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

(57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as lung cancer, are disclosed. Compositions may comprise one or more lung tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a lung tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as lung cancer. Diagnostic methods based on detecting a lung tumor protein, or mRNA encoding such a protein, in a sample are also provided.

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COMPOUNDS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER AND METHODS FOR THEIR USE

TECHNICAL FIELD

The present invention relates generally to compositions and methods for the treatment of lung cancer. The invention is more specifically related to nucleotide sequences that are preferentially expressed in lung tumor tissue, together with polypeptides encoded by such nucleotide sequences. The inventive nucleotide sequences and polypeptides may be used in vaccines and pharmaceutical compositions for the treatment of lung cancer.

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 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 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.

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 compounds and methods for the therapy and diagnosis 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 SEQ ID NOS: 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277, 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359, 361, 364, 369, 372, 373, 377, 379 and 386; (b) variants of a sequence recited in SEQ ID NOS: 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277, 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359, 361, 364, 369, 372, 373, 377, 379 and 386; and (c) complements of a sequence of (a) or (b).

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 contiguous 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 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 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 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.

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 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 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 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. Isolated 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 isolated 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.

SEQUENCE IDENTIFIERS

SEQ ID NO: 1 is the determined cDNA sequence for L363C1.cons

SEQ ID NO: 2 is the determined cDNA sequence for L263C2.cons

SEQ ID NO: 3 is the determined cDNA sequence for L263C2c

SEQ ID NO: 4 is the determined cDNA sequence for L263C1.cons

SEQ ID NO: 5 is the determined cDNA sequence for L263C1b

SEQ ID NO: 6 is the determined cDNA sequence for L164C2.cons

SEQ ID NO: 7 is the determined cDNA sequence for L164C1.cons

SEQ ID NO: 8 is the determined cDNA sequence for L366C1a

SEQ ID NO: 9 is the determined cDNA sequence for L260C1.cons

SEQ ID NO: 10 is the determined cDNA sequence for L163C1c

SEQ ID NO: 11 is the determined cDNA sequence for L163C1b

SEQ ID NO: 12 is the determined cDNA sequence for L255C1.cons

SEQ ID NO: 13 is the determined cDNA sequence for L255C1b

SEQ ID NO: 14 is the determined cDNA sequence for L355C1.cons

SEQ ID NO: 15 is the determined cDNA sequence for L366C1.cons

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SEQ ID NO: 17 is the determined cDNA sequence for LT86-1

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SEQ ID NO: 19 is the determined cDNA sequence for LT86-3

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SEQ ID NO: 21 is the determined cDNA sequence for LT86-5

SEQ ID NO: 22 is the determined cDNA sequence for LT86-6

SEQ ID NO: 23 is the determined cDNA sequence for LT86-7

SEQ ID NO: 24 is the determined cDNA sequence for LT86-8

SEQ ID NO: 25 is the determined cDNA sequence for LT86-9

SEQ ID NO: 26 is the determined cDNA sequence for LT86-10

SEQ ID NO: 27 is the determined cDNA sequence for LT86-11

SEQ ID NO: 28 is the determined cDNA sequence for LT86-12

SEQ ID NO: 29 is the determined cDNA sequence for LT86-13

SEQ ID NO: 30 is the determined cDNA sequence for LT86-14

SEQ ID NO: 31 is the determined cDNA sequence for LT86-15

SEQ ID NO: 32 is the predicted amino acid sequence for LT86-1

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SEQ ID NO: 35 is the predicted amino acid sequence for LT86-4

SEQ ID NO: 36 is the predicted amino acid sequence for LT86-5

SEQ ID NO: 37 is the predicted amino acid sequence for LT86-6

SEQ ID NO: 38 is the predicted amino acid sequence for LT86-7

SEQ ID NO: 39 is the predicted amino acid sequence for LT86-8

SEQ ID NO: 40 is the predicted amino acid sequence for LT86-9

SEQ ID NO: 41 is the predicted amino acid sequence for LT86-10

SEQ ID NO: 42 is the predicted amino acid sequence for LT86-11

SEQ ID NO: 43 is the predicted amino acid sequence for LT86-12

SEQ ID NO: 44 is the predicted amino acid sequence for LT86-13

SEQ ID NO: 45 is the predicted amino acid sequence for LT86-14

SEQ ID NO: 46 is the predicted amino acid sequence for LT86-15

SEQ ID NO: 47 is a $(dT)_{12}AG$ primer

SEQ ID NO: 48 is a primer

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SEQ ID NO: 50 is the determined 5' cDNA sequence for L86S-12

SEQ ID NO: 51 is the determined 5' cDNA sequence for L86S-16

SEQ ID NO: 52 is the determined 5' cDNA sequence for L86S-25

SEQ ID NO: 53 is the determined 5' cDNA sequence for L86S-36

SEQ ID NO: 54 is the determined 5' cDNA sequence for L86S-40

SEQ ID NO: 55 is the determined 5' cDNA sequence for L86S-46

SEQ ID NO: 56 is the predicted amino acid sequence for L86S-3

SEQ ID NO: 57 is the predicted amino acid sequence for L86S-12

SEQ ID NO: 58 is the predicted amino acid sequence for L86S-16

SEQ ID NO: 59 is the predicted amino acid sequence for L86S-25

SEQ ID NO: 60 is the predicted amino acid sequence for L86S-36

SEQ ID NO: 61 is the predicted amino acid sequence for L86S-40

SEQ ID NO: 62 is the predicted amino acid sequence for L86S-46

SEQ ID NO: 63 is the determined 5' cDNA sequence for L86S-30

SEQ ID NO: 64 is the determined 5' cDNA sequence for L86S-41

SEQ ID NO: 65 is the predicted amino acid sequence from the 5' end of LT86-9

SEQ ID NO: 66 is the determined extended cDNA sequence for LT86-4

SEQ ID NO: 67 is the predicted extended amino acid sequence for LT86-4

SEQ ID NO: 68 is the determined 5' cDNA sequence for LT86-20

SEQ ID NO: 69 is the determined 3' cDNA sequence for LT86-21

SEQ ID NO: 70 is the determined 5' cDNA sequence for LT86-22

SEQ ID NO: 71 is the determined 5' cDNA sequence for LT86-26

SEQ ID NO: 72 is the determined 5' cDNA sequence for LT86-27

SEQ ID NO: 73 is the predicted amino acid sequence for LT86-20

SEQ ID NO: 74 is the predicted amino acid sequence for LT86-21

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SEQ ID NO: 76 is the predicted amino acid sequence for LT86-26

SEQ ID NO: 77 is the predicted amino acid sequence for LT86-27

SEQ ID NO: 78 is the determined extended cDNA sequence for L86S-12

SEQ ID NO: 79 is the determined extended cDNA sequence for L86S-36

SEQ ID NO: 80 is the determined extended cDNA sequence for L86S-46

SEQ ID NO: 81 is the predicted extended amino acid sequence for L86S-12

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SEQ ID NO: 83 is the predicted extended amino acid sequence for L86S-46

SEQ ID NO: 84 is the determined 5'cDNA sequence for L86S-6

SEQ ID NO: 85 is the determined 5'cDNA sequence for L86S-11

SEQ ID NO: 86 is the determined 5'cDNA sequence for L86S-14

SEQ ID NO: 87 is the determined 5'cDNA sequence for L86S-29

SEQ ID NO: 88 is the determined 5'cDNA sequence for L86S-34

SEQ ID NO: 89 is the determined 5'cDNA sequence for L86S-39

SEQ ID NO: 90 is the determined 5'cDNA sequence for L86S-47

SEQ ID NO: 91 is the determined 5'cDNA sequence for L86S-49

SEQ ID NO: 92 is the determined 5'cDNA sequence for L86S-51

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SEQ ID NO: 104 is the determined 5' cDNA sequence for SLT-T3
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SEQ ID NO: 113 is the predicted amino acid sequence for SLT-T3
SEQ ID NO: 114 is the predicted amino acid sequence for SLT-T10
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SEQ ID NO: 140 is the determined cDNA sequence for PSLT-011
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SEQ ID NO: 189 is a first predicted amino acid sequence for SAL-66

SEQ ID NO: 190 is a second predicted amino acid sequence for SAL-66

SEQ ID NO: 191 is the predicted amino acid sequence for SAL-82

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SEQ ID NO: 234 is the determined 5' cDNA sequence for LT4690-55
SEQ ID NO: 235 is the determined cDNA sequence for LT4690-59
SEQ ID NO: 236 is the determined cDNA sequence for LT4690-63
SEQ ID NO: 237 is the determined cDNA sequence for LT4690-71
SEQ ID NO: 238 is the determined cDNA sequence for 2LT-3
SEQ ID NO: 239 is the determined cDNA sequence for 2LT-6
SEQ ID NO: 240 is the determined cDNA sequence for 2LT-22
SEQ ID NO: 241 is the determined cDNA sequence for 2LT-25
SEQ ID NO: 242 is the determined cDNA sequence for 2LT-26
SEQ ID NO: 243 is the determined cDNA sequence for 2LT-31
SEQ ID NO: 244 is the determined cDNA sequence for 2LT-36
SEQ ID NO: 245 is the determined cDNA sequence for 2LT-42
SEQ ID NO: 246 is the determined cDNA sequence for 2LT-44
SEQ ID NO: 247 is the determined cDNA sequence for 2LT-54
SEQ ID NO: 248 is the determined cDNA sequence for 2LT-55
SEQ ID NO: 249 is the determined cDNA sequence for 2LT-57
SEQ ID NO: 250 is the determined cDNA sequence for 2LT-58

SEQ ID NO: 251 is the determined cDNA sequence for 2LT-59
SEQ ID NO: 252 is the determined cDNA sequence for 2LT-62
SEQ ID NO: 253 is the determined cDNA sequence for 2LT-63
SEQ ID NO: 254 is the determined cDNA sequence for 2LT-65
SEQ ID NO: 255 is the determined cDNA sequence for 2LT-66
SEQ ID NO: 256 is the determined cDNA sequence for 2LT-70
SEQ ID NO: 257 is the determined cDNA sequence for 2LT-73
SEQ ID NO: 258 is the determined cDNA sequence for 2LT-74
SEQ ID NO: 259 is the determined cDNA sequence for 2LT-76
SEQ ID NO: 260 is the determined cDNA sequence for 2LT-77
SEQ ID NO: 261 is the determined cDNA sequence for 2LT-78
SEQ ID NO: 262 is the determined cDNA sequence for 2LT-80
SEQ ID NO: 263 is the determined cDNA sequence for 2LT-85
SEQ ID NO: 264 is the determined cDNA sequence for 2LT-87
SEQ ID NO: 265 is the determined cDNA sequence for 2LT-89
SEQ ID NO: 266 is the determined cDNA sequence for 2LT-94
SEQ ID NO: 267 is the determined cDNA sequence for 2LT-95
SEQ ID NO: 268 is the determined cDNA sequence for 2LT-98
SEQ ID NO: 269 is the determined cDNA sequence for 2LT-100
SEQ ID NO: 270 is the determined cDNA sequence for 2LT-103
SEQ ID NO: 271 is the determined cDNA sequence for 2LT-105
SEQ ID NO: 272 is the determined cDNA sequence for 2LT-107
SEQ ID NO: 273 is the determined cDNA sequence for 2LT-108
SEQ ID NO: 274 is the determined cDNA sequence for 2LT-109
SEQ ID NO: 275 is the determined cDNA sequence for 2LT-118
SEQ ID NO: 276 is the determined cDNA sequence for 2LT-120
SEQ ID NO: 277 is the determined cDNA sequence for 2LT-121
SEQ ID NO: 278 is the determined cDNA sequence for 2LT-122
SEQ ID NO: 279 is the determined cDNA sequence for 2LT-124
SEQ ID NO: 280 is the determined cDNA sequence for 2LT-126
SEQ ID NO: 281 is the determined cDNA sequence for 2LT-127

SEQ ID NO: 282 is the determined cDNA sequence for 2LT-128
SEQ ID NO: 283 is the determined cDNA sequence for 2LT-129
SEQ ID NO: 284 is the determined cDNA sequence for 2LT-133
SEQ ID NO: 285 is the determined cDNA sequence for 2LT-137
SEQ ID NO: 286 is the determined cDNA sequence for LT4690-71
SEQ ID NO: 287 is the determined cDNA sequence for LT4690-82
SEQ ID NO: 288 is the determined full-length cDNA sequence for SSLT-74
SEQ ID NO: 289 is the determined cDNA sequence for SSLT-78
SEQ ID NO: 290 is the determined cDNA sequence for SCC1-8.
SEQ ID NO: 291 is the determined cDNA sequence for SCC1-12.
SEQ ID NO: 292 is the determined cDNA sequence for SCC1-336
SEQ ID NO: 293 is the determined cDNA sequence for SCC1-344
SEQ ID NO: 294 is the determined cDNA sequence for SCC1-345
SEQ ID NO: 295 is the determined cDNA sequence for SCC1-346
SEQ ID NO: 296 is the determined cDNA sequence for SCC1-348
SEQ ID NO: 297 is the determined cDNA sequence for SCC1-350
SEQ ID NO: 298 is the determined cDNA sequence for SCC1-352
SEQ ID NO: 299 is the determined cDNA sequence for SCC1-354
SEQ ID NO: 300 is the determined cDNA sequence for SCC1-355
SEQ ID NO: 301 is the determined cDNA sequence for SCC1-356
SEQ ID NO: 302 is the determined cDNA sequence for SCC1-357
SEQ ID NO: 303 is the determined cDNA sequence for SCC1-501
SEQ ID NO: 304 is the determined cDNA sequence for SCC1-503
SEQ ID NO: 305 is the determined cDNA sequence for SCC1-513
SEQ ID NO: 306 is the determined cDNA sequence for SCC1-516
SEQ ID NO: 307 is the determined cDNA sequence for SCC1-518
SEQ ID NO: 308 is the determined cDNA sequence for SCC1-519
SEQ ID NO: 309 is the determined cDNA sequence for SCC1-522
SEQ ID NO: 310 is the determined cDNA sequence for SCC1-523
SEQ ID NO: 311 is the determined cDNA sequence for SCC1-525
SEQ ID NO: 312 is the determined cDNA sequence for SCC1-527

SEQ ID NO: 313 is the determined cDNA sequence for SCC1-529
SEQ ID NO: 314 is the determined cDNA sequence for SCC1-530
SEQ ID NO: 315 is the determined cDNA sequence for SCC1-531
SEQ ID NO: 316 is the determined cDNA sequence for SCC1-532
SEQ ID NO: 317 is the determined cDNA sequence for SCC1-533
SEQ ID NO: 318 is the determined cDNA sequence for SCC1-536
SEQ ID NO: 319 is the determined cDNA sequence for SCC1-538
SEQ ID NO: 320 is the determined cDNA sequence for SCC1-539
SEQ ID NO: 321 is the determined cDNA sequence for SCC1-541
SEQ ID NO: 322 is the determined cDNA sequence for SCC1-542
SEQ ID NO: 323 is the determined cDNA sequence for SCC1-546
SEQ ID NO: 324 is the determined cDNA sequence for SCC1-549
SEQ ID NO: 325 is the determined cDNA sequence for SCC1-551
SEQ ID NO: 326 is the determined cDNA sequence for SCC1-552
SEQ ID NO: 327 is the determined cDNA sequence for SCC1-554
SEQ ID NO: 328 is the determined cDNA sequence for SCC1-558
SEQ ID NO: 329 is the determined cDNA sequence for SCC1-559
SEQ ID NO: 330 is the determined cDNA sequence for SCC1-561
SEQ ID NO: 331 is the determined cDNA sequence for SCC1-562
SEQ ID NO: 332 is the determined cDNA sequence for SCC1-564
SEQ ID NO: 333 is the determined cDNA sequence for SCC1-565
SEQ ID NO: 334 is the determined cDNA sequence for SCC1-566
SEQ ID NO: 335 is the determined cDNA sequence for SCC1-567
SEQ ID NO: 336 is the determined cDNA sequence for SCC1-568
SEQ ID NO: 337 is the determined cDNA sequence for SCC1-570
SEQ ID NO: 338 is the determined cDNA sequence for SCC1-572
SEQ ID NO: 339 is the determined cDNA sequence for SCC1-575
SEQ ID NO: 340 is the determined cDNA sequence for SCC1-576
SEQ ID NO: 341 is the determined cDNA sequence for SCC1-577
SEQ ID NO: 342 is the determined cDNA sequence for SCC1-578
SEQ ID NO: 343 is the determined cDNA sequence for SCC1-582

