctcatgctag	cctcacgaaa	ctggaataag	ccttcgaaaa	gaaattgtcc	ttgaagcttg	300
tatctgatat	cagcactgga	ttgtagaact	tggtgctgat	tttgaccttg	tattgaagtt	360
aactgttccc	cttgggtatta	acgtgtcagg	gctgagtgnt	c		401

<210> 274

<211> 401

<212> DNA

<213> 人

<400> 274

ccacccacac	ccaccgcgc	ctcgttgcgc	tcttctccgg	gagccagtc	gcgccaccgc	60
cgccgcccag	gccatgcgca	cctcgcgag	ccatgtccac	caggtccgtg	tcctcgtcct	120
cctaccgcag	gatgttcggc	ggccccgca	cgcgagccg	gccgagctcc	agccggagct	180
acgtgactac	gtccaccgc	acctaagcc	tgggcagcgc	gctgcgccc	agcaccagcc	240
gcagcctcta	gcctcgtcc	ccggggggcg	tgtatgccac	gcgctcctct	gccgtgcgcc	300
tgccggagcag	cgtgcccggg	gtgcggctcc	tgccaggactc	ggtggacttc	tcgctggccg	360

acgccatcaa caccgagttc aagaacaccc gcaccaacga g

401

<210> 275

<211> 401

<212> DNA

<213> 人

<400> 275

ccacttccac cactttgtgg agcagtgcct tcagcgcaac cgggatgcca ggtatccctg	60
ctggcctggg cctgggcttc gggagagcag aggggtgctca ggagggttaag gccaggggtg	120
gaagggactt acctcccaaa ggttctgcag ggggaatctgg agctacacac aggagggatc	180
agctcctggg tgtgtcagag gccagcctgg ggagctctgg cactgcttc ccatgagctg	240
agggagaggg agaggggacc cgaggctgag gcataagtgg caggatttcg ggaagctggg	300
gacacggcag tgatgctgog gtctctcttc ccttttcct ccaggcccag tgccagcacc	360
ctctgaacc actctttctt caagcagatc aagcgacgtg c	401

<210> 276

<211> 401

<212> DNA

<213> 人

<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 gctcttcttc tagcagccag	120
tatactttct gtcagccaga aactgtatctt tcactctcagc ctagtgatga tgaatcaagt	180
agtgatgaaa ccagtaatac gccagtcctt gccttttagac gacgccgtgc taggaagaag	240
accgtttctg cttcagaatc tgaagaccgg ctagtgtgtg aadaagaaac tgaaccttct	300
aaggagttga gtaaacgtca gttcagtagt ggtctcaata agtgtgttat acttgctttg	360
gtgattgcaa tcagcatggg atttggccat ttctatggca c	401

<210> 277

<211> 401

<212> DNA

<213> 人

<220>

<221> misc feature

<222> (1)...(401)

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

<400> 277

aactttggca acatatctca gcaaaaacta cagctatgtt attcatgcca aaataaaagc	60
tgtgcagagg agtggctgca atgaggtcac aacgggtggtg gatgtaaaag agatcttcaa	120
gtcctcatca cccatccctc gaactcaagt cccgctcatt acaaattctt cttgccagtg	180
tccacacatc ctgccccatc aagatgttct catcatgtgt taagagnggc gctcaaggat	240
gatgcttctt gaaaattgct tagttgaaaa atggagagat cagcttagta aaagatccat	300
acagtgggaa gagaggctgc aggaacagcg ganaacagtt caggacaaga agaaaaacagc	360
cgggcgcacc agtcgtagta atcccccaa accaaaggga a	401

<210> 278

<211> 401

<212> DNA

<213> 人

<220>

<221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 278
 aatgagtgtg agaccacaaa tgaatgccgg gaggatgaaa tgtgttggaa ttatcatggc 60
 ggcttccgtt gttatocacg aatcccttgt caagatccct acattctaac accagagAAC 120
 cgatgtgttt gccagtcctc aatgccatg tgcgagAAC tgcccagtc aatagtctac 180
 aaatacatga gcatccgagc 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> 人

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 279
 aaattattgc ctctgataca tacctaagtn aacanaacat taatacctaa gtaaacataa 60
 cattaacttg aggggttgag nttctaantg aaactgtatt tgaaactttt aagtatactt 120
 taggaacaaa gcatgaacgg cagtctagaa taccagaAAC atctacttgg gtagcttggn 180
 gccattatcc tgtggaatct gatatgtctg gnagcatgtc attgatggga catgaagaca 240
 tctttggaaa tgatgagatt atttcctgtg ttaaaaaaaa aaaaaatctt aaattcctac 300
 aatgtgaaac tgaaactaat aattttgata ctgatgtatg ggacagcgta tctgtaccag 360
 gctctaaata acaaaagnta gggngacaag nacatgttcc t 401

<210> 280
 <211> 326
 <212> DNA
 <213> 人

<400> 280
 gaagtggAat tgtataattc aattcgataa ttgatctcat gggctttccc tggaggaaag 60
 gttttttttt ttgttttttt tttaagaaact tgaaacttgt aaactgagat gtctgtagct 120
 tttttgccca tctgtagtgt atgtgaagat ttcaaaaact gagagcaact tttctttgtt 180
 tagaattatg agaaaggcac tagatgactt taggatttgc atttttccct ttattgcctc 240
 atttcttgtg acgccttgtt ggggagggaa atctgtttat ttttctctac aaataaaaag 300
 ctaagattct atatcgcaaa aaaaaa 326

<210> 281
 <211> 374
 <212> DNA
 <213> 人

<400> 281
 caacgcgttt gcaaatattc ccctggtagc ctacttccct acccccgaat attggtaaga 60
 tcgagcaatg gcttcaggac atgggtttct ttctcctgtg atcattcaag tgctcactgc 120
 atgaagactg gcttgtctca gtgtttcaac ctacaccagg ctgtctcttg gtccacacct 180
 cgctccctgt tagtgccgta tgacagcccc catcaaatga ccttggccaa gtcacggttt 240
 ctctgtgtgc aaggtttgtt ggctgattgg tggaaagttag ggtggaccaa aggaggccac 300
 gtgagcagtc agcaccagtt ctgcaccagc agcgcctcog tcctagtggg tgttccctgtt 360
 tctcctggcc ctgg 374

<210> 282

<211> 404

<212> DNA

<213> 人

<220>

<221> misc feature

<222> (1)...(404)

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

<400> 282

```

agtgtggtgg aattcccgca tcttanncgc cgactcacac aaggcagagt ngccatggag      60
aaaattccag tgtcagcatt cttgctcctt gtggccctct cctacactct ggccagagat      120
accacagtca aacctgnagc caaaaaggac acaaaggact ctgcacccaa actgccccan      180
acctcttcca gaggttgggg tgaccaactc atctggactc anacatatga agaagctcta      240
tataaatcca agacaagcaa caaaccttgg atgattatct atcaattgga tgagtgccca      300
cacagtcaag ctttaaagaa agtgtttgct gaaaataaag aaatccagaa attggcagag      360
cagtttgtcc tcttcaatct ggtttatgaa acaactgaca aaca                                404