SEQ ID NO: 344 is the determined cDNA sequence for SCC1-583
SEQ ID NO: 345 is the determined cDNA sequence for SCC1-586
SEQ ID NO: 346 is the determined cDNA sequence for SCC1-588
SEQ ID NO: 347 is the determined cDNA sequence for SCC1-590
SEQ ID NO: 348 is the determined cDNA sequence for SCC1-591
SEQ ID NO: 349 is the determined cDNA sequence for SCC1-592
SEQ ID NO: 350 is the determined cDNA sequence for SCC1-593
SEQ ID NO: 351 is the determined cDNA sequence for SCC1-594
SEQ ID NO: 352 is the determined cDNA sequence for SCC1-595
SEQ ID NO: 353 is the determined cDNA sequence for SCC1-596
SEQ ID NO: 354 is the determined cDNA sequence for SCC1-598
SEQ ID NO: 355 is the determined cDNA sequence for SCC1-599
SEQ ID NO: 356 is the determined cDNA sequence for SCC1-602
SEQ ID NO: 357 is the determined cDNA sequence for SCC1-604
SEQ ID NO: 358 is the determined cDNA sequence for SCC1-605
SEQ ID NO: 359 is the determined cDNA sequence for SCC1-606
SEQ ID NO: 360 is the determined cDNA sequence for SCC1-607
SEQ ID NO: 361 is the determined cDNA sequence for SCC1-608
SEQ ID NO: 362 is the determined cDNA sequence for SCC1-610
SEQ ID NO: 363 is the determined cDNA sequence for clone DMS79T1
SEQ ID NO: 364 is the determined cDNA sequence for clone DMS79T2
SEQ ID NO: 365 is the determined cDNA sequence for clone DMS79T3
SEQ ID NO: 366 is the determined cDNA sequence for clone DMS79T5
SEQ ID NO: 367 is the determined cDNA sequence for clone DMS79T6
SEQ ID NO: 368 is the determined cDNA sequence for clone DMS79T7
SEQ ID NO: 369 is the determined cDNA sequence for clone DMS79T9
SEQ ID NO: 370 is the determined cDNA sequence for clone DMS79T10
SEQ ID NO: 371 is the determined cDNA sequence for clone DMS79T11
SEQ ID NO: 372 is the determined cDNA sequence for clone 128T1
SEQ ID NO: 373 is the determined cDNA sequence for clone 128T2
SEQ ID NO: 374 is the determined cDNA sequence for clone 128T3

SEQ ID NO: 375 is the determined cDNA sequence for clone 128T4
SEQ ID NO: 376 is the determined cDNA sequence for clone 128T5
SEQ ID NO: 377 is the determined cDNA sequence for clone 128T7
SEQ ID NO: 378 is the determined cDNA sequence for clone 128T9
SEQ ID NO: 379 is the determined cDNA sequence for clone 128T10
SEQ ID NO: 380 is the determined cDNA sequence for clone 128T11
SEQ ID NO: 381 is the determined cDNA sequence for clone 128T12
SEQ ID NO: 382 is the determined cDNA sequence for clone NCIH69T3
SEQ ID NO: 383 is the determined cDNA sequence for clone NCIH69T5
SEQ ID NO: 384 is the determined cDNA sequence for clone NCIH69T6
SEQ ID NO: 385 is the determined cDNA sequence for clone NCIH69T7
SEQ ID NO: 386 is the determined cDNA sequence for clone NCIH69T9
SEQ ID NO: 387 is the determined cDNA sequence for clone NCIH69T10
SEQ ID NO: 388 is the determined cDNA sequence for clone NCIH69T11
SEQ ID NO: 389 is the determined cDNA sequence for clone NCIH69T12

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to 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 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 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 of human lung tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NOS: 1-31, 49-55, 63,64, 66, 68-72, 78-80, 84-92 and 217-389.

LUNG TUMOR PROTEIN POLYNUCLEOTIDES

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

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a lung tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native lung tumor protein or a portion thereof.

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

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

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

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

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

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

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 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 ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured 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 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 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.

Certain nucleic acid sequences of cDNA molecules encoding portions of lung tumor proteins are provided in SEQ ID NO: 1-31, 49-55, 63,64, 66, 68-72, 78-80, 84-92 and 217-389. The isolation of these sequences is described in detail below.

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 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*. 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.

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 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 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 limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). 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.

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., 243-247 (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). 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 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 sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ^{125}I-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 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 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.

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

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

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above 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 and higher eukaryotic cells. Preferably, the host 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 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, 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 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 tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

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

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

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

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

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). 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 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 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 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 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 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 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, 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 more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y, ^{123}I, ^{125}I, ^{131}I, ^{186}Re, ^{188}Re, ^{211}At, and ^{212}Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria 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 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 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, 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, 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 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 *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 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 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 kill target cells coated with the 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 al., *Cancer Res. 54*:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a lung tumor polypeptide (100 ng/ml - 100 μg/ml, preferably 200 ng/ml - 25 μg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a lung tumor polypeptide, polynucleotide or polypeptide-expressing APC may be $CD4^+$ and/or $CD8^+$. Lung tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

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

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is 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 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 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. 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 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) 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 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, *Bortadella 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); 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.

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, TNFα, 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 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 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. 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. Another preferred adjuvant is a saponin, preferably QS21, 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. 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 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. 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 TNFα to cultures of monocytes 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, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce maturation and proliferation of dendritic cells.

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 correlates with the high expression of Fcγ receptor, mannose receptor and DEC-205 marker. 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).

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. 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 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.

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 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 μg 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 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 biological sample (for example, blood, sera, 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 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 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) 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 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 μg, and preferably about 100 ng to about 1 μg, 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 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. 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.

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 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 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.

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.

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 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. 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 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 1μg, and more preferably from about 50 ng to about 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 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 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. 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, 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.

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 (*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.

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 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 sequence recited in SEQ ID NOS: 1-31, 49-55, 63,64, 66, 68-72, 78-80, 84-92 and 217-389. 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).

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

As noted above, to improve sensitivity, multiple lung tumor protein 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 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 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, 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 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 way of limitation.

EXAMPLES

Example 1

PREPARATION OF LUNG TUMOR-SPECIFIC cDNA SEQUENCES USING DIFFERENTIAL DISPLAY RT-PCR

This example illustrates the preparation of cDNA molecules encoding lung tumor-specific polypeptides using a differential display screen.

Tissue samples were prepared from lung tumor and normal tissue of a patient with lung cancer that was confirmed by pathology after removal of samples from the patient. Normal RNA and tumor RNA was extracted from the samples and mRNA was isolated and converted into cDNA using a $(dT)_{12}AG$ (SEQ ID NO: 47) anchored 3' primer. Differential display PCR was then executed using a randomly chosen primer (SEQ ID NO: 48). Amplification conditions were standard buffer containing 1.5 mM $MgCl_2$, 20 pmol of primer, 500 pmol dNTP and 1 unit of Taq DNA polymerase (Perkin-Elmer, Branchburg, NJ). Forty cycles of amplification were performed using 94 °C denaturation for 30 seconds, 42 °C annealing for 1 minute and 72 °C extension for 30 seconds. Bands that were repeatedly observed to be specific to the RNA fingerprint pattern of the tumor were cut out of a silver stained gel, subcloned into the pGEM-T vector (Promega, Madison, WI) and sequenced. The isolated 3' sequences are provided in SEQ ID NO: 1-16.

Comparison of these sequences to those in the public databases using the BLASTN program, revealed no significant homologies to the sequences provided in SEQ ID NO: 1-11. To the best of the inventors' knowledge, none of the isolated DNA sequences have previously been shown to be expressed at a greater level in human lung tumor tissue than in normal lung tissue.

Example 2

USE OF PATIENT SERA TO IDENTIFY DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS

This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by expression screening of lung tumor samples with autologous patient sera.

A human lung tumor directional cDNA expression library was constructed employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the library was taken from a late SCID mouse passaged human squamous epithelial lung carcinoma and poly A+ RNA was isolated using the Message Maker kit (Gibco BRL, Gaithersburg, MD). The resulting library was screened using *E. coli*-absorbed autologous patient serum, as described in Sambrook et al., (*Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989), with the secondary antibody being goat anti-human IgG-A-M (H + L) conjugated with alkaline phosphatase, developed with NBT/BCIP (Gibco BRL). Positive plaques expressing immunoreactive antigens were purified. Phagemid from the plaques was rescued and the nucleotide sequences of the clones was determined.

Fifteen clones were isolated, referred to hereinafter as LT86-1 – LT86-15. The isolated cDNA sequences for LT86-1 – LT86-8 and LT86-10 - LT86-15 are provided in SEQ ID NO: 17-24 and 26-31, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 32-39 and 41-46, respectively. The determined cDNA sequence for LT86-9 is provided in SEQ ID NO: 25, with the corresponding predicted amino acid sequences from the 3' and 5' ends being provided in SEQ ID NO: 40 and 65, respectively. These sequences were compared to those in the gene bank as described above. Clones LT86-3, LT86-6 – LT86-9, LT86-11 – LT86-13 and LT86-15 (SEQ ID NO: 19, 22-25, 27-29 and 31, respectively) were found to show some homology to previously identified expressed sequence tags (ESTs), with clones LT86-6, LT86-8, LT86-11, LT86-12 and LT86-15 appearing to be similar or identical to each other. Clone LT86-3 was found to show some homology with a human transcription repressor. Clones LT86-6, 8, 9, 11, 12 and 15 were found to show some homology to a yeast RNA Pol II transcription regulation mediator. Clone LT86-13 was found to show some homology with a *C. elegans* leucine aminopeptidase. Clone LT86-9 appears to contain two inserts, with the 5' sequence showing homology to the previously identified antisense sequence of interferon alpha-induced P27, and the 3' sequence being similar to LT86-6. Clone LT86-14 (SEQ ID NO: 30) was found to show some homology to the trithorax gene and has an "RGD" cell attachment sequence and a beta-Lactamase A site which functions in hydrolysis of penicillin. Clones LT86-1, LT86-2, LT86-4, LT86-5 and LT86-10 (SEQ ID NOS: 17, 18, 20, 21 and 26. respectively) were found to show homology to previously identified genes. A subsequently determined extended cDNA sequence for LT86-4 is provided in SEQ ID NO: 66, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 67.

Subsequent studies led to the isolation of five additional clones, referred to as LT86-20, LT86-21, LT86-22, LT86-26 and LT86-27. The determined 5' cDNA sequences for LT86-20, LT86-22, LT86-26 and LT86-27 are provided in SEQ ID NO: 68 and 70-72, respectively, with the determined 3' cDNA sequences for LT86-21 being provided in SEQ ID NO: 69. The corresponding predicted amino acid sequences for LT86-20, LT86-21, LT86-22, LT86-26 and LT86-27 are provided in SEQ ID NO: 73-77, respectively. LT86-22 and LT86-27 were found to be highly similar to each other. Comparison of these sequences to those in the gene bank as described above, revealed no significant homologies to LT86-22 and LT86-27. LT86-20, LT86-21 and LT86-26 were found to show homology to previously identified genes.

In further studies, a cDNA expression library was prepared using mRNA from a lung small cell carcinoma cell line in the lambda ZAP Express expression vector (Stratagene), and screened as described above, with a pool of two lung small cell carcinoma patient sera. The sera pool was adsorbed with *E. coli* lysate and human PBMC lysate was added to the serum to block antibody to proteins found in normal tissue. Seventy-three clones were isolated. The determined cDNA sequences of these clones are provided in SEQ ID NO: 290-362. The sequences of SEQ ID NO: 289-292, 294, 296-297, 300, 302, 303, 305, 307-315, 317-320, 322-325, 327-332, 334, 335, 338-341, 343-352, 354-358, 360 and 362 were found to show some homology to previously isolated genes. The sequences of SEQ ID NO: 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359 and 361 were found to show some homology to previously identified ESTs.

Example 3

USE OF MOUSE ANTISERA TO IDENTIFY DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS

This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by screening of lung tumor cDNA libraries with mouse anti-tumor sera.

A directional cDNA lung tumor expression library was prepared as described above in Example 2. Sera was obtained from SCID mice containing late passaged human squamous cell and adenocarcinoma tumors. These sera were pooled and injected into normal mice to produce anti-lung tumor serum. Approximately 200,000 PFUs were screened from the unamplified library using this antiserum. Using a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (BRL Labs.), approximately 40 positive plaques were identified. Phage was purified and phagemid excised for 9 clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined cDNA sequences for 7 of the isolated clones (hereinafter referred to as L86S-3, L86S-12, L86S-16, L86S-25, L86S-36, L86S-40 and L86S-46) are provided in SEQ ID NO: 49-55, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 56-62, respectively. The 5' cDNA sequences for the remaining 2 clones (hereinafter referred to as L86S-30 and L86S-41) are provided in SEQ ID NO: 63 and 64. L86S-36 and L86S-46 were subsequently determined to represent the same gene. Comparison of these sequences with those in the public database as described above, revealed no significant homologies to clones L86S-30, L86S-36 and L86S-46 (SEQ ID NO: 63, 53 and 55, respectively). L86S-16 (SEQ ID NO: 51) was found to show some homology to an EST previously identified in fetal lung and germ cell tumor. The remaining clones were found to show at least some degree of homology to previously identified human genes. Subsequently determined extended cDNA sequences for L86S-12, L86S-36 and L86S-46 are provided in SEQ ID NO: 78-80, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 81-83.

Subsequent studies led to the determination of 5' cDNA sequences for an additional nine clones, referred to as L86S-6, L86S-11, L86S-14, L86S-29, L86S-34, L86S-39, L86S-47, L86S-49 and L86S-51 (SEQ ID NO: 84-92, respectively). The corresponding predicted amino acid sequences are provided in SEQ ID NO: 93-101, respectively. L86S-30, L86S-39 and L86S-47 were found to be similar to each other. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to L86S-14. L86S-29 was found to show some homology to a previously identified EST. L86S-6, L86S-11, L86S-34, L86S-39, L86S-47, L86S-49 and L86S-51 were found to show some homology to previously identified genes.

In further studies, a directional cDNA library was constructed using a Stratagene kit with a Lambda Zap Express vector. Total RNA for the library was isolated from two primary squamous lung tumors and poly A+ RNA was isolated using an oligo dT column. Antiserum was developed in normal mice using a pool of sera from three SCID mice implanted with human squamous lung carcinomas. Approximately 700,000 PFUs were screened from the unamplified library with *E. coli* absorbed mouse anti-SCID tumor serum. Positive plaques were identified as described above. Phage was purified and phagemid excised for 180 clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined cDNA sequences for 23 of the isolated clones are provided in SEQ ID NO: 126-148. Comparison of these sequences with those in the public database as described above revealed no significant homologies to the sequences of SEQ ID NO: 139 and 143-148. The sequences of SEQ ID NO: 126-138 and 140-142 were found to show homology to previously identified human polynucleotide sequences.

Example 4

USE OF MOUSE ANTISERA TO SCREEN LUNG TUMOR LIBRARIES PREPARED FROM SCID MICE

This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by screening of lung tumor cDNA libraries prepared from SCID mice with mouse anti-tumor sera.

A directional cDNA lung tumor expression library was prepared using a Stratagene kit with a Lambda Zap Express vector. Total RNA for the library was taken from a late passaged lung adenocarcinoma grown in SCID mice. Poly A+ RNA was isolated using a Message Maker Kit (Gibco BRL). Sera was obtained from two SCID mice implanted with lung adenocarcinomas. These sera were pooled and injected into normal mice to produce anti-lung tumor serum. Approximately 700,000 PFUs were screened from the unamplified library with *E. coli*-absorbed mouse anti-SCID tumor serum. Positive plaques were identified with a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (Gibco BRL). Phage was purified and phagemid excised for 100 clones with insert in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined 5' cDNA sequences for 33 of the isolated clones are provided in SEQ ID NO: 149-181. The corresponding predicted amino acid sequences for SEQ ID NO: 149, 150, 152-154, 156-158 and 160-181 are provided in SEQ ID NO: 182, 183, 186, 188-193 and 194-215, respectively. The clone of SEQ ID NO: 151 (referred to as SAL-25) was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 184 and 185. The clone of SEQ ID NO: 153 (referred to as SAL-50) was found to contain two open reading frames encoding the predicted amino acid sequences of SEQ ID NO: 187 and 216. Similarly, the clone of SEQ ID NO: 155 (referred to as SAL-66) was found to contain two open reading frames encoding the predicted amino acid sequences of SEQ ID NO: 189 and 190. Comparison of the isolated sequences with those in the public database revealed no significant homologies to the sequences of SEQ ID NO: 151, 153 and 154. The sequences of SEQ ID NO: 149, 152, 156, 157 and 158 were found to show some homology to previously isolated expressed sequence tags (ESTs). The sequences of SEQ ID NO: 150, 155 and 159-181 were found to show homology to sequences previously identified in humans.

Using the procedures described above, two directional cDNA libraries (referred to as LT46-90 and LT86-21) were prepared from two late passaged lung squamous carcinomas grown in SCID mice and screened with sera obtained from SCID mice implanted with human squamous lung carcinomas. The determined cDNA sequences for the isolated clones are provided in SEQ ID NO: 217-237 and 286-289. SEQ ID NO: 286 was found to be a longer sequence of LT4690-71 (SEQ ID NO: 237). Comparison of these sequences with those in the public databases revealed no known homologies to the sequences of SEQ ID NO: 219, 220, 225, 226, 287 and 288. The sequences of SEQ ID NO: 218, 221, 222 and 224 were found to show some homology to previously identified sequences of unknown function. The sequence of SEQ ID NO: 236 was found to show homology to a known mouse mRNA sequence. The sequences of SEQ ID NO: 217, 223, 227-237, 286 and 289 showed some homology to known human DNA and/or RNA sequences.

In further studies using the techniques described above, one of the cDNA libraries described above (LT86-21) was screened with *E. coli*-absorbed mouse anti-SCID tumor serum. This serum was obtained from normal mice immunized with a pool of 3 sera taken from SCID mice implanted with human squamous lung carcinomas. The determined cDNA sequences for the isolated clones are provided in SEQ ID NO: 238-285. Comparison of these sequences with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 253, 260, 277 and 285. The sequences of SEQ ID NO: 249, 250, 256, 266, 276 and 282 were found to show some homology to previously isolated expressed sequence tags (ESTs). The sequences of SEQ ID NO: 238-248, 251, 252, 254, 255, 257-259, 261-263, 265, 267-275, 278-281, 283 and 284 were found to show some homology to previously identified DNA or RNA sequences.

Example 5

DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for representative lung tumor polypeptides 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. 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 tumor from 3 patients, lung adenocarcinoma, prostate tumor, colon tumor and lung tumor), and different normal tissues, including lung from four patients, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, myocardium, retina and testes. L86S-46 was found to be expressed at high levels in lung squamous tumor, colon tumor and prostate tumor, and was undetectable in the other tissues examined. L86S-5 was found to be expressed in the lung tumor samples and in 2 out of 4 normal lung samples, but not in the other normal or tumor tissues tested. L86S-16 was found to be expressed in all tissues except normal liver and normal stomach. Using real-time PCR, L86S-46 was found to be over-expressed in lung squamous tissue and normal tonsil, with expression being low or undetectable in all other tissues examined.

Example 6

ISOLATION OF DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS

DNA sequences encoding antigens potentially involved in squamous cell lung tumor formation were isolated as follows.

A lung tumor directional cDNA expression library was constructed employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the library was taken from a pool of two human squamous epithelial lung carcinomas and poly A+ RNA was isolated using oligo-dT cellulose (Gibco BRL, Gaithersburg, MD). Phagemid were rescued at random and the cDNA sequences of isolated clones were determined.

The determined cDNA sequence for the clone SLT-T1 is provided in SEQ ID NO: 102, with the determined 5' cDNA sequences for the clones SLT-T2, SLT-T3, SLT-T5, SLT-T7, SLT-T9, SLT-T10, SLT-T11 and SLT-T12 being provided in SEQ ID NO: 103-110, respectively. The corresponding predicted amino acid sequence for SLT-T1, SLT-T2, SLT-T3, SLT-T10 and SLT-T12 are provided in SEQ ID NO: 111-115, respectively. Comparison of the sequences for SLT-T2, SLT-T3, SLT-T5, SLT-T7, SLT-T9 and SLT-T11 with those in the public databases as described above, revealed no significant homologies. The sequences for SLT-T10 and SLT-T12 were found to show some homology to sequences previously identified in humans.

The sequence of SLT-T1 was determined to show some homology to a PAC clone of unknown protein function. The cDNA sequence of SLT-T1 (SEQ ID NO: 102) was found to contain a mutator (MUTT) domain. Such domains are known to function in removal of damaged guanine from DNA that can cause A to G transversions (see, for example, el-Deiry, W.S., 1997 *Curr. Opin. Oncol. 9*:79-87; Okamoto, K. et al. 1996 *Int. J. Cancer 65*:437-41; Wu, C. et al. 1995 *Biochem. Biophys. Res. Commun. 214*:1239-45; Porter, D.W. et al. 1996 *Chem. Res. Toxicol. 9*:1375-81). SLT-T1 may thus be of use in the treatment, by gene therapy, of lung cancers caused by, or associated with, a disruption in DNA repair.

In further studies, DNA sequences encoding antigens potentially involved in adenocarcinoma lung tumor formation were isolated as follows. A human lung tumor directional cDNA expression library was constructed employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the library was taken from a late SCID mouse passaged human adenocarcinoma and poly A+ RNA was isolated using the Message Maker kit (Gibco BRL, Gaithersburg, MD). Phagemid were rescued at random and the cDNA sequences of isolated clones were determined.

The determined 5' cDNA sequences for five isolated clones (referred to as SALT-T3, SALT-T4, SALT-T7, SALT-T8, and SALT-T9) are provided in SEQ ID NO: 116-120, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 121-125. SALT-T3 was found to show 98% identity to the previously identified human transducin-like enhancer protein TLE2. SALT-T4 appears to be the human homologue of the mouse H beta 58 gene. SALT-T7 was found to have 97% identity to human 3-mercaptopyruvate sulfurtransferase and SALT-T8 was found to show homology to human interferon-inducible protein 1-8U. SALT-T9 shows approximately 90% identity to human mucin MUC 5B.

cDNA sequences encoding antigens potentially involved in small cell lung carcinoma development were isolated as follows. cDNA expression libraries were constructed with mRNA from the small cell lung carcinoma cell lines NCIH69, NCIH128 and DMS79 (all available from the American Type Culture Collection, Manassas, VA) employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Phagemid were rescued at random and the cDNA sequences of 27 isolated clones were determined. Comparison of the determined cDNA sequences revealed no significant homologies to the sequences of SEQ ID NO: 372 and 373. The sequences of SEQ ID NO: 364, 369, 377, 379 and 386 showed some homology to previously isolated ESTs. The sequences of the remaining 20 clones showed some homology to previously identified genes. The cDNA sequences of these clones are provided in SEQ ID NO: 363, 365-368, 370, 371, 374-376, 378, 380-385 and 387-389, wherein SEQ ID NO: 363, 366-368, 370, 375, 376, 378, 380-382, 384 and 385 are full-length sequences.

Example 7

SYNTHESIS OF POLYPEPTIDES

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. 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 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.

Example 8

ISOLATION AND CHARACTERIZATION OF DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS BY T-CELL EXPRESSION CLONING

Lung tumor antigens may also be identified by T cell expression cloning. One source of tumor specific T cells is from surgically excised tumors from human patients.

A non-small cell lung carcinoma was minced and enzymatically digested for several hours to release tumor cells and infiltrating lymphocytes (tumor infiltrating T cells, or TILs). The cells were washed in HBSS buffer and passed over a Ficoll (100%/75%/HBSS) discontinuous gradient to separate tumor cells and lymphocytes from non-viable cells. Two bands were harvested from the interfaces; the upper band at the 75%/HBSS interface contained predominantly tumor cells, while the lower band at the 100%/75%/HBSS interface contained a majority of lymphocytes. The TILs were expanded in culture, either in 24-well plates with culture media supplemented with 10 ng/ml IL-7 and 100 U/ml IL-2, or alternatively, 24-well plates that have been pre-coated with the anti-CD3 monoclonal antibody OKT3. The resulting TIL cultures were analyzed by FACS to confirm that a high percentage were CD8+ T cells (>90% of gated population) with only a small percentage of CD4+ cells.

In addition, non-small cell lung carcinoma cells were expanded in culture using standard techniques to establish a tumor cell line, which was later confirmed to be a lung carcinoma cell line by immunohistochemical analysis. This tumor cell line was transduced with a retroviral vector to express human CD80, and characterized by FACS analysis to confirm high expression levels of CD80, and class I and II MHC molecules.

The specificity of the TIL lines to lung tumor was confirmed by INF-γ and/or TNF-α cytokine release assays. TIL cells from day 21 cultures were co-cultured with either autologous or allogeneic tumor cells, EBV-immortalized LCL, or control cell lines Daudi and K562, and the culture supernatant monitored by ELISA for the presence of cytokines. The TIL specifically recognized autologous tumor but not allogeneic tumor. In addition, there was no recognition of EBV-immortalized LCL or the control cell lines, indicating that the TIL lines are tumor specific and are potentially recognizing a tumor antigen presented by autologous MHC molecules.

The characterized tumor-specific TIL lines were expanded to suitable numbers for T cell expression cloning using soluble anti-CD3 antibody in culture with irradiated EBV transformed LCLs and PBL feeder cells in the presence of 20 U/ml IL-2. Clones from the expanded TIL lines were generated by standard limiting dilution techniques. Specifically, TIL cells were seeded at 0.5 cells/well in a 96-well U bottom plate and stimulated with CD-80-transduced autologous tumor cells, EBV transformed LCL, and PBL feeder cells in the presence of 50 U/ml IL-2. These clones were further analyzed for tumor specificity by ^{51}Cr microcytotoxicity and IFN-γ bioassays. The MHC restriction element recognized by the TIL clones may be determined by antibody blocking studies.

CTL lines or clones prepared as described above may be employed to identify tumor specific antigens. For example, autologous fibroblasts or LCL from a patient may be transfected or transduced with polynucleotide fragments derived from a lung tumor cDNA library to generate target cells expressing tumor polypeptides. The target cells expressing tumor polypeptides in the context of MHC will be recognized by the CTL line or clone, resulting in T-cell activation which can be monitored by cytokine detection assays. The tumor gene being expressed by the target cell and recognized by the tumor-specific CTL may then be isolated.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention.

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 NOs: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648 and 668;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs:_ 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479, 483, 488, 491, 492, 497, 498, 500, 510, 519, 527, 528, 543, 545, 547, 553, 556, 559, 561, 564, 565, 568, 569, 574-577, 579, 580, 584, 585, 587, 592, 595, 598, 603, 608, 610, 613, 621-623, 626, 642, 648 and 668 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 NOs: 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277, 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359, 361, 364, 369, 372, 373, 377, 379 and 386, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polynucleotide encoding at least 15 amino acid 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 Nos: 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277, 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359, 361, 364, 369, 372, 373, 377, 379 and 386, or a complement of any of the foregoing sequences.

4. 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 NOs:_ 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277, 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359, 361, 364, 369, 372, 373, 377, 379 and 386, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NOs:_ 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277, 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359, 361, 364, 369, 372, 373, 377, 379 and 386.

6. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NOs:_ 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277, 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359, 361, 364, 369, 372, 373, 377, 379 and 386 under moderately stringent conditions.

7. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 3-6.

8. An expression vector, comprising a polynucleotide according to any one of claims 3-8.

9. A host cell transformed or transfected with an expression vector according to claim 8.

10. 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 NOs:_ 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277, 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359, 361, 364, 369, 372, 373, 377, 379 and 386, or a complement of any of the foregoing polynucleotide sequences.

11. A fusion protein, comprising at least one polypeptide according to claim 1.

12. A fusion protein according to claim 11, 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.

13. A fusion protein according to claim 11, wherein the fusion

protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

14. A fusion protein according to claim 11, wherein the fusion protein comprises an affinity tag.

15. An isolated polynucleotide encoding a fusion protein according to claim 11.

16. A pharmaceutical composition, comprising a physiologically 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 3;

(c) an antibody according to claim 10;

(d) a fusion protein according to claim 11; and

(e) a polynucleotide according to claim 15.

17. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

(a) a polypeptide according to claim 1;

(b) a polynucleotide according to claim 3;

(c) an antibody according to claim 10;

(d) a fusion protein according to claim 11; and

(e) a polynucleotide according to claim 15.

18. A vaccine according to claim 17, wherein the immunostimulant is an adjuvant.

19. A vaccine according to any claim 17, wherein the immunostimulant induces a predominantly Type I response.

20. 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 16.

21. 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 17.

22. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

23. A pharmaceutical composition according to claim 22, wherein the antigen presenting cell is a dendritic cell or a macrophage.

24. 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:

(a) sequences recited in SEQ ID NOs: 217-389;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 217-389 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii);

in combination with an immunostimulant.

25. A vaccine according to claim 24, wherein the immunostimulant is an adjuvant.

26. A vaccine according to claim 24, wherein the immunostimulant induces a predominantly Type I response.

27. A vaccine according to claim 24, wherein the antigen-presenting cell is a dendritic cell.

28. A method for inhibiting the development of a cancer in a patient, 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:

(a) sequences recited in SEQ ID NOs: 217-389;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 217-389 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii)encoded by a polynucleotide recited in any one of SEQ ID NOs: 217-389;

and thereby inhibiting the development of a cancer in the patient.

29. A method according to claim 28, wherein the antigen-presenting cell is a dendritic cell.

30. A method according to any one of claims 20, 21 and 28, wherein the cancer is lung cancer.

31. 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 NOs: 217-389; 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.

32. A method according to claim 31, wherein the biological sample is blood or a fraction thereof.

33. 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 31.

34. 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 NOs: 217-389;

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 217-389 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.

35. An isolated T cell population, comprising T cells prepared according to the method of claim 34.

36. 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 35.

37. 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 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 NOs: 217-389;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 217-389 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 (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.

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 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:

(1) sequences recited in SEQ ID NOs: 217-389;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 217-389 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 express a polypeptide of (i);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

(c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

39. A method 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 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 NOs: 217-389 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; 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.

40. A method according to claim 39, wherein the binding agent is an antibody.

41. A method according to claim 42, wherein the antibody is a monoclonal antibody.

42. A method according to claim 39, wherein the cancer is lung cancer.

43. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 217-389 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

44. A method according to claim 43, wherein the binding agent is an antibody.

45. A method according to claim 44, wherein the antibody is a monoclonal antibody.

46. A method according to claim 43, wherein the cancer is a lung cancer.

47. A method 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, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 217-389 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 presence or absence of a cancer in the patient.

48. A method according to claim 47, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

49. A method according to claim 47, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

50. 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 polynucleotide sequence recited in any one of SEQ ID NOs: 217-389 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 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.