```

<210> 283

<211> 184

<212> DNA

<213> 人

<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 ccccaaaaaa ttggaatttt      120
tttttcaaca ctcttacacc tgttatggaa aatgtcaacc ttgtgaagaa aacaaaaata      180
aaaa                                              184

```

<210> 284

<211> 421

<212> DNA

<213> 人

<220>

<221> misc feature

<222> (1)...(421)

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

<400> 284

```

ctattaatcc tgccacaata tttttaakta cgtacaaaga tctgacatgt caccacagga      60
cccatttcac ccactgctct gtttggccgc cagtcttttg tctctctctt cagcaatggg      120
gaggcggata ccctttctct ggggaanana aatccatggg ttgttgccct tgccaataac      180
aaaaatggtg gaaagtggag tggcaagct gttgccattg gcctctttca cgtgaaccac      240
gtcaaaaagat ccagggtgcc tctctctgtt ggtgatcaca ccaattcttc ctagggttagc      300
acctccagtc accatacaca ggttaccagt gtcgaacttg atgaaatcag taatcttgcc      360
agtctctaaa tcaatctgaa tggatatcatt caccttgatg aggggatcgg ggtagcggat      420
g                                              421

```

<210> 285

<211> 361

<212> DNA

<213> 人

<220>

<221> misc_feature
 <222> (1)...(361)
 <223> n = A,T,C or G

<400> 285
 ctgggtggta actcttttatt tcattgtccg gaanaaagat gggagtggga acaggggtgga 60
 cactgtgcag gcttcagctt ccactccggg caggattcag gctatctggg accgcagggg 120
 ctgccaggtg cacagccctg gctcccaggg caggcaggca aggtgacggg actggaagcc 180
 cttttcanag ccttggagga gctgggtccgt ccacaagcaa tgagtgccac tctgcagttt 240
 gcaggggatg gataaacagg gaaacactgt gcatttcctca cagccaacag tgtaggtctt 300
 ggtgaagccc cggcgctgag ctaagctcag gctgttccag ggagccacga aactgcaggt 360
 a

<210> 286
 <211> 336
 <212> DNA
 <213> 人

<220>
 <221> misc_feature
 <222> (1)...(336)
 <223> n = A,T,C or G

<400> 286
 tttagagtggc agcgcccttta tttgtggggg ccttcaaggc agggctcgtgg ggggcagcgg 60
 ggaggaanag ccganaaact gtgtgaccgg ggcctcaggt ggtgggcatt gggggctcct 120
 cttgcanatg cccattggca tcaccgggtg agccattggg ggcagcgggt accggctcct 180
 tcttgttcaa catagggtag gtggcagcca cgggtccaac tcgcttgagg ctgggccctg 240
 ggcgctccat tttgtgttcc angagcatgt ggttctgtgg cgggagcccc acgcagggcc 300
 tgaggatgtt ctcgatgcag ctgcgctggc ggaaaa 336

<210> 287
 <211> 301
 <212> DNA
 <213> 人

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 287
 tgggtaccac atttntttat ttgaagggaat ggnacaaatc aaanaactta agnggatgtt 60
 ttggtacaac ttatanaaaa ggnaaaggaa accccaacat gcatgcnctg ccttgngnac 120
 cagggaagtc accccacggc tatggggaaa ttancccgag gcttancttt cattatcact 180
 gtctcccagg gngngcttgt caaaaanata ttccnccaag ccaaattcgg gcgctcccat 240
 nttgcnaag ttggtcacgt ggtcacccaa ttctttgatg gctttcacct gctcattcag 300
 g 301

<210> 288
 <211> 358
 <212> DNA
 <213> 人

<220>
 <221> misc_feature
 <222> (1)...(358)
 <223> n = A,T,C or G

<400> 288

```

aagtttttaa acttttttatt tgcattattaa aaaaatttgn cttccaata attaaaatca      60
tttgaacaaa aaaaaaaatg gcaactotgat taaactgcat tacagcctgc aggacacctt      120
gggccagctt ggtttttactc tanattttcac tgtcgtccca cccacttct tccacccac      180
ttttccttc accaacatgc aagttctttc cttccctgcc agccanatag atagacagat      240
gggaaaggca ggcggggcct tgcgtgtcag tagttctttg atgtgaaagg ggcagcacag      300
tcattttaac ttgatccaac ctctttgcat cttacaaagt taaacagcta aaagaagt      358

```

<210> 289

<211> 462

<212> DNA

<213> 人

<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 agaggggtgca      120
ggctgagggg ggaagggtaa naggaaggaa ggccatcctg gatccccaca tttcagtctc      180
anatgaggac aaagggactc ccaagcccc aaatcatcan aaacaccaa ggagcaggag      240
gagcttgagc agggcccagg gagcctcana gccataccag ccactgtcta cttcccatcc      300
tctctccca ttccctgtct gcttcanaac acctcccagc taagcccagc ctccattccc      360
ccaatcctgg cccttgccag cttgacagtc acagtgcctg gaattccacc actgaggctt      420
ctcccagttg gattaggacg tcgccctgtt agcatgctgc cc                                462

```

<210> 290

<211> 481

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(481)

<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 ttttccagct ctgtgggtctg tctttggatc agcaataatt gcctgaacag      240
ctactatggc ttggttgatt tttgtctgta gctctctgag ctctctatg tgcagcaatc      300
gcanaatttg agcagcttca ttaanaactg catctcctgt gtcaaaacca anaatatgtt      360
tgtctaaagc aacaggtaag cctctctttg tttgatttgc cttancaact gcctcctgtg      420
tcaggcgtc ctgaacccaa atccgaattg cettaagcat taccaggtaa tcatcatgac      480
g                                481

```

<210> 291

<211> 381

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(381)

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

<400> 291

```

tcatagtaat gtaaaacat ttgtttaatt ctaaatcaaa tcactttcac aacagtgaac      60

```

```

attagtgact ggttaaggng tgccactgta catatcatca tttctgact ggggtcagga      120
cctggtccta gtccacaagg gtggcaggag gaggggtggag gctaanaaca cagaaaacac      180
acaaaanaaa ggaagctgc cttggcanaa ggatgaggng gtgagcttgc cgaaggatgg      240
tggaagggg gctccctgtt ggggccgagc caggagtccc aagtcagctc tctgcctta      300
cttagctcct ggcanagggt gagtggggac ctacgaggtt caaatcaaa tggcatttgg      360
ccagcctggc tttactaaca g                                     381

```