51. A method according to claim 50, wherein the amount of

polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

53. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 10; and

(b) a detection reagent comprising a reporter group.

54. A kit according to claim 53, wherein the antibodies are immobilized on a solid support.

55. A kit according to claim 53, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

56. A kit according to claim 53, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

57. 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 NOs:_ 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277, 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359, 361, 364, 369, 372, 373, 377, 379 and 386, or a complement of any of the foregoing polynucleotides.

58. A oligonucleotide according to claim 57, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID

NOs:_ 218-222, 224-226, 249, 250, 253, 256, 266, 276, 277. 282, 285, 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353. 359, 361. 364, 369, 372, 373, 377, 379 and 386.

59. A diagnostic kit, comprising:

(a) an oligonucleotide according to claim 58; and

(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

SEQUENCE LISTING

<110> Corixa Corporation
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<120> COMPOUNDS FOR THERAPY AND DIAGNOSIS OF
LUNG CANCER AND METHODS FOR THEIR USE

<130> 210121.475PC

<140> PCT
<141> 2000-03-30

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atcgtaacta ctagtgactt ctgaggttta cagttngaat atgttctcnn aggtttatca 420
agttntgtta ttgatgatng gtaatctaca cctctggaag ctgtngaatg tgaaaaagat 480
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tgtttcnagg gggcntgggg ggtttaaaaa aatgtttctn ttnccntaaa aatgtttacc 600
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<212> DNA
<213> Homo sapien

<220>
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<222> (1)...(369)
<223> n = A,T,C or G

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aattcattaa ctttgtggtt gaagggagca gcgtcngaaa ctgctttagc acagtgggag 180
gaaaacaaac agattcatct ccggaaacca aaggaaaggg tragtgggtt tttattagcc 240
agctgtatcc tagatggtca atttccagtg gatgaataca ccttacgtac gtttctcttg 300
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<212> DNA
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<212> DNA
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<220>
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accgccccna ttaagaatta gagcaagcag tgaggtgaag ccttgtcctt gcttttaaca 180
tagaaagtga tccaaattca ccaaacttga cttnnggttt tgcagtgtgg cctcctgatt 240
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<210> 9
<211> 449
<212> DNA
<213> Homo sapien

<220>
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aagttcagga cacaagcttc tggcccatgc agagcagagg ccatgagggg tcacagcatg 240
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<210> 10
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<213> Homo sapien

<220>
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gctcactact gtggatatgt atgtnttgac cgatnacaca ggctgattta gggaagagat 420
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<210> 11
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tcaggcatct gggacttgat gtgggtntgg gatttgaaat cagagcacct nggtctctst 180
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<212> DNA
<213> Homo sapien

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<211> 488
<212> DNA
<213> Homo sapien

<400> 20

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<213> Homo sapien

<400> 21

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<212> DNA
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<211> 633
<212> DNA
<213> Homo sapien

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<211> 1328
<212> DNA
<213> Homo sapien

<400> 24
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<211> 1758
<212> DNA
<213> Homo sapien

<400> 25
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<211> 493
<212> DNA
<213> Homo sapien

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<213> Homo sapien

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<210> 28
<211> 1333
<212> DNA
<213> Homo sapien

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<211> 813
<212> DNA
<213> Homo sapien

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<211> 1316
<212> DNA
<213> Homo sapien

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<211> 1355
<212> DNA
<213> Homo sapien

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agatggttgg aatcgagtac atcctttttgc atgctcaaga gcccattctt ttcatcattc 240
ggaagcaaca gcggcagtcc cctgcccaag ttatcccact agctgattac tatatcattg 300
ctggagtgat ctatcaggca ccagacttgg gatcagttat aaactctaga gtgcttactg 360
cagtgcatgg tattcagtca gcttttgatg aagctatgtc atactgtcga tatcatcctt 420
ccaaagggta ttggtggcac ttcaaagatc atgaagagca agataaagtc agacctaaag 480
ccaaaaggaa agaagaacca agctctattt ttcagagaca acgtgtggat gctttacttt 540
tagacctcag acaaaaattt ccacccaaat ttgtgcagct aaagcctgga gaaaagcctg 600
ttccagtgga tcaaacaaag aaagaggcag aacctatacc agaaactgta aaacctgagg 660
agaaggagac cacaaagaat gtacaacaga cagtgagtgc taaaggcccc cctgaaaaac 720
ggatgagact tcagtgagta ctggacaaaa gagaagcctg gaagactcct catgctagtt 780
atcatacctc agtactgtgg ctcttgagct ttgaagtact ttattgtaac cttcttattt 840
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aatcccagca ctttgggagg ccatggcggg tggatcactt gaggtcagaa gttcaagacc 960
agcctgacca atatggtgaa accccgtctc tactaaaaat acaaaaatta gccgggcgtg 1020
gtggcgggcg cccatagtcc cagctactcg ggaggctgag acaggagact tgcttgaacc 1080
cgggaggtgg aggttgccct gagctgatta tcatgctgtt gcactccagc ttgggcgaca 1140
gaacgagact ttgtctcaaa aaaagaagaa aagatattat tcccatcatg atttcttgtg 1200
aatatttgtt atatgtcttc tggtaacctt tcctctcccg gacttgaagc aacctcacac 1260

```
actcacatgt ttactggtag atatgtttta aaagcaaaat aaaggtattt gtttttccaa    1320
aaaaaaaaaa aaaaaaaaaa aaaaaaaaac tcgag                               1355

       <210> 32
       <211> 80
       <212> PRT
       <213> Homo sapien

       <400> 32
Val Ser Arg Ile Arg Gly Gly Ala Lys Lys Arg Lys Lys Lys Ser Tyr
 1               5                   10                  15
Thr Thr Pro Lys Lys Asp Lys His Gln Arg Lys Lys Val Gln Pro Ala
            20                  25                  30
Val Leu Lys Tyr Tyr Lys Val Asp Glu Asn Gly Lys Ile Ser Cys Leu
        35                  40                  45
Arg Arg Glu Cys Pro Ser Asp Glu Cys Gly Ala Gly Val Phe Met Ala
    50                  55                  60
Ser His Phe Asp Arg His Tyr Cys Gly Lys Cys Cys Leu Thr His Cys
65                  70                  75                  80

       <210> 33
       <211> 130
       <212> PRT
       <213> Homo sapien

       <400> 33
Glu Ile Ser Asn Glu Val Arg Lys Phe Arg Thr Leu Thr Glu Leu Ile
 1               5                   10                  15
Leu Asp Ala Gln Glu His Val Lys Asn Pro Tyr Lys Gly Lys Lys Leu
            20                  25                  30
Lys Lys His Pro Asp Phe Pro Lys Lys Pro Leu Thr Pro Tyr Phe Arg
        35                  40                  45
Phe Phe Met Glu Lys Arg Ala Lys Tyr Ala Lys Leu His Pro Gln Met
    50                  55                  60
Ser Asn Leu Asp Leu Thr Lys Ile Leu Ser Lys Lys Tyr Lys Glu Leu
65                  70                  75                  80
Pro Glu Lys Lys Lys Met Lys Tyr Val Pro Asp Phe Gln Arg Arg Glu
                85                  90                  95
Thr Gly Val Arg Ala Lys Pro Gly Pro Ile Gln Gly Gly Ser Pro Pro
            100                 105                 110
Pro Tyr Pro Glu Cys Gln Glu Ser Asp Ile Pro Glu Lys Pro Gln Asp
        115                 120                 125
Pro Pro
    130

       <210> 34
       <211> 506
       <212> PRT
       <213> Homo sapien

       <400> 34
Asn Ser Glu Lys Glu Ile Pro Val Leu Asn Glu Leu Pro Val Pro Met
 1               5                   10                  15
Val Ala Arg Tyr Ile Arg Ile Asn Pro Gln Ser Trp Phe Asp Asn Gly
            20                  25                  30
```

```
Ser Ile Cys Met Arg Met Glu Ile Leu Gly Cys Pro Leu Pro Asp Pro
        35                  40                  45
Asn Asn Tyr Tyr His Arg Arg Asn Glu Met Thr Thr Thr Asp Asp Leu
    50                  55                  60
Asp Phe Lys His His Asn Tyr Lys Glu Met Arg Gln Leu Met Lys Val
65                  70                  75                  80
Val Asn Glu Met Cys Pro Asn Ile Thr Arg Ile Tyr Asn Ile Gly Lys
                85                  90                  95
Ser His Gln Gly Leu Lys Leu Tyr Ala Val Glu Ile Ser Asp His Pro
            100                 105                 110
Gly Glu His Glu Val Gly Glu Pro Glu Phe His Tyr Ile Ala Gly Ala
        115                 120                 125
His Gly Asn Glu Val Leu Gly Arg Glu Leu Leu Leu Leu Leu Leu His
    130                 135                 140
Phe Leu Cys Gln Glu Tyr Ser Ala Gln Asn Ala Arg Ile Val Arg Leu
145                 150                 155                 160
Val Glu Glu Thr Arg Ile His Ile Leu Pro Ser Leu Asn Pro Asp Gly
                165                 170                 175
Tyr Glu Lys Ala Tyr Glu Gly Gly Ser Glu Leu Gly Gly Trp Ser Leu
            180                 185                 190
Gly Arg Trp Thr His Asp Gly Ile Asp Ile Asn Asn Asn Phe Pro Asp
        195                 200                 205
Leu Asn Ser Leu Leu Trp Glu Ala Glu Asp Gln Gln Asn Ala Pro Arg
    210                 215                 220
Lys Val Pro Asn His Tyr Ile Ala Ile Pro Glu Trp Phe Leu Ser Glu
225                 230                 235                 240
Asn Ala Thr Val Ala Thr Glu Thr Arg Ala Val Ile Ala Trp Met Glu
                245                 250                 255
Lys Ile Pro Phe Val Leu Gly Gly Asn Leu Gln Gly Gly Glu Leu Val
            260                 265                 270
Val Ala Tyr Pro Tyr Asp Met Val Arg Ser Leu Trp Lys Thr Gln Glu
        275                 280                 285
His Thr Pro Thr Pro Asp Asp His Val Phe Arg Trp Leu Ala Tyr Ser
    290                 295                 300
Tyr Ala Ser Thr His Arg Leu Met Thr Asp Ala Arg Arg Arg Val Cys
305                 310                 315                 320
His Thr Glu Asp Phe Gln Lys Glu Glu Gly Thr Val Asn Gly Ala Ser
                325                 330                 335
Trp His Thr Val Ala Gly Ser Leu Asn Asp Phe Ser Tyr Leu His Thr
            340                 345                 350
Asn Cys Phe Glu Leu Ser Ile Tyr Val Gly Cys Asp Lys Tyr Pro His
        355                 360                 365
Glu Ser Glu Leu Pro Glu Glu Trp Glu Asn Asn Arg Glu Ser Leu Ile
    370                 375                 380
Val Phe Met Glu Gln Val His Arg Gly Ile Lys Gly Ile Val Arg Asp
385                 390                 395                 400
Leu Gln Gly Lys Gly Ile Ser Asn Ala Val Ile Ser Val Glu Gly Val
                405                 410                 415
Asn His Asp Ile Arg Thr Ala Ser Asp Gly Asp Tyr Trp Arg Leu Leu
            420                 425                 430
Asn Pro Gly Glu Tyr Val Val Thr Ala Lys Ala Glu Gly Phe Ile Thr
        435                 440                 445
Ser Thr Lys Asn Cys Met Val Gly Tyr Asp Met Gly Ala Thr Arg Cys
    450                 455                 460
Asp Phe Thr Leu Thr Lys Thr Asn Leu Ala Arg Ile Arg Glu Ile Met
```

```
465                 470                 475                 480
Glu Thr Phe Gly Lys Gln Pro Val Ser Leu Pro Ser Arg Arg Leu Lys
                485                 490                 495
Leu Arg Gly Arg Lys Arg Arg Gln Arg Gly
            500                 505
```

<210> 35
<211> 96
<212> PRT
<213> Homo sapien

<400> 35

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

<210> 36
<211> 129
<212> PRT
<213> Homo sapien

<400> 36

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

<210> 37
<211> 238
<212> PRT
<213> Homo sapien

<400> 37
Asn Leu Leu Gly Ile Ser Trp Val Asp Ser Ser Trp Ile Pro Ile Leu
1 5 10 15
Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser Glu Arg Ser Asn Pro Phe
20 25 30
Tyr Asp Arg Thr Cys Asn Asn Glu Val Val Lys Met Gln Arg Leu Thr
35 40 45
Leu Glu His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His
50 55 60
Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser
65 70 75 80
Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val
85 90 95
Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu
100 105 110
Thr Ala Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr
115 120 125
Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His
130 135 140
Glu Glu Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro
145 150 155 160
Ser Ser Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu
165 170 175
Arg Gln Lys Phe Pro Pro Lys Phe Val Gln Leu Lys Pro Gly Glu Lys
180 185 190
Pro Val Pro Val Asp Gln Thr Lys Lys Glu Ala Glu Pro Ile Pro Glu
195 200 205
Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys Asn Val Gln Gln Thr
210 215 220
Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met Arg Leu Gln
225 230 235

<210> 38
<211> 202
<212> PRT
<213> Homo sapien

<400> 38
Lys Gly Ser Glu Gly Glu Asn Pro Leu Thr Val Pro Gly Arg Glu Lys
1 5 10 15
Glu Gly Met Leu Met Gly Val Lys Pro Gly Glu Asp Ala Ser Gly Pro
20 25 30
Ala Glu Asp Leu Val Arg Arg Ser Glu Lys Asp Thr Ala Ala Val Val
35 40 45
Ser Arg Gln Gly Ser Ser Leu Asn Leu Phe Glu Asp Val Gln Ile Thr
50 55 60
Glu Pro Glu Ala Glu Pro Glu Ser Lys Ser Glu Pro Arg Pro Pro Ile
65 70 75 80
Ser Ser Pro Arg Ala Pro Gln Thr Arg Ala Val Lys Pro Arg Leu His
85 90 95
Pro Val Lys Pro Met Asn Ala Thr Ala Thr Lys Val Ala Asn Cys Ser
100 105 110
Leu Gly Thr Ala Thr Ile Ile Gly Glu Asn Leu Asn Asn Glu Val Met
115 120 125
Met Lys Lys Tyr Ser Pro Ser Asp Pro Ala Phe Ala Tyr Ala Gln Leu

130 135 140
Thr His Asp Glu Leu Ile Gln Leu Val Leu Lys Gln Lys Glu Thr Ile
145 150 155 160
Ser Lys Lys Glu Phe Gln Val Arg Glu Leu Glu Asp Tyr Ile Asp Asn
165 170 175
Leu Leu Val Arg Val Met Glu Glu Thr Pro Asn Ile Leu Arg Ile Pro
180 185 190
Thr Gln Val Gly Lys Lys Ala Gly Lys Met
195 200

<210> 39
<211> 243
<212> PRT
<213> Homo sapien

<400> 39
Val Asn Ala Leu Gly Ile Met Ala Ala Val Asp Ile Arg Asp Asn Leu
1 5 10 15
Leu Gly Ile Ser Trp Val Asp Ser Ser Trp Ile Pro Ile Leu Asn Ser
20 25 30
Gly Ser Val Leu Asp Tyr Phe Ser Glu Arg Ser Asn Pro Phe Tyr Asp
35 40 45
Arg Thr Cys Asn Asn Glu Val Val Lys Met Gln Arg Leu Thr Leu Glu
50 55 60
His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His Ala Gln
65 70 75 80
Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser Pro Ala
85 90 95
Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val Ile Tyr
100 105 110
Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu Thr Ala
115 120 125
Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr Cys Arg
130 135 140
Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His Glu Glu
145 150 155 160
Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro Ser Ser
165 170 175
Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu Arg Gln
180 185 190
Lys Ile Ser Thr Gln Ile Cys Ala Val Asp Gln Thr Lys Lys Glu Ala
195 200 205
Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys
210 215 220
Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met
225 230 235 240
Arg Leu Gln