```

<210> 292
<211> 371
<212> DNA
<213> 人

<220>
<221> misc_feature
<222> (1)...(371)
<223> n = A,T,C or G

```

```

<400> 292
gaaaaataa tccgtttaat tgaaaaacct gnaggatact attccactcc cccanatgag      60
gaggctgagg anaccaaacc cctacatcac ctctgtagca cttctgatac tcttcaagag      120
gcagcaggca agacaattc ccaaaacctc nacaaaagca attccaaggg ctgctgcagc      180
taccaccanc acatttttcc tcagccagcc cccaattctc tccacacagc cctccttatg      240
gatgccttc tcgttgaat taatcccaca gccacagta acattaatgc ancaggagtc      300
ggggactcgg ttcttcgaca tggaaaggat tttctcccaa tctgtgtagt tagcagcccc      360
acagcactta a                                     371

```

```

<210> 293
<211> 361
<212> DNA
<213> 人

<220>
<221> misc_feature
<222> (1)...(361)
<223> n = A,T,C or G

```

```

<400> 293
gatttaaaag aaacacttt attgttcagc aattaaaagt tagccaaata tgtatttttc      60
tcataatttt attgngatgt tatcaacatc aagtaaaatg ctcatthtca tcatttgctt      120
ctgttcatgt tttcttgaac acgtcttcaa ttttcttcc aaatgctgc atgccacact      180
tgaggtaacg aagcanaagt atttttaaac atgacagcta anaacattca tctacagcaa      240
cctatatgct caatacatgc cgggtgatcc tagtagtttt ttcacaacct tctacaagtt      300
tttggaanaa atctgttatg atgactttca tacaccttca cctcaaaggc tttcttgcac      360
c                                     361

```

```

<210> 294
<211> 391
<212> DNA
<213> 人

<220>
<221> misc_feature
<222> (1)...(391)
<223> n = A,T,C or G

```

```

<400> 294
tattttaaag tttaattatg attcanaaaa aatcgagcga ataactttct ctgaaaaaat      60
atattgactc tgtatanacc acagttattg gggganaagg gctggtaggt taaattatcc      120
tattttttat tctgaaaatg atattaatan aaagtcccggt ttccagtctg attataanga      180
tacatatgcc caaatggct ganaataaat acaacaggaa atgcaaaagc tgtaagcta      240

```

```

agggcattgca ananaaaatc tcanaatacc caaagnggca acaaggaacg tttggctgga      300
atttgaagtt atttcagtca tctttgtctt tggtccatg tttcaggatg cgtgtgaact      360
cgatgtaatt gaaattcccc tttttatcaa t                                     391

```

<210> 295

<211> 343

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(343)

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

<400> 295

```

ttcttttgtt ttattgataa cagaaactgt gcataattac agatttgatg aggaatctgc      60
aaataataaa gaattgtgtc actgccagca aaatacaatt attccatgcc ctctcaacat      120
acaaatatag agttcttcac accanattggc tctggtgtaa caaagccatt ttanattgtt      180
aattgtgctt ctacaaaacc ttcanagcat gaggtagttt cttttacct cnatattttc      240
cacatttcca ttattacact tttagttagc taaaatcctt ttaacatagc ctgaggatga      300
tctttcacia aagccaagcc tcatttacia agggtttatt tct                                     343

```

<210> 296

<211> 241

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(241)

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

<400> 296

```

ttcttggata ttggttggtt ttgtgaaaaa gtttttgttt ttcttctcag tcaactgaat      60
tatttctcta ctttgccctc ctgatgccca catgananaa cttaanataa tttctaacag      120
cttccacttt ggaaaaaaaaaa aaacctgtt ttcctcatgg aaocccagga gttgaaagtg      180
gatanatcgc tctcaaaatc taaggctctg ttcagcttta cattatgtta cctgacgttt      240
t                                     241

```

<210> 297

<211> 391

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(391)

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

<400> 297