<210> 40
<211> 245
<212> PRT
<213> Homo sapien

<400> 40

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

<210> 41
<211> 163
<212> PRT
<213> Homo sapien

<400> 41

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

```
Arg Ser Cys Gly Pro Lys Leu Thr Asn Ser Pro Ala Val Phe Val Met
    130                 135                 140
Val Gly Leu Pro Arg Pro Gly Gln Asp Leu Leu Leu His Glu Ser Leu
145                 150                 155                 160
Leu Ala Ala


      &lt;210&gt; 42
      &lt;211&gt; 243
      &lt;212&gt; PRT
      &lt;213&gt; Homo sapien

      &lt;400&gt; 42
Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser Ser
 1               5                  10                  15
Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser Glu
            20                  25                  30
Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val Lys
        35                  40                  45
Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile Glu
    50                  55                  60
Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys
65                  70                  75                  80
Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr
                85                  90                  95
Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile
            100                 105                 110
Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe Asp
        115                 120                 125
Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp
    130                 135                 140
His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala Lys
145                 150                 155                 160
Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp Ala
                165                 170                 175
Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln Leu
            180                 185                 190
Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu Ala
        195                 200                 205
Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys
    210                 215                 220
Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met
225                 230                 235                 240
Arg Leu Gln


      &lt;210&gt; 43
      &lt;211&gt; 244
      &lt;212&gt; PRT
      &lt;213&gt; Homo sapien

      &lt;400&gt; 43
Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser
 1               5                  10                  15
Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser
```

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

<210> 44
<211> 109
<212> PRT
<213> Homo sapien

<400> 44
Glu Leu His Phe Ser Glu Phe Thr Ser Ala Val Ala Asp Met Lys Asn
1 5 10 15
Ser Val Ala Asp Arg Asp Asn Ser Pro Ser Ser Cys Ala Gly Leu Phe
20 25 30
Ile Ala Ser His Ile Gly Phe Asp Trp Pro Gly Val Trp Val His Leu
35 40 45
Asp Ile Ala Ala Pro Val His Ala Gly Glu Arg Ala Thr Gly Phe Gly
50 55 60
Val Ala Leu Leu Leu Ala Leu Phe Gly Arg Ala Ser Glu Asp Pro Leu
65 70 75 80
Leu Asn Leu Val Ser Pro Leu Asp Cys Glu Val Asp Ala Gln Glu Gly
85 90 95
Asp Asn Met Gly Arg Asp Ser Lys Arg Arg Arg Leu Val
100 105

<210> 45
<211> 324
<212> PRT
<213> Homo sapien

<400> 45

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

<210> 46
<211> 244
<212> PRT
<213> Homo sapien

<400> 46

Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser
1 5 10 15
Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser
20 25 30

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

<210> 47
<211> 14
<212> DNA
<213> Homo sapien

<400> 47
tttttttttt ttag 14

<210> 48
<211> 10
<212> DNA
<213> Homo sapien

<400> 48
cttcaacctc 10

<210> 49
<211> 496
<212> DNA
<213> Homo sapien

<400> 49
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gcaccatgta ccgagcactt cggctcctcg cgcgctcgcg tcccctcgtg cgggctccag     60
ccgcagcctt agcttcggct cccggcttgg gtggcgcggc cgtgccctcg ttttggcctc    120
cgaacgcggc tcgaatggca agccaaaatt ccttccggat agaatatgat acctttggtg    180
aactaaaggt gccaaatgat aagtattatg gcgcccagac cgtgagatct acgatgaact    240
```

ttaagattgg aggtgtgaca gaacgcatgc caaccccagt tattaaagct tttggcatct 300
tgaagcgagc ggccgctgaa gtaaaccagg attatggtct tgatccaaag attgctaatg 360
caataatgaa ggcagcagat gaggtagctg aaggtaaatt aaatgatcat tttcctctcg 420
tggtatggca gactggatca ggaactcaga caaatatgaa tgtaaatgaa gtcattagcc 480
aatagagcaa ttgaaa 496

<210> 50
<211> 499
<212> DNA
<213> Homo sapien

<400> 50
agaaaaagtc tatgtttgca gaaatacaga tccaagacaa agacaggatg ggcactgctg 60
gaaaagttat taaatgcaaa gcagctgtgc tttgggagca gaagcaaccc ttctccattg 120
aggaaataga agttgcccca ccaaagacta aagaagttcg cattaagatt ttggccacag 180
gaatctgtcg cacagatgac catgtgataa aaggaacaat ggtgtccaag tttccagtga 240
ttgtgggaca tgaggcaact gggattgtag agagcattgg agaaggagtg actacagtga 300
aaccaggtga caaagtcatc cctctctttc tgccacaatg tagagaatgc aatgcttgtc 360
gcaacccaga tggcaacctt tgcattagga gcgatattac tggtcgtgga gtactggctg 420
atggcaccac cagatttaca tgcaagggcg aaccagtcca ccacttcatg aacaccagta 480
catttaccga gtacacagt 499

<210> 51
<211> 887
<212> DNA
<213> Homo sapien

<400> 51
gagtctgagc agaaaggaaa agcagccttg gcagccacgt tagaggaata caaagccaca 60
gtggccagtg accagataga gatgaatcgc ctgaaggctc agctggagaa tgaaaagcag 120
aaagtggcag agctgtattc tatccataac tctggagaca aatctgatat tcaggacctc 180
ctggagagtg tcaggctgga caaagaaaaa gcagagactt tggctagtag cttgcaggaa 240
gatctggctc atacccgaaa tgatgccaat cgattacagg atgccattgc taaggtagag 300
gatgaatacc gagccttcca agaagaagct aagaaacaaa ttgaagattt gaatatgacg 360
ttagaaaaat taagatcaga cctggatgaa aaagaaacag aaaggagtga catgaaagaa 420
accatctttg aacttgaaga tgaagtagaa caacatcgtg ctgtgaaact tcatgacaac 480
ctcattattt ctgatctaga gaatacagtt aaaaaactcc aggaccaaaa gcacgacatg 540
gaaagagaaa taaagacact ccacagaaga cttcgggaag aatctgcgga atggcggcag 600
tttcaggctg atctccagac tgcagtagtc attgcaaatg acattaaatc tgaagcccaa 660
gaggagattg gtgatctaaa gcgccggtta catgaggctc aagaaaaaaa tgagaaactc 720
acaaaagaat tggaggaaat aaagtcacgc aagcaagagg aggagcgagg cgggtataca 780
attacatgaa tgccgttgag agagatttgg cagccttaag gcagggaatg ggactgagta 840
gaaggtcctc gacttcctca gagccaactc ctacagtaaa aaccctc 887

<210> 52
<211> 491
<212> DNA
<213> Homo sapien

<400> 52
ggcacgagct tttccaaaaa tcatgctgct cctttctcta aagttcttac attttataga 60
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cctgctatag ctcagttttc agttcagaaa gtcactcctc agtctgatgg ctccagttca 180
aaagtgaaag tcaaagttcg agtaaatgtc catggcattt tcagtgtgtc cagtgcatct 240
ttagtggagg ttcacaagtc tgaggaaaat gaggagccaa tggaaacaga tcagaatgca 300

aaggaggaag agaagatgca agtggaccag gaggaaccac atgttgaaga gcaacagcag 360
cagacaccag gcagaaaata aggcagagtc tgaagaaatg gagacctctc aagctggatc 420
caaggataaa aagatggacc aaccacccca agccaagaag gcaaaagtga agaccagtac 480
tgtggacctg g 491

<210> 53
<211> 787
<212> DNA
<213> Homo sapien

<400> 53
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caggggtagt gatcctggca gtcaccatag ctctacttgt ttacttttta gcttttgatc 180
aaaaatctta cttttatagg agcagttttc aactcctaaa tgttgaatat aatagtcagt 240
taaattcacc agctacacag gaatacagga ctttgagtgg aagaattgaa tctctgatta 300
ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac 360
tgaggcaaga tggtagtggt gtgagagcgg atgttgtcat gaaatttcaa ttcactagaa 420
ataacaatgg agcatcaatg aaaagcagaa ttgagtctgt tttacgacaa atgctgaata 480
actctggaaa cctggaaata aacccttcaa ctgagataac atcacttact gaccaggctg 540
cagcaaattg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc 600
agagaatcct tggaggcact gaggctgagg agggaagctg gccgtggcaa gtcagtctgc 660
ggctcaataa tgcccaccac tgtggaggca gcctgatcaa taacatgtgg atcctgacag 720
cagctcactg cttcagaagc aactctaatc ctcgtgactg gattgccacg tctggtattt 780
ccacaac 787

<210> 54
<211> 386
<212> DNA
<213> Homo sapien

<400> 54
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gagccaatgg aaacagatca gaatgcaaag gaggaagaga agatgcaagt ggaccaggag 120
gaaccacatg ttgaagagca acagcagcag acaccagcag aaaataaggc agagtctgaa 180
gaaatggaga cctctcaagc tggatccaag gataaaaaga tggaccaacc accccaagcc 240
aagaaggcaa aagtgaagac cagtactgtg gacctgccaa tcgagaatca gctattatgg 300
cagatagaca gagagatgct caacttgtac attgaaaatg agggtaagat gatcatgcag 360
gataaactgg agaaggagcg gaatga 386

<210> 55
<211> 1462
<212> DNA
<213> Homo sapien

<400> 55
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cacgtgtaac ttcgacttca agatttctga atccatatgt agtatgtttc attgtcgtcg 120
caggggtagt gatcctggca gtcaccatag ctctacttgt ttacttttta gcttttgatc 180
aaaaatctta cttttatagg agcagttttc aactcctaaa tgttgaatat aatagtcagt 240
taaattcacc agctacacag gaatacagga ctttgagtgg aagaattgaa tctctgatta 300
ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac 360
tgaggcaaga tggtagtggt gtgagagcgg atgttgtcat gaaatttcaa ttcactagaa 420
ataacaatgg agcatcaatg aaaagcagaa ttgagtctgt tttacgacaa atgctgaata 480
actctggaaa cctggaaata aacccttcaa ctgagataac atcacttact gaccaggctg 540

cagcaaattg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc 600
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cagctcactg cttcagaagc aactctaatc ctcgtgactg gattgccacg tctggtattt 780
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ggatagtaag ctggggagat cagtgtggcc tgccggataa gccaggagtg tatactcgag 1260
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ctgttgcaaa gtctgtatgc aggtgtgcct gtcttaaatt ccaaagcttt acatttcaac 1380
tgaaaaagaa actagaaatg tcctaattta acatcttgtt acataaatat ggtttaacaa 1440
aaaaaaaaaa aaaaaactcg ag 1462

<210> 56
<211> 159
<212> PRT
<213> Homo sapien

<400> 56
Thr Met Tyr Arg Ala Leu Arg Leu Leu Ala Arg Ser Arg Pro Leu Val
1 5 10 15
Arg Ala Pro Ala Ala Ala Leu Ala Ser Ala Pro Gly Leu Gly Gly Ala
20 25 30
Ala Val Pro Ser Phe Trp Pro Pro Asn Ala Ala Arg Met Ala Ser Gln
35 40 45
Asn Ser Phe Arg Ile Glu Tyr Asp Thr Phe Gly Glu Leu Lys Val Pro
50 55 60
Asn Asp Lys Tyr Tyr Gly Ala Gln Thr Val Arg Ser Thr Met Asn Phe
65 70 75 80
Lys Ile Gly Gly Val Thr Glu Arg Met Pro Thr Pro Val Ile Lys Ala
85 90 95
Phe Gly Ile Leu Lys Arg Ala Ala Ala Glu Val Asn Gln Asp Tyr Gly
100 105 110
Leu Asp Pro Lys Ile Ala Asn Ala Ile Met Lys Ala Ala Asp Glu Val
115 120 125
Ala Glu Gly Lys Leu Asn Asp His Phe Pro Leu Val Val Trp Gln Thr
130 135 140
Gly Ser Gly Thr Gln Thr Asn Met Asn Val Asn Glu Val Ile Ser
145 150 155

<210> 57
<211> 165
<212> PRT
<213> Homo sapien

<400> 57
Lys Lys Ser Met Phe Ala Glu Ile Gln Ile Gln Asp Lys Asp Arg Met
1 5 10 15
Gly Thr Ala Gly Lys Val Ile Lys Cys Lys Ala Ala Val Leu Trp Glu
20 25 30
Gln Lys Gln Pro Phe Ser Ile Glu Glu Ile Glu Val Ala Pro Pro Lys

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

      <210> 58
      <211> 259
      <212> PRT
      <213> Homo sapien

      <400> 58
Glu Ser Glu Gln Lys Gly Lys Ala Ala Leu Ala Ala Thr Leu Glu Glu
 1               5                  10                  15
Tyr Lys Ala Thr Val Ala Ser Asp Gln Ile Glu Met Asn Arg Leu Lys
            20                  25                  30
Ala Gln Leu Glu Asn Glu Lys Gln Lys Val Ala Glu Leu Tyr Ser Ile
        35                  40                  45
His Asn Ser Gly Asp Lys Ser Asp Ile Gln Asp Leu Leu Glu Ser Val
    50                  55                  60
Arg Leu Asp Lys Glu Lys Ala Glu Thr Leu Ala Ser Ser Leu Gln Glu
65                  70                  75                  80
Asp Leu Ala His Thr Arg Asn Asp Ala Asn Arg Leu Gln Asp Ala Ile
                85                  90                  95
Ala Lys Val Glu Asp Glu Tyr Arg Ala Phe Gln Glu Glu Ala Lys Lys
            100                 105                 110
Gln Ile Glu Asp Leu Asn Met Thr Leu Glu Lys Leu Arg Ser Asp Leu
        115                 120                 125
Asp Glu Lys Glu Thr Glu Arg Ser Asp Met Lys Glu Thr Ile Phe Glu
    130                 135                 140
Leu Glu Asp Glu Val Glu Gln His Arg Ala Val Lys Leu His Asp Asn
145                 150                 155                 160
Leu Ile Ile Ser Asp Leu Glu Asn Thr Val Lys Lys Leu Gln Asp Gln
                165                 170                 175
Lys His Asp Met Glu Arg Glu Ile Lys Thr Leu His Arg Arg Leu Arg
            180                 185                 190
Glu Glu Ser Ala Glu Trp Arg Gln Phe Gln Ala Asp Leu Gln Thr Ala
        195                 200                 205
Val Val Ile Ala Asn Asp Ile Lys Ser Glu Ala Gln Glu Glu Ile Gly
    210                 215                 220
Asp Leu Lys Arg Arg Leu His Glu Ala Gln Glu Lys Asn Glu Lys Leu
225                 230                 235                 240
Thr Lys Glu Leu Glu Glu Ile Lys Ser Arg Lys Gln Glu Glu Glu Arg
```

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                245                 250                 255
Gly Gly Tyr


      <210> 59
      <211> 125
      <212> PRT
      <213> Homo sapien

      <400> 59
Gly Thr Ser Phe Ser Lys Asn His Ala Ala Pro Phe Ser Lys Val Leu
 1               5                  10                  15
Thr Phe Tyr Arg Lys Glu Pro Phe Thr Leu Glu Ala Tyr Tyr Ser Ser
            20                  25                  30
Pro Gln Asp Leu Pro Tyr Pro Asp Pro Ala Ile Ala Gln Phe Ser Val
        35                  40                  45
Gln Lys Val Thr Pro Gln Ser Asp Gly Ser Ser Ser Lys Val Lys Val
    50                  55                  60
Lys Val Arg Val Asn Val His Gly Ile Phe Ser Val Ser Ser Ala Ser
65                  70                  75                  80
Leu Val Glu Val His Lys Ser Glu Glu Asn Glu Glu Pro Met Glu Thr
                85                  90                  95
Asp Gln Asn Ala Lys Glu Glu Glu Lys Met Gln Val Asp Gln Glu Glu
            100                 105                 110
Pro His Val Glu Glu Gln Gln Gln Gln Thr Pro Gly Arg
        115                 120                 125