```

gttggtggctg anaatgctgg agatgctcag ttctctccct cacaaggtag gccacaaatt      60
cttggtggctg ccctcacatc tggggtcttc aggcaccagc catgcctgcc gaggagtgtc      120
gtcaggacan accatgtccg tgctaggccc aggcacagcc caaccactcc tcatccaagt      180
ctctcccagg tttctggtcc cgatgggcaa ggatgacccc tccagtggct ggtacccccc      240
catcccaact cccctcacat gctctcactc tccatcaggt ccccaatcct ggcttccctc      300
ttcacgaact ctcaaagaaa aggaaggata aaacctaat aaaccagaca gaagcagctc      360
tggaagagta caaaaagaca gccagaggtg t                                     391

```

<210> 298

<211> 321

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(321)

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

<400> 298

caagccaaac	tgtntccagc	tttatttaan	atactttcca	taaacaatca	tggtatttca	60
ggcaggacat	gggcanacaa	tcgttaacag	tatacaacaa	ctttcaaact	cccttnttca	120
atggactacc	aaaaatcaaa	aagccactat	aaaacccaat	gaagtcttca	tctgatgctc	180
tgaacagggg	aagtttaaag	ngaggggtga	catttcacat	ttagcatggt	gtttaacaac	240
ttttcacaag	cgcaccctga	ctttcaggaa	gtgaaatgaa	aatggcanaa	tttatctgaa	300
natccacaat	ctaaaaatgg	a				321

<210> 299

<211> 401

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(401)

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

<400> 299

tatcataaag	agtgttgaag	tttattttatt	atagcaccat	tgagacattt	tgaaattgga	60
attggtaaaa	aaataaaaca	aaaagcattt	gaattgtatt	tgngngaaca	gcaaaaaaag	120
agaagtatca	tttttctttg	tcaatttata	ctgtttccaa	acatttttga	aataaataac	180
tggaattttg	tcggtcactt	gcactgggtg	acaagattag	aadaagagga	acacatatgg	240
agttaaattt	tttttgtttg	gatttcanat	agagtgttgt	ttataaaaag	caaacagggc	300
caacgtccac	accaaattct	tgatcaggac	caccaatgtc	atagggngca	atatctacaa	360
taggtagtct	cacagccttg	cgtgttcgat	attcaaagac	t		401

<210> 300

<211> 188

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(188)

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

<400> 300

tgaatgcttt	gtcatattta	gaaagttaaa	gtgcaataat	gtttgaanac	aataagtggg	60
ggtgtatctt	gttttctaata	agataaactt	ttttgtcttt	gctttatctt	attagggagt	120
tgtatgtcag	tgtataaaac	atactgtgtg	gtataacagg	cttaataaat	tctttaaaag	180
gaaaaaaa						188

<210> 301

<211> 291

<212> DNA

<213> 人

<400> 301

aagattttgt	tttattttat	tatggctaga	aagacactgt	tatagccaaa	atcggcaatg	60
acactaaaga	aatcctctgt	gcttttcaat	atgcaaatat	atttcttcca	agagttgccc	120
tggtgtgact	tcaagagttc	atgttaactt	cttttctgga	aacttccttt	tcttagttgt	180

tgtattcttg aagagcctgg gccatgaaga gcttgccctaa gttttgggca gtgaactcct 240
tgatgttctg gcagtaagtg tttatctggc ctgcaatgag cagcgagtcc a 291

<210> 302
<211> 341
<212> DNA
<213> 人

<220>
<221> misc feature
<222> (1)...(341)
<223> n = A,T,C or G

<400> 302
tgatttttca taatttttatt aaatnatcac tgggaaaact aatgggttcgc gtatcacaca 60
attacactac aatctgatat gagtggtaaa accagccaat ggaatccagg taaagtacaa 120
aaacgccacc ttttattgtc ctgtcttatt tctcgggaag gagggttcta ctttacacat 180
ttcatgagcc agcagtgagc ttgagttaca atgtgtaggt tccttgtggg tatagctgca 240
gaagaagcca tcaaatctct gaggacttga catctctcgg aaagaagcaa actagtggat 300
ccccggggct gcaggaattc gatatcaagc ttatcgatac c 341

<210> 303
<211> 361
<212> DNA
<213> 人

<220>
<221> misc feature
<222> (1)...(361)
<223> n = A,T,C or G

<400> 303
tgcagacagt aaatnaattt tatttgngtt cacagaacat actaggcgat ctcgacagtc 60
gctccgtgac agcccaccaa cccccaccc tntacctcgc agccacccta aaggcgactt 120
caanaanatg gaaggatctc acggatctca ttctaatgg tccgccgaag tctcacacag 180
tanacagacg gagttganat gctggaggat gcagtcacct cctaaactta cgacccacca 240
ccanacttca tcccagccgg gacgtcctcc cccaccggag tcttccccat ttcttctect 300
actttgccgc agttccaggn gtctgtcttc caccagtccc acaaagctca ataaatacca 360
a 361

<210> 304
<211> 301
<212> DNA
<213> 人

<220>
<221> misc feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 304
ctcttttaca cagcctttat ttncggccct tgatcctgct cggatgctgg tggaggccct 60
tagctccgcc cgcaggctc tgtgccgct ccccgaggc gcanattcat gaacacggtg 120
ctcaggggct tgaggccgta ctccccagc gggagctggg cctccagggg cttccccctc 180
aaggtcagcc anaacaggtc gtccctgcac ccctccagcc cggctcactg ctgcttcagg 240
tgggccacgg tctgcgtcag ccgcacctcg taggtgctgc tggggccctt gttattcctc 300
a 301

<210> 305
<211> 331

<212> DNA

<213> 人

<220>

<221> misc_feature

<222> (1)...(331)

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

<400> 305

ganaggctag	taacatcagt	tttattgggt	tggggnggca	accatagcct	ggctgggggn	60
ggggctggcc	ctcacagggt	gttgagttcc	agcaggggtct	ggteccaagg	ctggtgaatc	120
tcgacgttct	cctccttggc	actggccaa	gtctcttcta	ggtcacgat	ggttttctcc	180
aactttgcc	canacctctc	ggcaaaactct	gctcgggtct	canrctcctt	cagcttctcc	240
tccaacaggt	tgatctcctc	ttcatattta	tcttctttgg	gggnatactc	ctcctctgag	300
gccatcaggg	acttgagggc	ctgggtccatg	g			331

<210> 306

<211> 457

<212> DNA

<213> 人

<400> 306

aatatgtaaa	ggtaataact	tttattatat	taaagacaat	gcaaacgaaa	aacagaattg	60
agcagtgcaa	aattttaagg	actgttttgt	tctcaaagtt	gcaagtttca	aagccaaaag	120
aattatatgt	atcaaatata	taagtaaaaa	aaagttagac	tttcaagcct	gtaatcccag	180
cactttggga	ggctgaggca	ggtggatcac	taacattaaa	aagacaacat	tagattttgt	240
cgatttatag	caattttata	aatatataac	tttgtcactt	ggatcctgaa	gcaaaataat	300
aaagtgaatt	tgggattttt	gtacttggta	aaaagtttaa	caccctaaat	tcacaactag	360
tggatccccc	gggctgcagg	aattegatat	caagcttatc	gataccgtcg	acctcgaggg	420
ggggcccggt	acccaattcg	ccctatagtg	agtcgta			457

<210> 307