      <210> 60
      <211> 246
      <212> PRT
      <213> Homo sapien

      <400> 60
Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro
 1               5                  10                  15
Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val
            20                  25                  30
Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr
        35                  40                  45
Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln
    50                  55                  60
Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile
65                  70                  75                  80
Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln
                85                  90                  95
Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val
            100                 105                 110
Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly
        115                 120                 125
Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn
    130                 135                 140
Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu
145                 150                 155                 160
Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly
                165                 170                 175
```

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Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu
            180                 185                 190
Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn
        195                 200                 205
Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr
    210                 215                 220
Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala
225                 230                 235                 240
Thr Ser Gly Ile Ser Thr
                245

      <210> 61
      <211> 128
      <212> PRT
      <213> Homo sapien

      <400> 61
Gly Ile Phe Ser Val Ser Ser Ala Ser Leu Val Glu Val His Lys Ser
 1               5                  10                  15
Glu Glu Asn Glu Glu Pro Met Glu Thr Asp Gln Asn Ala Lys Glu Glu
            20                  25                  30
Glu Lys Met Gln Val Asp Gln Glu Glu Pro His Val Glu Glu Gln Gln
        35                  40                  45
Gln Gln Thr Pro Ala Glu Asn Lys Ala Glu Ser Glu Glu Met Glu Thr
    50                  55                  60
Ser Gln Ala Gly Ser Lys Asp Lys Lys Met Asp Gln Pro Pro Gln Ala
65                  70                  75                  80
Lys Lys Ala Lys Val Lys Thr Ser Thr Val Asp Leu Pro Ile Glu Asn
                85                  90                  95
Gln Leu Leu Trp Gln Ile Asp Arg Glu Met Leu Asn Leu Tyr Ile Glu
            100                 105                 110
Asn Glu Gly Lys Met Ile Met Gln Asp Lys Leu Glu Lys Glu Arg Asn
        115                 120                 125

      <210> 62
      <211> 418
      <212> PRT
      <213> Homo sapien

      <400> 62
Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro
 1               5                  10                  15
Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val
            20                  25                  30
Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr
        35                  40                  45
Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln
    50                  55                  60
Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile
65                  70                  75                  80
Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln
                85                  90                  95
Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val
            100                 105                 110
Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly
```

```
        115                 120                 125
Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn
    130                 135                 140
Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu
145                 150                 155                 160
Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly
                165                 170                 175
Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu
            180                 185                 190
Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn
        195                 200                 205
Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr
    210                 215                 220
Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala
225                 230                 235                 240
Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg
                245                 250                 255
Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp
            260                 265                 270
Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile
        275                 280                 285
His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser
    290                 295                 300
Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr
305                 310                 315                 320
Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val
                325                 330                 335
Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu
            340                 345                 350
Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser
        355                 360                 365
Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val
    370                 375                 380
Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly
385                 390                 395                 400
Val Tyr Thr Arg Val Thr Ala Tyr Ile Asp Trp Ile Arg Gln Gln Thr
                405                 410                 415
Gly Ile
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<210> 63
<211> 776
<212> DNA
<213> Homo sapien

<400> 63

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aggcagtagc agtggatcgg gccaagaagg aggcagctga gaaggaacag gaacttttaa   120
aacagaaatt acaggagcag ccagcaacag atggaggctc aagataagag tcgcaaggaa   180
aactagccaa ctgaaggaga agctgcagat ggagagagaa cacctactga gagagcagat   240
tatgatgttg gagcacacgc agaaggtcca aaatgattgg cttcatgaag gatttaagaa   300
gaagtatgag gagatgaatg cagagataag tcaatttaaa cgtatgattg atactacaaa   360
aaatgatgat actccctgga ttgcacgaac cttggacaac cttgccgatg agctaactgc   420
aatattgtct gctcctgcta aattaattgg tcatggtgtc aaaggtgtga gctcactctt   480
taaaaagcat aagctcccct tttaaggata ttatagattg tacatatatg ctttggacta   540
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tttttgatct gtatgttttt cattttcatt cagcaagttt ttttttttt tcagagtctt 600
actctgttgc ccaggctgga gtacagtggt gcaatctcag ctcactgcaa cctctgcctc 660
ctgggttcaa gagattcacc tgcctcagcc ccctagtagc tgggattata ggtgtacacc 720
accacaccca gctaatttt gtatttttag tagagatggg gtttcactat gttggc 776

<210> 64
<211> 160
<212> DNA
<213> Homo sapien

<400> 64
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gcccctcagt agcctcggcc caagaggcct gctttccact cgctagcccc gccgggggtc 120
cgtgtcctgt ctcggtggcc ggacccgggc ccgagcccga 160

<210> 65
<211> 72
<212> PRT
<213> Homo sapien

<400> 65
Leu Ser Ala Met Gly Phe Thr Ala Ala Gly Ile Ala Ser Ser Ser Ile
1 5 10 15
Ala Ala Lys Met Met Ser Ala Ala Ala Ile Ala Asn Gly Gly Gly Val
20 25 30
Ala Ser Gly Ser Leu Val Ala Thr Leu Gln Ser Leu Gly Ala Thr Gly
35 40 45
Leu Ser Gly Leu Thr Lys Phe Ile Leu Gly Ser Ile Gly Ser Ala Ile
50 55 60
Ala Ala Val Ile Ala Arg Phe Tyr
65 70

<210> 66
<211> 2581
<212> DNA
<213> Homo sapien

<400> 66
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gctggacagc tggaggatga acggagaagc cgactgcccc acagacctgg aaatggccgc 180
ccccaaaggc caagaccgtt ggtcccagga agacatgctg actttgctgg aatgcatgaa 240
gaacaacctt ccatccaatg acagctccaa gttcaaaacc accgaatcac acatggactg 300
ggaaaaagta gcatttaaag acttttctgg agacatgtgc aagctcaaat gggtggagat 360
ttctaatgag gtgaggaagt tccgtacatt gacagaattg atcctcgatg ctcaggaaca 420
tgttaaaaat ccttacaaag gcaaaaaact caagaaacac ccagacttcc caaagaagcc 480
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gaagaagaag atgaaatata ttcaggactt ccagagagag aaacaggagt tcgagcgaaa 660
cctggcccga ttcagggagg atcaccccga cctaatccag aatgccaaga aatcggacat 720
cccagagaag cccaaaaccc cccagcagct gtggtacacc cacgagaaga aggtgtatct 780
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gggtatcacc aagtccaccc tcaccaaggc cgaacgccag ctcaaggaca agtttgacgg 1020

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gcgacccacc aagccacctc cgaacagcta ctcgctgtac tgcgcagagc tcatggccaa    1080
catgaaggac gtgcccagca cagagcgcat ggtgctgtgc agccagcagt ggaagctgct    1140
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catgaccaag ctgcgaggcc caaaccccaa atccagccgg actactctgc agtccaagtc    2160
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agagcccagg agctcccctc cccaactgac cacctttgtt tcttccccat gttctgtccc    2520
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<210> 67
<211> 764
<212> PRT
<213> Homo sapien

<400> 67

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

```
                165                 170                 175
Ala Arg Phe Arg Glu Asp His Pro Asp Leu Ile Gln Asn Ala Lys Lys
            180                 185                 190
Ser Asp Ile Pro Glu Lys Pro Lys Thr Pro Gln Gln Leu Trp Tyr Thr
        195                 200                 205
His Glu Lys Lys Val Tyr Leu Lys Val Arg Pro Asp Ala Thr Thr Lys
    210                 215                 220
Glu Val Lys Asp Ser Leu Gly Lys Gln Trp Ser Gln Leu Ser Asp Lys
225                 230                 235                 240
Lys Arg Leu Lys Trp Ile His Lys Ala Leu Glu Gln Arg Lys Glu Tyr
                245                 250                 255
Glu Glu Ile Met Arg Asp Tyr Ile Gln Lys His Pro Glu Leu Asn Ile
            260                 265                 270
Ser Glu Glu Gly Ile Thr Lys Ser Thr Leu Thr Lys Ala Glu Arg Gln
        275                 280                 285
Leu Lys Asp Lys Phe Asp Gly Arg Pro Thr Lys Pro Pro Pro Asn Ser
    290                 295                 300
Tyr Ser Leu Tyr Cys Ala Glu Leu Met Ala Asn Met Lys Asp Val Pro
305                 310                 315                 320
Ser Thr Glu Arg Met Val Leu Cys Ser Gln Gln Trp Lys Leu Leu Ser
                325                 330                 335
Gln Lys Glu Lys Asp Ala Tyr His Lys Lys Cys Asp Gln Lys Lys Lys
            340                 345                 350
Asp Tyr Glu Val Glu Leu Leu Arg Phe Leu Glu Ser Leu Pro Glu Glu
        355                 360                 365
Glu Gln Gln Arg Val Leu Gly Glu Glu Lys Met Leu Asn Ile Asn Lys
    370                 375                 380
Lys Gln Ala Thr Ser Pro Ala Ser Lys Lys Pro Ala Gln Glu Gly Gly
385                 390                 395                 400
Lys Gly Gly Ser Glu Lys Pro Lys Arg Pro Val Ser Ala Met Phe Ile
                405                 410                 415
Phe Ser Glu Glu Lys Arg Arg Gln Leu Gln Glu Glu Arg Pro Glu Leu
            420                 425                 430
Ser Glu Ser Glu Leu Thr Arg Leu Leu Ala Arg Met Trp Asn Asp Leu
        435                 440                 445
Ser Glu Lys Lys Lys Ala Lys Tyr Lys Ala Arg Glu Ala Ala Leu Lys
    450                 455                 460
Ala Gln Ser Glu Arg Lys Pro Gly Gly Glu Arg Glu Glu Arg Gly Lys
465                 470                 475                 480
Leu Pro Glu Ser Pro Lys Arg Ala Glu Glu Ile Trp Gln Gln Ser Val
                485                 490                 495
Ile Gly Asp Tyr Leu Ala Arg Phe Lys Asn Asp Arg Val Lys Ala Leu
            500                 505                 510
Lys Ala Met Glu Met Thr Trp Asn Asn Met Glu Lys Lys Glu Lys Leu
        515                 520                 525
Met Trp Ile Lys Lys Ala Ala Glu Asp Gln Lys Arg Tyr Glu Arg Glu
    530                 535                 540
Leu Ser Glu Met Arg Ala Pro Pro Ala Ala Thr Asn Ser Ser Lys Lys
545                 550                 555                 560
Met Lys Phe Gln Gly Glu Pro Lys Lys Pro Pro Met Asn Gly Tyr Gln
                565                 570                 575
Lys Phe Ser Gln Glu Leu Leu Ser Asn Gly Glu Leu Asn His Leu Pro
            580                 585                 590
Leu Lys Glu Arg Met Val Glu Ile Gly Ser Arg Trp Gln Arg Ile Ser
        595                 600                 605
```

```
Gln Ser Gln Lys Glu His Tyr Lys Lys Leu Ala Glu Glu Gln Gln Lys
    610                 615                 620
Gln Tyr Lys Val His Leu Asp Leu Trp Val Lys Ser Leu Ser Pro Gln
625                 630                 635                 640
Asp Arg Ala Ala Tyr Lys Glu Tyr Ile Ser Asn Lys Arg Lys Ser Met
                645                 650                 655
Thr Lys Leu Arg Gly Pro Asn Pro Lys Ser Ser Arg Thr Thr Leu Gln
            660                 665                 670
Ser Lys Ser Glu Ser Glu Glu Asp Asp Glu Glu Asp Glu Asp Asp Glu
        675                 680                 685
Asp Glu Asp Glu Glu Glu Glu Asp Asp Glu Asn Gly Asp Ser Ser Glu
    690                 695                 700
Asp Gly Gly Asp Ser Ser Glu Ser Ser Ser Glu Asp Glu Ser Glu Asp
705                 710                 715                 720
Gly Asp Glu Asn Glu Glu Asp Asp Glu Asp Glu Asp Asp Asp Glu Asp
                725                 730                 735
Asp Asp Glu Asp Glu Asp Asn Glu Ser Glu Gly Ser Ser Ser Ser Ser
            740                 745                 750
Ser Ser Leu Gly Asp Ser Ser Asp Phe Asp Ser Asn
        755                 760
```

<210> 68
<211> 434
<212> DNA
<213> Homo sapien

<400> 68

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ctaagatgct ggatgctgaa gacatcgtcg gaactgcccg gccagatgag aaagccatta     60
tgacttatgt gtctagcttc tatcatgcct tctctggagc ccagaaggca gaaacagcag    120
ccaatcgcat ctgcaaagtg ttggcggtca atcaagagaa cgagcagctt atggaagact    180
atgagaagct ggccagtgat ctgttggagt ggatccgccg caccatccca tggctggaga    240
atcgggtgcc tgagaacacc atgcatgcca tgcagcagaa gctggaggac ttccgagact    300
atagacgcct gcacaagccg cccaaggtgc aggagaagtg ccagctggag atcaacttta    360
acacgctgca gaccaaactg cggctcagca accggcctgc cttcatgccc tccgagggca    420
ggatggtctc ggat                                                      434
```

<210> 69
<211> 244
<212> DNA
<213> Homo sapien

<400> 69

```
aggcagcatg ctcgttgaga gtcatcacca ctccctaatc tcaagtacgc agggacacaa     60
acactgcgga aggccgcagg gtcctctgcc taggaaaacc agagaccttt gttcacttgt    120
ttatgtgctg accttccctc cactattgtc ctgtgaccct gccaatcccc cctttgtgag    180
aaacacccaa gaatgatcaa taaaaaataa attaatttag gaaaaaaaaa aaaaaaaact    240
cgag                                                                 244
```

<210> 70
<211> 437
<212> DNA
<213> Homo sapien

<400> 70

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ctgggacggg agcgtccagc gggactcgaa ccccagatgt gaaggcgttt ctggaaagtc     60
```

cttggtccct ggatccagcg tcggccagcc cagagcccgt gccgcacatc cttgcgtcct 120
ccaggcagtg ggaccccgcg agctgcacgt ccctgggcac ggacaagtgt gaggcactgt 180
tggggctgtg ccaggtgcgg ggtgggctgc cccctttctc agaaccttcc agcctggtgc 240
cgtggccccc aggccggagt cttcctaagg ctgtgaggcc accсctgtcc tggcctccgt 300
tctcgcagca gcagaccttg cccgtgatga gcggggaggc ccttggctgg ctgggccagg 360
ctggttccct ggccatgggg gctgcacctc tgggggagcc agccaaggag gaccccatgc 420
tggcgcagga agccggg 437

<210> 71
<211> 271
<212> DNA
<213> Homo sapien

<400> 71
gcgcagagtt ctgtcgtcca ccatcgagtg aggaagagag cattggttcc cctgagatag 60
aagagatggc tctcttcagt gcccagtctc catacattaa cccgatcatc ccctttactg 120
gaccaatcca aggagggctg caggagggac ttcaggtgac cctccagggg actaccgaga 180
gttttgcaca aaagtttgtg gtgaactttt cagaacagct tcaatggaga tgacttggcc 240
ttccacttca accccggtta tgaggaagga g 271

<210> 72
<211> 290
<212> DNA
<213> Homo sapien

<400> 72
ccgagcccta cccggaggtc tccagaatcc ccaccgtcag gggatgcaac ggctccctgt 60
ctggtgccct ctcctgctgc gaggactcgg cccagggctc gggcccgccc aaggccccta 120
cggtggccga gggtcccagc tcctgccttc ggcggaacgt gatcagcgag agggagcgca 180
ggaagcggat gtcgttgagc tgtgagcgtc tgcgggccct gctgccccag ttcgatggcc 240
ggcgggagga catggcctcg gtcctggaga tgtctgttgc aattcctgcg 290

<210> 73
<211> 144
<212> PRT
<213> Homo sapien

<400> 73
Lys Met Leu Asp Ala Glu Asp Ile Val Gly Thr Ala Arg Pro Asp Glu
1 5 10 15
Lys Ala Ile Met Thr Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly
20 25 30
Ala Gln Lys Ala Glu Thr Ala Ala Asn Arg Ile Cys Lys Val Leu Ala
35 40 45
Val Asn Gln Glu Asn Glu Gln Leu Met Glu Asp Tyr Glu Lys Leu Ala
50 55 60
Ser Asp Leu Leu Glu Trp Ile Arg Arg Thr Ile Pro Trp Leu Glu Asn
65 70 75 80
Arg Val Pro Glu Asn Thr Met His Ala Met Gln Gln Lys Leu Glu Asp
85 90 95
Phe Arg Asp Tyr Arg Arg Leu His Lys Pro Pro Lys Val Gln Glu Lys
100 105 110
Cys Gln Leu Glu Ile Asn Phe Asn Thr Leu Gln Thr Lys Leu Arg Leu
115 120 125
Ser Asn Arg Pro Ala Phe Met Pro Ser Glu Gly Arg Met Val Ser Asp

130 135 140

<210> 74
<211> 64
<212> PRT
<213> Homo sapien

<400> 74
Gly Ser Met Leu Val Glu Ser His His His Ser Leu Ile Ser Ser Thr
1 5 10 15
Gln Gly His Lys His Cys Gly Arg Pro Gln Gly Pro Leu Pro Arg Lys
20 25 30
Thr Arg Asp Leu Cys Ser Leu Val Tyr Val Leu Thr Phe Pro Pro Leu
35 40 45
Leu Ser Cys Asp Pro Ala Lys Ser Pro Phe Val Arg Asn Thr Gln Glu
50 55 60

<210> 75
<211> 145
<212> PRT
<213> Homo sapien

<400> 75
Gly Thr Gly Ala Ser Ser Gly Thr Arg Thr Pro Asp Val Lys Ala Phe
1 5 10 15
Leu Glu Ser Pro Trp Ser Leu Asp Pro Ala Ser Ala Ser Pro Glu Pro
20 25 30
Val Pro His Ile Leu Ala Ser Ser Arg Gln Trp Asp Pro Ala Ser Cys
35 40 45
Thr Ser Leu Gly Thr Asp Lys Cys Glu Ala Leu Leu Gly Leu Cys Gln
50 55 60
Val Arg Gly Gly Leu Pro Pro Phe Ser Glu Pro Ser Ser Leu Val Pro
65 70 75 80
Trp Pro Pro Gly Arg Ser Leu Pro Lys Ala Val Arg Pro Pro Leu Ser
85 90 95
Trp Pro Pro Phe Ser Gln Gln Gln Thr Leu Pro Val Met Ser Gly Glu
100 105 110
Ala Leu Gly Trp Leu Gly Gln Ala Gly Ser Leu Ala Met Gly Ala Ala
115 120 125
Pro Leu Gly Glu Pro Ala Lys Glu Asp Pro Met Leu Ala Gln Glu Ala
130 135 140
Gly
145

<210> 76
<211> 69
<212> PRT
<213> Homo sapien

<400> 76
Ala Glu Phe Cys Arg Pro Pro Ser Ser Glu Glu Glu Ser Ile Gly Ser
1 5 10 15
Pro Glu Ile Glu Glu Met Ala Leu Phe Ser Ala Gln Ser Pro Tyr Ile
20 25 30
Asn Pro Ile Ile Pro Phe Thr Gly Pro Ile Gln Gly Gly Leu Gln Glu

```
        35                  40                  45
Gly Leu Gln Val Thr Leu Gln Gly Thr Thr Glu Ser Phe Ala Gln Lys
    50                  55                  60
Phe Val Val Asn Phe
65
```

<210> 77
<211> 96
<212> PRT
<213> Homo sapien

<400> 77

```
Glu Pro Tyr Pro Glu Val Ser Arg Ile Pro Thr Val Arg Gly Cys Asn
 1               5                  10                  15
Gly Ser Leu Ser Gly Ala Leu Ser Cys Cys Glu Asp Ser Ala Gln Gly
            20                  25                  30
Ser Gly Pro Pro Lys Ala Pro Thr Val Ala Glu Gly Pro Ser Ser Cys
        35                  40                  45
Leu Arg Arg Asn Val Ile Ser Glu Arg Glu Arg Arg Lys Arg Met Ser
    50                  55                  60
Leu Ser Cys Glu Arg Leu Arg Ala Leu Leu Pro Gln Phe Asp Gly Arg
65                  70                  75                  80
Arg Glu Asp Met Ala Ser Val Leu Glu Met Ser Val Ala Ile Pro Ala
                85                  90                  95
```

<210> 78
<211> 2076
<212> DNA
<213> Homo sapien

<400> 78

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agaaaaagtc tatgtttgca gaaatacaga tccaagacaa agacaggatg ggcactgctg      60
gaaaagttat taaatgcaaa gcagctgtgc tttgggagca gaagcaaccc ttctccattg     120
aggaaataga agttgcccca ccaaagacta aagaagttcg cattaagatt ttggccacag     180
gaatctgtcg cacagatgac catgtgataa aaggaacaat ggtgtccaag tttccagtga     240
ttgtgggaca tgaggcaact gggattgtag agagcattgg agaaggagtg actacagtga     300
aaccaggtga caaagtcatc cctctcttc tgccacaatg tagagaatgc aatgcttgtc      360
gcaacccaga tggcaacctt tgcattagga gcgatattac tggtcgtgga gtactggctg     420
atggcaccac cagatttaca tgcaagggca aaccagtcca ccacttcatg aacaccagta     480
catttaccga gtacacagtg gtggatgaat cttctgttgc taagattgat gatgcagctc     540
ctcctgagaa agtctgttta attggctgtg ggttttccac tggatatggc gctgctgtta     600
aaactggcaa ggtcaaacct ggttccactt gcgtcgtctt tggcctgaga ggagttggcc     660
tgtcagtcat catgggctgt aagtcagctg gtgcatctag gatcattggg attgacctca     720
acaaagacaa atttgagaag gccatggctg taggtgccac tgagtgtatc agtcccaagg     780
actctaccaa acccatcagt gaggtgctgt cagaaatgac aggcaacaac gtgggataca     840
cctttgaagt tattgggcat cttgaaacca tgattgatgc cctggcatcc tgccacatga     900
actatgggac cagcgtggtt gtaggagttc ctccatcagc caagatgctc acctatgacc     960
cgatgttgct cttcactgga cgcacatgga agggatgtgt ctttggaggt ttgaaaagca    1020
gagatgatgt cccaaaacta gtgactgagt tcctggcaaa gaaatttgac ctggaccagt    1080
tgataactca tgtcttacca tttaaaaaaa tcagtgaagg atttgagctg ctcaattcag    1140
gacaaagcat tcgaacggtc ctgacgtttt gagatccaaa gtggcaggag gtctgtgttg    1200
tcatggtgaa ctggagtttc tcttgtgaga gttccctcat ctgaaatcat gtatctgtct    1260
cacaaataca agcataagta gaagatttgt tgaagacata gaacccttat aaagaattat    1320
taacctttat aaacatttaa agtcttgtga gcacctggga attagtataa taacaatgtt    1380
aatatttttg atttacattt tgtaaggcta taattgtatc ttttaagaaa acatacactt    1440
```

```
ggatttctat gttgaaatgg agatttttaa gagttttaac cagctgctgc agatatatat   1500
ctcaaaacag atatagcgta taaagatata gtaaatgcat ctcctagagt aatattcact   1560
taacacattg aaactattat tttttagatt tgaatataaa tgtatttttt aaacacttgt   1620
tatgagttaa cttggattac attttgaaat cagttcattc catgatgcat attactggat   1680
tagattaaga aagacagaaa agattaaggg acgggcacat ttttcaacga ttaagaatca   1740
tcattacata acttggtgaa actgaaaaag tatatcatat gggtacacaa ggctatttgc   1800
cagcatatat taatatttta gaaaatattc cttttgtaat actgaatata aacatagagc   1860
tagaatcata ttatcatact tatcataatg ttcaatttga tacagtagaa ttgcaagtcc   1920
ttaagtccct attcactgtg cttagtagtg actccattta ataaaaagtg tttttagttt   1980
ttaacaacta cactgatgta tttatatata tttataacat gttaaaaatt tttaaggaaa   2040
ttaaaaatta tataaaaaaa aaaaaaaaaa ctcgag                             2076
```

<210> 79
<211> 2790
<212> DNA
<213> Homo sapien

<400> 79

```
aagcagttga gtaggcagaa aaaagaacct cttcattaag gattaaaatg tataggccag     60
cacgtgtaac ttcgacttca agatttctga atccatatgt agtatgtttc attgtcgtcg    120
caggggtagt gatcctggca gtcaccatag ctctacttgt ttacttttta gcttttgatc    180
aaaaatctta cttttatagg agcagttttc aactcctaaa tgttgaatat aatagtcagt    240
taaattcacc agctacacag gaatacagga ctttgagtgg aagaattgaa tctctgatta    300
ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac    360
tgaggcaaga tggtagtggt gtgagagcgg atgttgtcat gaaatttcaa ttcactagaa    420
ataacaatgg agcatcaatg aaaagcagaa ttgagtctgt tttacgacaa atgctgaata    480
actctggaaa cctggaaata aacccttcaa ctgagataac atcacttact gaccaggctg    540
cagcaaattg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc    600
agagaatcct tggaggcact gaggctgagg agggaagctg gccgtggcaa gtcagtctgc    660
ggctcaataa tgcccaccac tgtggaggca gcctgatcaa taacatgtgg atcctgacag    720
cagctcactg cttcagaagc aactctaatc ctcgtgactg gattgccacg tctggtattt    780
ccacaacatt tcctaaacta agaatgagag taagaaatat tttaattcat aacaattata    840
aatctgcaac tcatgaaaat gacattgcac ttgtgagact tgagaacagt gtcaccttta    900
ccaaagatat ccatagtgtg tgtctcccag ctgctaccca gaatattcca cctggctcta    960
ctgcttatgt aacaggatgg ggcgctcaag aatatgctgg ccacacagtt ccagagctaa   1020
ggcaaggaca ggtcagaata ataagtaatg atgtatgtaa tgcaccacat agttataatg   1080
gagccatctt gtctggaatg ctgtgtgctg gagtacctca aggtggagtg gacgcatgtc   1140
agggtgactc tggtggccca ctagtacaag aagactcacg gcggctttgg tttattgtgg   1200
ggatagtaag ctggggagat cagtgtggcc tgccggataa gccaggagtg tatactcgag   1260
tgacagccta ccttgactgg attaggcaac aaactgggat ctagtgcaac aagtgcatcc   1320
ctgttgcaaa gtctgtatgc aggtgtgcct gtcttaaatt ccaaagcttt acatttcaac   1380
tgaaaaagaa actagaaatg tcctaattta acatcttgtt acataaatat ggtttaacaa   1440
acactgttta acctttcttt attattaaag gttttctatt ttctccagag aactatatga   1500
atgttgcata gtactgtggc tgtgtaacag aagaaacaca ctaaactaat tacaaagtta   1560
acaatttcat tacagttgtg ctaaatgccc gtagtgagaa gaacaggaac cttgagcatg   1620
tatagtagag gaacctgcac aggtctgatg ggtcagaggg gtcttctctg ggtttcactg   1680
aggatgagaa gtaagcaaac tgtggaaaca tgcaaaggaa aaagtgatag aataatattc   1740
aagacaaaaa gaacagtatg aggcaagaga aatagtatgt atttaaaatt tttggttact   1800
caatatctta tacttagtat gagtcctaaa attaaaaatg tgaaactgtt gtactatacg   1860
tataacctaa ccttaattat tctgtaagaa catgcttcca taggaaatag tggataattt   1920
tcagctattt aaggcaaaag ctaaaatagt tcactcctca actgagaccc aaagaattat   1980
agatattttt catgatgacc catgaaaaat atcactcatc tacataaagg agagactata   2040
tctattttat agagaagcta agaaatatac ctacacaaac ttgtcaggtg ctttacaact   2100
acatagtact ttttaacaac aaaataataa ttttaagaat gaaaatttta atcatcggga   2160
agaacgtccc actacagact tcctatcact ggcagttata tttttgagcg taaaagggtc   2220
```

gtcaaacgct aaatctaagt aatgaattga aagtttaaag agggggaaga gttggtttgc 2280
aaaggaaaag tttaaatagc ttaatatcaa tagaatgatc ctgaagacag aaaaaacttt 2340
gtcactcttc ctctctcatt ttctttctct ctctctcccc ttctcataca catgcctccc 2400
cgaccaaaga atataatgta aattaaatcc actaaaatgt aatggcatga aaatctctgt 2460
agtctgaatc actaatattc ctgagttttt atgagctcct agtacagcta aagtttgcct 2520
atgcatgatc atctatgcgt cagagcttcc tccttctaca agctaactcc ctgcatctgg 2580
gcatcaggac tgctccatac atttgctgaa aacttcttgt atttcctgat gtaaaattgt 2640
gcaaacacct acaataaagc catctacttt tagggaaagg gagttgaaaa tgcaaccaac 2700
tcttggcgaa ctgtacaaac aaatctttgc tatactttat ttcaaataaa ttctttttga 2760
aatgaaaaaa aaaaaaaaaa aaaactcgag 2790

<210> 80
<211> 1460
<212> DNA
<213> Homo sapien

<400> 80
ctcaaagcag ttgagtaggc agaaaaaaga acctcttcat taaggattaa aatgtatagg 60
ccagcacgtg taacttcgac ttcaagattt ctgaatccat atgtagtatg tttcattgtc 120
gtcgcagggg tagtgatcct ggcagtcacc atagctctac ttgtttactt tttagctttt 180
gatcaaaaat cttactttta taggagcagt tttcaactcc taaatgttga atataatagt 240
cagttaaatt caccagctac acaggaatac aggactttga gtggaagaat tgaatctctg 300
attactaaaa cattcaaaga atcaaattta agaaatcagt tcatcagagc tcatgttgcc 360
aaactgaggc aagatggtag tggtgtgaga gcggatgttg tcatgaaatt tcaattcact 420
agaaataaca atggagcatc aatgaaaagc agaattgagt ctgttttacg acaaatgctg 480
aataactctg gaaacctgga aataaaccct tcaactgaga taacatcact tactgaccag 540
gctgcagcaa attggcttat taatgaatgt ggggccggtc cagacctaat aacattgtct 600
gagcagagaa tccttggagg cactgaggct gaggagggaa gctggccgtg gcaagtcagt 660
ctgcggctca ataatgccca ccactgtgga ggcagcctga tcaataacat gtggatcctg 720
acagcagctc actgcttcag aagcaactct aatcctcgtg actggattgc cacgtctggt 780
atttccacaa catttcctaa actaagaatg agagtaagaa atattttaat tcataacaat 840
tataaatctg caactcatga aaatgacatt gcacttgtga gacttgagaa cagtgtcacc 900
tttaccaaag atatccatag tgtgtgtctc ccagctgcta cccagaatat tccacctggc 960
tctactgctt atgtaacagg atggggcgct caagaatatg ctggccacac agttccagag 1020
ctaaggcaag gacaggtcag aataataagt aatgatgtat gtaatgcacc acatagttat 1080
aatggagcca tcttgtctgg aatgctgtgt gctggagtac ctcaaggtgg agtggacgca 1140
tgtcagggtg actctggtgg cccactagta caagaagact cacggcggct ttggtttatt 1200
gtggggatag taagctgggg agatcagtgt ggcctgccgg ataagccagg agtgtatact 1260
cgagtgacag cctacccttga ctggattagg caacaaactg ggatctagtg caacaagtgc 1320
atccctgttg caaagtctgt atgcaggtgt gcctgtctta aattccaaag ctttacattt 1380
caactgaaaa agaaactaga aatgtcctaa tttaacatct tgttacataa atatggttta 1440
acaaaaaaaa aaaaaaaaaa 1460