<211> 491

<212> DNA

<213> 人

<400> 307

gtgcttggac	ggaacccggc	gctcgttccc	caccccggcc	ggdcgccc	agccagccct	60
ccgtcacctc	ttcacccgac	cctcggactg	ccccaaaggc	ccgcgcgcgc	ctccagcgcc	120
gcgcagccac	cgccgcgcgc	gcccctcttc	cttagtgccc	gccatgacga	ccgcgtccac	180
ctcgcagggtg	cgccagaa	accaccagga	ctcagaggcc	gccatcaacc	gccagatcaa	240
cctggagctc	tacgcctcct	acgtttacct	gtccatgtct	taotactttg	accgcgatga	300
tgtggctttg	aagaactttg	ccaaatactt	tcttcaocaa	tctcatgagg	agagggaaca	360
tgctgagaaa	ctgatgaagc	tgacgaacca	acgaggtggc	cgaatcttcc	ttcaggatat	420
caagaaacca	gactgtgatg	actgggagag	cgggctgaat	gcaatggagt	gtgcattaca	480
tttggaaaaa	a					491

<210> 308

<211> 421

<212> DNA

<213> 人

<400> 308

ctcagcgctt	cttctttctt	ggtttgatcc	tgactgctgt	catggcggtgc	cctctggaga	60
aggccctgga	tgtgatgggtg	tccaccttcc	acaagtactc	gggcaagag	ggtgacaagt	120
tcaagctcaa	caagtccagaa	ctaaaggagc	tgtgaccocg	ggagctgccc	agcttcttgg	180
ggaaaaggac	agatgaagct	gctttccaga	agctgatgag	caacttggac	agcaacaggg	240
acaacgaggt	ggacttccaa	gagtactgtg	tcttctgtgc	ctgcacgcgc	atgatgtgta	300
acgaattctt	tgaaggcttc	ccagataaagc	agcccaaggaa	gaatatgaaa	ctcctctgat	360
gtgggttgggg	ggtctgccag	ctggggccct	ccctgtcgcc	agtgggcact	tttttttttc	420

c

421

<210> 309

<211> 321

<212> DNA

<213> 人

<400> 309

accaa	atggc	ggatg	acgcc	ggtgc	agcgg	ggggg	ccccg	gggcc	cctgg	ggccct	ggga	60
tgggg	aaacc	cggtg	gcttc	cgcgg	aggtt	tccgg	cagtgg	catcc	ggggc	cgggg	tcgcg	120
gccgt	ggacg	gggcc	ggggc	cgagg	ccgcg	gagct	cgccg	aggca	aggcc	gaggata	aagg	180
agtgg	atgcc	cgtca	ccaag	ttggg	ccgct	tggtc	aagga	catga	agatc	aagtc	ccctg	240
aggag	atcta	tctct	tctcc	ctgcc	catta	aggaat	caga	gatcat	tgat	ttcttc	cctgg	300
gggcct	ctct	caagg	atgag	g								321

<210> 310

<211> 381

<212> DNA

<213> 人

<400> 310

ttaac	cagcc	atatt	ggctc	aataa	atagc	ttcgg	taagg	agtta	atttc	cttct	agaaa	60
tcagt	gccta	ttttt	cctgg	aaact	caatt	ttaaa	tagtc	caatt	ccatc	tgaag	ccaag	120
ctgtt	gtcat	tttca	ttcgg	tgaca	ttctc	tccca	tgaca	cccag	aaggg	gcaga	agaac	180
cacat	ttttc	attta	tagat	gtttg	catcc	tttgt	attaa	aattat	ttttg	aaggg	gttgc	240
ctcatt	ggat	ggctt	ttttt	ttttt	cctcc	agggg	agaag	ggaga	aatgt	acttg	gaaat	300
taatg	tatgt	ttaca	tctct	ttgca	aattc	ctgtac	atag	agata	tattt	tttaag	tgtg	360
aatgt	aaaca	catact	gtga	a								381

<210> 311

<211> 538

<212> DNA

<213> 人

<400> 311

tttga	attta	cacca	agaac	ttctc	aataa	aagaa	aatca	tgaat	gctcc	acaatt	ttcaa	60
catacc	acaa	gaga	agttaa	tttct	taaca	ttgtg	ttcta	tgatt	atttg	taaga	ccctc	120
accaag	ttct	gatat	ctttt	aaaga	catag	ttcaa	aattg	ctttt	gaaaa	tctgt	attct	180
tga	aatatc	cttgt	tgtgt	attag	gtttt	taaata	accag	ctaa	aggatt	acctc	actga	240
gtcat	cagta	ccctc	ctatt	cagct	cccca	agatg	atgtg	ttttt	gctta	cccta	agaga	300
ggttt	ttctc	ttattt	tttag	ataatt	caag	tgctt	agata	aattat	gtttt	tcttt	aagtg	360
tttat	ggtaa	actct	tttaa	agaaa	attta	atatg	ttata	gctga	atctt	tttgg	taact	420
ttaaa	ctttt	atcata	gact	ctgtac	atat	gttca	aatta	gctgc	ttgcc	tgatg	tgtgt	480
atcat	cggtg	ggatg	acaga	acaa	acatat	ttatg	atcat	gaata	aatgtg	ctttg	taa	538

<210> 312

<211> 176

<212> DNA

<213> 人

<400> 312

ggagg	agcag	ctgag	agata	gggtc	agtga	atgcg	gttca	gcctg	ctacc	tctct	gtctc	60
tcatag	aacc	attgc	cttag	aattat	tgtg	tgaca	cgttt	tttgt	tgggt	aagct	gtaag	120
gtttt	gttct	ttgtg	aacat	gggtat	ttttg	agggg	agggg	ggagg	gagta	gggaag		176

<210> 313

<211> 396

<212> DNA

<213> 人

<400> 313

ccagcacc	caggccctgg	gggacctggg	ttctcagact	gccaaagaag	ccttgccatc	60
tggcgctccc	atggctcttg	caacatctcc	ccttcgtttt	tgaggggggc	atgccggggg	120
agccaccagc	ccctcactgg	gttcggagga	gagtcaggaa	gggcacaagca	cgacaaagca	180
gaaacatcgg	atttggggaa	cgctgtcaa	tccttgtgc	cgagggctg	ggcgggagag	240
actgttctgt	tccttgtgta	actgtgttgc	tgaaagacta	cctcgttctt	gtcttgatgt	300
gtcaccgggg	caactgctg	ggggcgggga	tgggggcagg	gtggaagcgg	ctccccattt	360
tataccaang	gtgctacatc	tatgtgatgg	gtgggg			396

<210> 314

<211> 311

<212> DNA

<213> 人

<400> 314

cctcaacatc	ctcagagagg	actggaagcc	agtccttacg	ataaactcca	taatttatgg	60
cctgcagtat	ctcttcttgg	agcccaaccc	cgaggaccca	ctgaacaagg	aggccgcaga	120
ggtcctgcag	aacaaccggc	gyctgtttga	gcagaaagtg	cagcgctcca	tgccgggtgg	180
ctacatcggc	tccacotact	ttgagcgtg	cctgaatatag	ggttggcgca	taccaccccc	240
cgccacggcc	acaagccctg	gcacccctg	caaatattta	ttggggggcca	tgggtagggg	300
tttggggggc	g					311

<210> 315

<211> 336

<212> DNA

<213> 人

<400> 315

tttagaacat	ggttatcatc	caagactact	ctaccctgca	acattgaact	ccaagagca	60
aatccacatt	cctcttgagt	tctgcagctt	ctgtgtaaat	agggcagctg	tcgtctatgc	120
cgtagaatca	catgatctga	ggaccattca	tggaagctgc	taaatagcct	agtcctggga	180
gtcttccata	aagtttttga	tggaagcaaac	aaacaggatt	aaactaggtt	tggttccttc	240
agccctctaa	aagcataggg	cttagcctgc	aggttctctt	gggctttctc	tgtgtgtgta	300
gttttgtaaa	cactatagca	tctgttaaga	tccagt			336

<210> 316

<211> 436

<212> DNA

<213> 人

<400> 316

aacatggtct	gctgacctta	agagagaogc	ttcctgcaga	acaggacctg	actacaaaga	60
atgtttccat	tggaaattgtt	ggtaaagaot	tggagtttac	aatctatgat	gatgatgatg	120
tgtctccatt	cctggaagggt	cttgaagaaa	gaaccacagag	aaaggcacag	cctgctcaac	180
ctgctgatga	acctgcagaa	aaggctgatg	aaccaatgga	acattaagtg	ataagccagt	240
ctatatatgt	attatcaaat	atgtaagaat	acaggcacca	catactgatg	acaataatct	300
atactttgaa	ccaaaagttg	cagagtgggtg	gaatgctatg	tttttaggaat	cagtcocagat	360
gtgagttttt	tccaagcaac	ctcactgaaa	cctatataat	ggaatacatt	tttctttgaa	420
agggctctgta	taatca					436

<210> 317

<211> 196

<212> DNA

<213> 人

<400> 317

tattccttgt	gaagatgata	tactattttt	gttaagcgtg	tctgtattta	tgtgtgagga	60
gctgctggct	tgcagtgcgc	gtgcagctgg	agagctgggtg	ccgggagatt	ggacggcctg	120
atgtccctc	ccctgccctg	gtccagggaa	gctggccgag	ggcctgggt	cctgaggggc	180
atctgcccc	ccccca					196

<210> 318
 <211> 381
 <212> DNA
 <213> 人
 <220>
 <221> misc feature
 <222> (1) ... (381)
 <223> n = A,T,C or G

<400> 318
 gacgcttnng ccgtaacgat gatoggagac atcctgctgt tcgggacgtt gctgatgaat 60
 gccggggcgg tgctgaactt taagctgaaa aagaaggaca cncggggctt tggggaggag 120
 tncagggagc ccaacacagg tgacaacatc cgggaattct tgctgancct cagatacttt 180
 cnaatcttca tencctctgt gaacatcttc atgatgttct gcatgattgt gctgntcggc 240
 tcttgaatcc cancgatgaa accannaact cactttcccg ggatgccgan tctccattcc 300
 tccattcctg atgacttcaa naatgttttt gaccaaaaaa ccgacaacct tcccagaaag 360
 tccaagctcg tgggtggngg a 381

<210> 319
 <211> 506
 <212> DNA
 <213> 人

<400> 319
 ctaagcttta cgaatggggt gacaacttat gataaaaact agagctagtg aattagccta 60
 tttgtaaata cctttgttat aattgatagg atacatcttg gacatggaat tgttaagcca 120
 cctctgagca gtgtatgtca ggaacttgctc attaggttgg cagcagaggg gcagaaggaa 180
 ttatacaggt agagatgtat gcagatgtgt ccataatatgt ccataattac attttgatag 240
 ccattgatgt atgcactctct tggctgtact ataagaacac attaattcaa tggaaataca 300
 ctttgctaat attttaatgg tatagatctg ctaatgaatt ctcttaaaaa catactgtat 360
 tctgttgctg tgtgtttcat tttaaattga gcattaaggg aatgcagcat ttaaatacaga 420
 actctgccaa tgcttttatc tagaggcgtg ttgccatttt tgtcttatat gaaatttctg 480
 tccaagaaa ggcaggatta catctt 506

<210> 320
 <211> 351
 <212> DNA
 <213> 人

<400> 320
 ctgacctgca ggacgaaacc atgaagagcc tgatccttct tggcatcctg gccgccttag 60
 cggtagtaac tttgtgttat gaatcacatg aaagcatgga atcttatgaa cttaatccct 120
 tcattaacag gagaastgca aataccttca tatccctca gcagagatgg agagctaaag 180
 tccaagagag gatccgagaa cgctctaagc ctgtccacga gctcaatagg gaagcctgtg 240
 atgactacag acttttgcaa cgctaagoca tggtttatgg atacaatgct gcctataatc 300
 gctacttcag gaagcgccga gggaccaaat gagactgagg gaagaaaaaa a 351

<210> 321
 <211> 421
 <212> DNA
 <213> 人

<400> 321
 ctoggaggcg ttcagctgct tcaagatgaa gctgaacatc tccttccag ccactggctg 60
 ccagaaactc attgaagtgg aagatgaacg caaacttctt actttctatg agaagcgtat 120
 ggccacagaa gttgttctg aagctctggg tgaagaatgg aagggttatg tggtecgat 180
 cagtggtggg aacgacaaac aaggtttccc catgaagcag ggtgtcttga cccatggcgc 240
 tgtccgcctg ctactgagta aagggcattc ctgttacaga ccaaggagaa ctggagaaag 300

aaagagaaaa tcagttcgtg gttgcattgt ggatgcaaat ctgagcgttc tcaacttggt 360
tattgtaaaa aaaggagaga aggatattcc tggactgact gatactacag tgcctcgccg 420
c 421

<210> 322
<211> 521
<212> DNA
<213> 人

<400> 322
agcagctctc ctgccacagc tctcaccccc ctgaaaatgt tcgectgctc caagtttgtc 60
tccactccct ccttggtcaa gagcacctca cagctgctga gccgtccgct atctgcagtg 120
gtgctgaaac gaccggagat actgacagat gagagcctca gcagcttggc agtctcatgt 180
ccccctacct cacttgtctc tagccgcagc ttccaaacca gcgccatttc aaggacatc 240
gacacagcag ccaagttcat tggagctggg gctgccacag ttgggggtggc tggttctggg 300
gctgggattg gaactgtgtt tgggagcctc atcattgggt atgccaggaa cctttctctg 360
aagcaacagc tcttctccta cgccattctg ggctttgccc tctcggaggc catggggctc 420
ttttgtctga tggtagcctt tctcatcctc tttgccatgt gaaggagccg tctccacctc 480
ccatagttct cccgcgtctg gttggccccg tgtgttccct t 521

<210> 323
<211> 435
<212> DNA
<213> 人

<400> 323
ccgaggtcgc acgcgtgaga cttctccgcc gcagacgccg ccgcgatgag ctacgtcgcc 60
tcttaectgc tggtgccct agggggcaac tctcccccga gcgccaaagg catcaagaag 120
atcttggaac gcgtgggtat cgaggcggac gacgacggc tcaacaagg tctcagttag 180
ctgaattgaa aaaacattga agacgtcatt gccagggtta ttggcaagct tgccagtgtg 240
cctgctggtg gggctgtagc cgtctctgct gccccaggct ctgcagcccc tgctgctggt 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> 人

<400> 324
aggagatcga ctttcggtgc ccgcaagacc agggctggaa ccgcgagatc acgctgcaga 60
tggtgcagta caagaatcgt caggccatcc tggcggtcaa atccacgcgg cagaagcagc 120
agcacctggt ccagcagcag cccccctcgc agccgcagcc gcagccgcag ctccagcccc 180
aaccaccagc tcagcctcag ccgcaacccc agccccaatc acaaccccag cctcagcccc 240
aaccacaagc tcagccccag cagctccacc cgtatccgca tccacatcca catccacact 300
ctcatcctca ctgcaccca caccctcacc cgcacccgca tccgcaccaa ataccgcacc 360
cacacccaca gccgcactcg cagccgcacg ggcaaccggt tctccgcagc acctccaaact 420
ctgectgaaa ggggcagctc ccgggcaaga caagggtttg aggacttgag gaagtgggac 480
gagcacattt ctattgtctt cacttggatc aaaagcaaaa c 521

<210> 325
<211> 451
<212> DNA
<213> 人

<400> 325
attttcatctt ccattaacct ggaagctttc atgaatatcc tcttctttta aaacatttta 60
acattattta aacagaaaaa gatgggctct ttctgggttag ttgttacatg atagcagaga 120
tatttttact tagattactt tgggaatgag agattgttgt cttgaactct ggcactgtac 180

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agtgaatgtg tctgtagttg tgtagtttg cattaagcat gtataacatt caagtatgtc 240
atccaaataa gaggcataata cattgaattg tttttaatcc tctgacaagt tgactcttcg 300
acccccaccc ccacccaaga ctttttaata gtaaatagag agagagagaa gagttaatga 360
acatgaggta gtgttccact ggcaggatga cttttcaata gctcaaatca atttcagtgc 420
ctttatcact tgaattatta acttaatttg a 451

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<210> 326
<211> 421
<212> DNA
<213> 人

<220>
<221> misc_feature
<222> (1)...(421)
<223> n = A,T,C or G

```

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<400> 326
cgcggtcgta agggctgagg attttttggtc cgcacgctcc tgctcctgac tcaccgctgt 60
tcgtctctgc cgaggaacaa gtcggtcagg aagcccgcgc gcacacagcca tggtttttaa 120
ggataccgga aaaacacccg tggagccgga ggtggcaatt caccgaattc gaatcacccct 180
aacaagccgc aacgtaaat ccttggaaaa ggtgtgtgct gacttgataa gaggcgcaaa 240
agaaaagaat ctcaaatgta aaggaccagt tcgaatgcct accaagactt tgagantcac 300
tacaagaaaa actccttgtg gtgaagggtc taagacgtgg gatcgtttcc agatgagaat 360
tcacaagcga ctcatcgact tgcacagtcc ttctgagatt gttaagcaga ttacttccat 420
c 421

```

```

<210> 327
<211> 456
<212> DNA
<213> 人

```

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<400> 327
atcttgacga ggctgcggtg tctgctgcta ttctccgagc ttgcgaatgc cgcctaagga 60
cgacaagaag aagaaggacg ctggaaagtc ggccaagaaa gacaaagacc cagtgaacaa 120
atccgggggc aaggccaana agaagaagtg gtccaaaggc aaagtccggg acaagctcaa 180
taacttagtc ttgtttgaca aagctaccta tgataaactc tgtaagggaag ttcccaacta 240
taaacttata accccagctg tggctctctga gagactgaag attcgaggct cccctggccag 300
ggcagccctt caggagctcc ttagtaaaag acttatcaaa ctggtttcaa agcacagagc 360
tcaagtaatt tacaccagaa ataccaaggy tggagatgct ccagctgctg gtgaagatgc 420
atgaataggt ccaaccagct gtacatttgg aaaaat 456

```

```

<210> 328
<211> 471
<212> DNA
<213> 人

```

```

<400> 328
gtggaagtga catcgtcttt aaacccctgg tggcaatccc tgacgcaccg ccgtgatgcc 60
caggaagac agggcgacct ggaagtcac ctacttccct aagatcatcc aactattgga 120
tgattatccg aaatgtttca ttgtgggagc agacaatgtg ggtccaagc agatgcagca 180
gatccgcatg tcccttcgag ggaaggctgt ggtgctgatg ggcaagaaca ccatgatgcg 240
caaggccatc cgagggcacc tggaaaaaa cccagctctg gagaaactgc tgcctcatat 300
ccgggggaat gtgggctttg tggtcaccaa ggaggacctc actgagatca gggacatggt 360
gctggccaat aagggtgccag ctgctgcccg tgctggtgoc attgccccat gtgaagtcac 420
tgtgccagcc cagaacactg gtctcggggc cgagaagacc tcctttttcc a 471

```

```

<210> 329
<211> 278
<212> DNA
<213> 人

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<220>
 <221> misc_feature
 <222> (1)...(278)
 <223> n = A,T,C or G

<400> 329
 gtttaaactt aagcttggtta ccgagctcgg atccactagt ccagtgtggt ggaattctag 60
 aaattgagat gcccccccag gccagcaaat gttccttttt gttcaaagtc tattttttatt 120
 ccttgatatt tttctttttt tttttttttt ttgnggatgg ggacttgtga atttttctaa 180
 aggtgctatt taacatggga gganagcgtg tgcggctcca gccagcccg ctgctcactt 240
 tccacctctt ctccacctgc ctctggcttc tcaggcct 278

<210> 330
 <211> 338
 <212> DNA
 <213> 人

<400> 330
 ctccaggcttc aacatogaat acgcccaggg ccccttggcc ctattcttca tagccgaata 60
 cacaacattt attataataa acaccctcac cactacnate ttctaggaa caacatatga 120
 cgcactctcc cctgaactct acacaacata ttttgcacc aagaccctac ttctaacctc 180
 cctgttctta tgaattcgaa cagcataccc ccgattccgc tacgaccaac tcatacacct 240
 cctatgaaaa aacttccctac cactcacctt agcattactt atatgatatg tctccatacc 300
 cattacaatc tccagcattc cccctcaaac ctaaaaaa 338

<210> 331
 <211> 2820
 <212> DNA
 <213> 人

<400> 331
 tggcaaaatc ctggagccag aagaaggac agcagcattg atcaatctta cagctaacat 60
 gttgtacctg gaaaacaatg cccagactca atttagttag ccacagtaca cgaacctggg 120
 gctcctgaac agcatggacc agcagattcg gaacggctcc tcgtccacca gtccctataa 180
 cacagaccac ggcgagaaca ggcgcacggc gccctggccc tacgcacagc ccagccccac 240
 ctctgatgct ctctctccat caccggccat cccctccaac accgactacc caggcccgca 300
 cagttccgac gtgtccttcc agcagtcgag caccggccaag tcggccacct ggacgtattc 360
 cactgaactg aagaactctt actgccaat tgcaaaagaca tgcdccatcc agatcaagggt 420
 gatgacccca cctcctcagg gagctgttat ccgagccatg cctgtctaca aaaaagctga 480
 gcacgtcaog gaggtgggtg agcgggtccc caaccatgag ctgagccgtg agttcaacga 540
 gggacagatt gcccctccta gtcattttag tcgagtagag gggacagacc atgccagta 600
 tgtagaagat cccatcacag gaagacagag tgtgtcggta ccttatgagc caccocagggt 660
 tggcactgaa ttcaogacag tcttgtacaa tttcatgtgt aacagcagtt gtgttggagg 720
 gatgaaccgc cgtccaattt taatcattgt tactctggaa accagagatg ggcaagtcc 780
 gggccgacgc tgctttgagg ccgggattctg tgccttgccc ggaagagaca ggaaggcgga 840
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 gcgcccgttt cgtcagaaca cacatgggtat ccagatgaca tccatcaaga aacgaagatc 960
 ccagatgat gaactgttat acttaaccag gaggggcccgt gagacttatg aaatgctgtt 1020
 gaagatcaaa gagtccttgg aactcatgca gtaccttcc cagcacacaa ttgaaacgta 1080
 caggcaacag caacagcagc agcaccagca cttacttcag aaacagacct caatacagtc 1140
 tccatcttca tatggttaaca gtcctccacc totgaacaaa atgaacagca tgaacaagct 1200
 gccttctgtg agccagctta tcaacctca gcagcgcaac gccctcactc ctacaacctc 1260
 tccatctgtg atgggagcca acattcccat gatgggcacc cacatggcaa tgggtggaga 1320
 catgaatgga ctacgcccc cccaggcact cctccccca ctctccatgc catccacctc 1380
 ccactgcaca ccccacctc cgtatccac agattgcagc attgtcagtt tcttagcgag 1440
 gttgggctgt tcatcatgtc tggactattt caogacccag ggggtgacca ccatctatca 1500
 gattgagcat tactccatgg atgatctggc aagtctgaaa atcctctgagc aatttcgaca 1560
 tgcgatctgg aagggcatcc tggaccacog gcagctccac gaattctcct ccccttctca 1620

tctcctgagg	accccaagca	gtgcctctac	agtcagtgtg	ggctccagtg	agacccgggg	1680
tgagcgtgtt	attgatgtg	tgcgattcac	cctccgccag	accatctctt	tcccaccccg	1740
agatgagtgg	aatgacttca	actttgacat	ggatgctcgc	cgcaataaag	aacagcgcat	1800
caaagaggag	ggggagttag	cctcaccatg	tgagctcttc	ctateccctct	cctaactgcc	1860
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tcttgtctga	tttcttaggg	gaaggagaag	taagaggcta	cctcttacct	aacatctgac	1980
ctggcatcta	attctgattc	tggctttaag	ccttcaaaac	tatagcttgc	agaactgtag	2040
ctgccatggc	taggtagnaag	tgagcaaaaa	agagttgggt	gtctccttaa	gctgcagaga	2100
tttctcattg	acttttataa	agcatgttca	cccttatagt	ctaagactat	atatataaat	2160
gtataaatat	acagtataga	tttttgggtg	gggggcattg	agtattgttt	aaaatgtaat	2220
ttaaatgaaa	gaaaattgag	ttgcactttt	tgaccatttt	tttaatttact	tgttttggat	2280
ggcttgtcta	tactccttcc	cttaaggggt	atcatgtatg	gtgataggta	tctagagctt	2340
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tgccacatca	aacctttgag	tagatccatt	tccattgctt	attaagttag	taagactgta	2460
gatatgtatt	cttttctcag	tgttggtata	ttttatatta	ctgacatttc	ttctagtgat	2520
gatggttcac	gttgggggtg	tttaatccag	ttataagaag	aagttcatgt	ccaaacgggtc	2580
ctctttagtt	tttggttggg	aatgaggaaa	attcttaaaa	ggcccatagc	agccagttca	2640
aaaaaccccg	acgtcatgta	tttgagcata	tcagtaaccc	ccttaaat	aataaccaga	2700
taccttatct	tacaatgttg	attgggaaaa	catttgctgc	ccattacaga	ggtattaaaa	2760
ctaaatttca	ctactagatt	gactaactca	aatcacatt	tgctactgtt	gtagaatttc	2820

<210> 332
 <211> 2270
 <212> DNA
 <213> 人

<400> 332						
tcgttgatat	caaagacagt	tgaaggaaat	gaattttgaa	acttcacggt	gtgccaccct	60
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totccatctt catatggtaa cagctcccca cctctgaaca aatgaacag catgaacaag 1140
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<210> 337
 <211> 1551
 <212> DNA
 <213> 人

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<400> 337
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ccatcagaag atggtgcgac aaacaagatt gagcttagca tggactgtat ccgcattgag 180
gactcggacc tgagtgcacc catgtggcca cagtacaga acctggggt cctgaacagc 240
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cagaacagcg tcacggcgcc ctgcacctac gcacagccca gctccacctt cgatgctctc 360
totccatcac ccgccatccc ctccaacacc gactaccag gcccgacag tttcgacgtg 420
tccttcagc agtcagacac cgcgaagtc gccacctga cgtattccac tgaactgaag 480
aaactctact gccaaattgc aagacatgc ccatccaga tcaaggtgat gacccacct 540
cctcaggag ctgttatccg cgcctgcct gtctacaaa aagctgagca cgtcacggag 600

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atcacaggaa gacagagtgt gctggtaoct tatgagccac cccaggttgg cactgaattc 780
acgcagctct tgtacaattt catgtgtaac agcagttgtg ttggagggat gaaccgccgt 840
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cagcagcagc accagcaact acttcagaaa cagacctcaa tacagtctcc atcttcatat 1260
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cagcttatca accctcagca gcgcaacgcc ctcactccta caaccattcc tgatggcatg 1380
ggagccaaca ttcccatgat gggcacccac atgccaatgg ctggagacat gaatggactc 1440
agccccaacc aggcactccc tccccactc tccatgccat ccacctccca ctgcacaccc 1500
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<210> 338
 <211> 586
 <212> FRT
 <213> 人

<400> 338

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      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 Pro 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
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
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
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 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 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
 465 470 475 480
 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
 565 570 575
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
 580 585
 <210> 339
 <211> 641
 <212> PRT
 <213> 人
 <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
 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
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
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
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> 人

<400> 340

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Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
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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

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
 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> 人
 <400> 341
 Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
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 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
His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala		
	85	90
Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala		
	100	105
Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly		
	115	120
Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr		
	130	135
Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn		
	145	150
Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn		
	165	170
Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val		
	180	185
Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val		
	195	200
Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg		
	210	215
Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val		
	225	230
Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg		
	245	250
Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp		
	260	265
Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Ser Arg Gln Asn Thr		
	275	280
His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp		
	290	295
Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu		
	305	310
Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His		
	325	330
Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu		
	340	345
Leu Gln Lys Gln		
	355	

<210> 342

<211> 690

<212> PRT

<213> 人

<400> 342

Met Asn Phe Glu Thr Ser Arg Cys Ala Thr Leu Gln Tyr Cys Pro Asp
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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

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
 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 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

01.10.31

610	615	620
Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val Ile Asp 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> 人		
<400> 343		
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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 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		
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
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 Tyr Pro Thr Asp Cys Ser Ile Val Arg Ile Trp Gln Val
 450 455 460

<210> 344
 <211> 516
 <212> PRT
 <213> 人

<400> 344

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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
 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
 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> 人

<400> 345

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Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
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Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln
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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 His Lys Val Arg Ile
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Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly
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Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn
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Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr
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Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala
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Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
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Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys
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<212> PRT
<213> 人

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Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser
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Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His
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 Val Asn Thr Asp Ser Glu Thr Ala Val Val Asn Val Thr Tyr Ser Ser
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 Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu
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 Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Thr Ala Ala
 145 150 155 160
 Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly Gln
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 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
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 Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln
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 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
 Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys
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 Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Asn Phe Val
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 Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln
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 Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu
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 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
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 Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp
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 Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe
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01-10-51

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Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His
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Gly Ala Asn Arg Phe
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