<210> 81
<211> 386
<212> PRT
<213> Homo sapien

<400> 81
Met Phe Ala Glu Ile Gln Ile Gln Asp Lys Asp Arg Met Gly Thr Ala
1 5 10 15
Gly Lys Val Ile Lys Cys Lys Ala Ala Val Leu Trp Glu Gln Lys Gln
20 25 30
Pro Phe Ser Ile Glu Glu Ile Glu Val Ala Pro Pro Lys Thr Lys Glu
35 40 45

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

<210> 82
<211> 418
<212> PRT
<213> Homo sapien

<400> 82
Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro
 1   5   10   15
Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val
            20   25   30

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

<210> 83
<211> 418
<212> PRT
<213> Homo sapien

<400> 83

Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro
1 5 10 15
Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val
20 25 30
Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr
35 40 45
Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln
50 55 60
Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile
65 70 75 80
Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln
85 90 95
Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val
100 105 110
Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly
115 120 125
Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn
130 135 140
Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu
145 150 155 160
Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly
165 170 175
Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu
180 185 190
Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn
195 200 205
Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr
210 215 220
Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala
225 230 235 240
Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg
245 250 255
Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp
260 265 270
Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile
275 280 285
His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser
290 295 300
Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr
305 310 315 320
Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val
325 330 335
Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu
340 345 350
Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser
355 360 365
Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val
370 375 380
Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly
385 390 395 400
Val Tyr Thr Arg Val Thr Ala Tyr Leu Asp Trp Ile Arg Gln Gln Thr
405 410 415
Gly Ile

<210> 84
<211> 489
<212> DNA
<213> Homo sapien

<400> 84
aaaagggtaa gcttgatgat taccaggaac gaatgaacaa aggggaaagg cttaatcaag 60
atcagctgga tgccgtttct aagtaccagg aagtcacaaa taatttggag tttgcaaaag 120
aattacagag gagtttcatg gcactaagtc aagatattca gaaaacaata aagaagacag 180
cacgtcggga gcagcttatg agagaagaag ctgaacagaa acgtttaaaa actgtacttg 240
agctacagta tgttttggac aaattgggag atgatgaagt gcggactgac ctgaaacaag 300
gtttgaatgg agtgccaata ttgtccgaag aggagttgtc attgttggat gaattctata 360
agctagtaga ccctgaacgg gacatgagct tgaggttgaa tgaacagtat gaacatgcct 420
ccattcacct gtgggacctg ctggaaggga aggaaaaacc tgtatgtgga accacctata 480
aagttctaa 489

<210> 85
<211> 304
<212> DNA
<213> Homo sapien

<400> 85
gggacctgga ggaggccacg ctgcagcatg aagccacagc agccaccctg aggaagaagc 60
acgcggacag cgtggccgag ctcggggagc agatcgacaa cctgcagcgg gtgaagcaga 120
agctggagaa ggagaagagc gagatgaaga tggagatcga tgacctcgct tgtaacatgg 180
aggtcatctc caaatctaag ggaaaccttg agaagatgtg ccgcacactg gaggaccaag 240
tgagtgagct gaagacccag gaggaggaac agcagcggct gatcaatgaa ctgactgcgc 300
agag 304

<210> 86
<211> 296
<212> DNA
<213> Homo sapien

<400> 86
gaaaatcctt cctttgaatg ggaatctcca agcagttgaa ttgggcgaaa aaagaacctc 60
ttccttaagg attaaaatgt ttagggcaac acgtgttact tccacttcca gatttctgaa 120
tccatatgtt gtatgtttcc ttgtcctccc aggggttgtg atcctggcag tccccatagc 180
tctacttgtt tactttttag cttttgatca aaaatcttac ttttattgga gcaattttcc 240
actcccaaat gttgaatata atagtccgtt taattccccc gcttcaccgg gaattc 296

<210> 87
<211> 904
<212> DNA
<213> Homo sapien

<400> 87
gtgtccagga aacgattcat gaacataaca agcttgctgc aaattcagat catctcatgc 60
agattcaaaa atgtgagttg gtcttgatcc acacctaccc agttggtgaa gacagccttg 120
tatctgatcg ttctaaaaaa gagttgtccc cggttttaac cagtgaagtt catagtgttc 180
gtgcaggacg gcatcttgct accaaattga atattttagt acagcaacat tttgacttgg 240
cttcaactac tattacaaat attccaatga aggaagaaca gcatgctaac acatctgcca 300
attatgatgt ggagctactt catcacaaag atgcacatgt agatttcctg aaaagtggtg 360

attcgcatct aggtggcggc agtcgagaag gctcgtttaa agaaacaata acattaaagt 420
ggtgtacacc aaggacaaat aacattgaat tacactattg tactggagct tatcggattt 480
cacctgtaga tgtaaatagt agaccttcct cctgccttac taattttctt ctaaatggtc 540
gttctgtttt attggaacaa ccacgaaagt caggttctaa agtcattagt catatgctta 600
gtagccatgg aggagagatt tttttgcacg tccttagcag ttctcgatcc attctagaag 660
atccaccttc aattagtgaa ggatgtggag gaagagttac agactaccgg attacagatt 720
ttggtgaatt tatgagggga aaacagatta actccttttc tacaccccag atataaaatc 780
gatggaagtc ttgaggtccc tttggaaccg agccaaaaga tcagttaaaa aaacataccc 840
gttactggcc tatgatttca aaaacccacc atttttaaca tgcaagcggt agttccgtta 900
acca 904

<210> 88
<211> 387
<212> DNA
<213> Homo sapien

<400> 88
cgtctctccc ccagtttgcc gttcacccgg agcgctcggg acttgccgat agtggtgacg 60
gcggcaacat gtctgtggct ttcgcggccc cgaggcagcg aggcaagggg gagatcactc 120
ccgctgcgat tcagaagatg ttggatgaca ataaccatct tattcagtgt ataatggact 180
ctcagaataa aggaaagacc tcagagtgtt ctcagtatca gcagatgttg cacacaaact 240
tggtatacct tgctacaata gcagattcta atcaaaatat gcagtctctt ttaccagcac 300
caccccacaca gaatatgcct atgggtcctg gagggatgaa tcagagcggg cctcccccac 360
ctccacgctc tcacaacatg ccttcaa 387

<210> 89
<211> 481
<212> DNA
<213> Homo sapien

<400> 89
tgttcttgga cctgcggtgc tatagagcag gctcttctag gttggcagtt gccatggaat 60
ctggacccaa aatgttggcc cccgtttgcc tggtggaaaa taacaatgag cagctattgg 120
tgaaccagca agctatacag attcttgaaa agatttctca gccagtggtg gtggtggcca 180
ttgtaggact gtaccgtaca gggaaatcct acttgatgaa ccatctggca ggacagaatc 240
atggcttccc tctgggctcc acggtgcagt ctgaaaccaa gggcatctgg atgtggtgcg 300
tgccccaccc atccaagcca aaccacaccc tggtccttct ggacaccgaa ggtctgggcg 360
atgtggaaaa gggtgaccct aagaatgact cctggatctt tgccctggct gtgctcctgt 420
gcagcacctt tgtctacaac agcatgagca ccatcaacca ccaggccctg gagcagctgc 480
a 481

<210> 90
<211> 491
<212> DNA
<213> Homo sapien

<400> 90
tgaaaactgt tcttggacct gcggtgctat agagcaggtt ggcagttgcc atggaatctg 60
gacccaaaat gttggccccc gtttgcctgg tggaaaataa caatgagcag ctattggtga 120
accagcaagc tatacagatt cttgaaaaga tttctcagcc agtggtggtg gtggccattg 180
taggactgta ccgtacaggg aaatcctact tgatgaacca tctggcagga cagaatcatg 240
gcttccctct gggctccacg gtgcagtctg aaaccaaggg catctggatg tggtgcgtgc 300
cccacccatc caagccaaac cacaccctgg tccttctgga caccgaaggt ctgggcgatg 360
tggaaaaggg tgaccctaag aatgactcct ggatctttgc cctggctgtg ctcctgtgca 420
gcacctttgt ctacaacagc atgagcacca tcaaccacca agccctggag cagctgcatt 480

atgtgacgga c 491

<210> 91
<211> 488
<212> DNA
<213> Homo sapien

<400> 91
ttcgacagtc agccgcatct tcttttgcgt cgccagccga gccacatcgc tcagacacca 60
tggggaaggt gaaggtcgga gtcaacggat ttggtcgtat tgggcgcctg gtcaccaggg 120
ctgcttttaa ctctggtaaa gtggatattg ttgccatcaa tgacccctc attgacctca 180
actacatggt ttacatgttc caatatgatt ccacccatgg caaattccat ggcaccgtcg 240
aggctgagaa cgggaagctt gtcatcaatg gaaatcccat caccatcttc caggagcgag 300
atccctccaa aatcaagtgg ggcgatgctg gcgctgagta cgtcgtggag tccactggcg 360
tcttcaccac catggagaag gctggggctc atttgcaggg gggagccaaa agggtcatca 420
tctctgcccc tctgctgatg ccccatgttc gtcatgggtg tgaaccatga gaagtatgac 480
acagcctc 488

<210> 92
<211> 384
<212> DNA
<213> Homo sapien

<400> 92
gacagtcagc cgcatcttct tttgcgtcgc cagccgagcc acatcgctca gacaccatgg 60
ggaaggtgaa ggtcggagtc aacggatttg gtcgtattgg gcgcctggtc accagggctg 120
cttttaactc tggtaaagtg gatattgttg ccatcaatga ccccttcatt gacctcaact 180
acatggttta catgttccaa tatgattcca cccatggcaa attccatggc accgtcgagg 240
ctgagaacgg gaagcttgtc atcaatggaa atcccatcac catcttccag gagcgagatc 300
cctccaaaat caagtggggc gatactggcg ctgagtacgt cgtggagtcc actggcgtct 360
tcaccaccat ggagaaggct gggg 384

<210> 93
<211> 162
<212> PRT
<213> Homo sapien

<400> 93
Lys Gly Lys Leu Asp Asp Tyr Gln Glu Arg Met Asn Lys Gly Glu Arg
1 5 10 15
Leu Asn Gln Asp Gln Leu Asp Ala Val Ser Lys Tyr Gln Glu Val Thr
20 25 30
Asn Asn Leu Glu Phe Ala Lys Glu Leu Gln Arg Ser Phe Met Ala Leu
35 40 45
Ser Gln Asp Ile Gln Lys Thr Ile Lys Lys Thr Ala Arg Arg Glu Gln
50 55 60
Leu Met Arg Glu Glu Ala Glu Gln Lys Arg Leu Lys Thr Val Leu Glu
65 70 75 80
Leu Gln Tyr Val Leu Asp Lys Leu Gly Asp Asp Glu Val Arg Thr Asp
85 90 95
Leu Lys Gln Gly Leu Asn Gly Val Pro Ile Leu Ser Glu Glu Glu Leu
100 105 110Ser Leu Leu Asp Glu
Phe Tyr Lys Leu Val Asp Pro Glu Arg Asp Met
115 120 125
Ser Leu Arg Leu Asn Glu Gln Tyr Glu His Ala Ser Ile His Leu Trp

```
    130                 135                 140
Asp Leu Leu Glu Gly Lys Glu Lys Pro Val Cys Gly Thr Thr Tyr Lys
145                 150                 155                 160
Val Leu


      <210> 94
      <211> 100
      <212> PRT
      <213> Homo sapien

      <400> 94
Asp Leu Glu Glu Ala Thr Leu Gln His Glu Ala Thr Ala Ala Thr Leu
 1               5                  10                  15
Arg Lys Lys His Ala Asp Ser Val Ala Glu Leu Gly Glu Gln Ile Asp
            20                  25                  30
Asn Leu Gln Arg Val Lys Gln Lys Leu Glu Lys Glu Lys Ser Glu Met
        35                  40                  45
Lys Met Glu Ile Asp Asp Leu Ala Cys Asn Met Glu Val Ile Ser Lys
    50                  55                  60
Ser Lys Gly Asn Leu Glu Lys Met Cys Arg Thr Leu Glu Asp Gln Val
65                  70                  75                  80
Ser Glu Leu Lys Thr Gln Glu Glu Glu Gln Gln Arg Leu Ile Asn Glu
                85                  90                  95
Leu Thr Ala Gln
            100

      <210> 95
      <211> 99
      <212> PRT
      <213> Homo sapien

      <400> 95
Lys Ile Leu Pro Leu Asn Gly Asn Leu Gln Ala Val Glu Leu Gly Glu
 1               5                  10                  15
Lys Arg Thr Ser Ser Leu Arg Ile Lys Met Phe Arg Ala Thr Arg Val
            20                  25                  30
Thr Ser Thr Ser Arg Phe Leu Asn Pro Tyr Val Val Cys Phe Leu Val
        35                  40                  45
Leu Pro Gly Val Val Ile Leu Ala Val Pro Ile Ala Leu Leu Val Tyr
    50                  55                  60
Phe Leu Ala Phe Asp Gln Lys Ser Tyr Phe Tyr Trp Ser Asn Phe Pro
65                  70                  75                  80
Leu Pro Asn Val Glu Tyr Asn Ser Pro Phe Asn Ser Pro Ala Ser Pro
                85                  90                  95
Gly Ile Pro


      <210> 96
      <211> 257
      <212> PRT
      <213> Homo sapien

      <400> 96
Val Gln Glu Thr Ile His Glu His Asn Lys Leu Ala Ala Asn Ser Asp
```

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

```
<210> 97
<211> 128
<212> PRT
<213> Homo sapien

<400> 97
Ser Leu Pro Gln Phe Ala Val His Pro Glu Arg Ser Gly Leu Ala Asp
 1               5                   10                  15
Ser Gly Asp Gly Gly Asn Met Ser Val Ala Phe Ala Ala Pro Arg Gln
            20                  25                  30
Arg Gly Lys Gly Glu Ile Thr Pro Ala Ala Ile Gln Lys Met Leu Asp
        35                  40                  45
Asp Asn Asn His Leu Ile Gln Cys Ile Met Asp Ser Gln Asn Lys Gly
    50                  55                  60
Lys Thr Ser Glu Cys Ser Gln Tyr Gln Gln Met Leu His Thr Asn Leu
65                  70                  75                  80
Val Tyr Leu Ala Thr Ile Ala Asp Ser Asn Gln Asn Met Gln Ser Leu
                85                  90                  95
Leu Pro Ala Pro Pro Thr Gln Asn Met Pro Met Gly Pro Gly Gly Met
            100                 105                 110
Asn Gln Ser Gly Pro Pro Pro Pro Pro Arg Ser His Asn Met Pro Ser
```

```
        115                 120                 125

      &lt;210&gt; 98
      &lt;211&gt; 159
      &lt;212&gt; PRT
      &lt;213&gt; Homo sapien

      &lt;400&gt; 98
Phe Leu Asp Leu Arg Cys Tyr Arg Ala Gly Ser Ser Arg Leu Ala Val
 1               5                  10                  15
Ala Met Glu Ser Gly Pro Lys Met Leu Ala Pro Val Cys Leu Val Glu
            20                  25                  30
Asn Asn Asn Glu Gln Leu Leu Val Asn Gln Gln Ala Ile Gln Ile Leu
        35                  40                  45
Glu Lys Ile Ser Gln Pro Val Val Val Val Ala Ile Val Gly Leu Tyr
    50                  55                  60
Arg Thr Gly Lys Ser Tyr Leu Met Asn His Leu Ala Gly Gln Asn His
65                  70                  75                  80
Gly Phe Pro Leu Gly Ser Thr Val Gln Ser Glu Thr Lys Gly Ile Trp
                85                  90                  95
Met Trp Cys Val Pro His Pro Ser Lys Pro Asn His Thr Leu Val Leu
            100                 105                 110
Leu Asp Thr Glu Gly Leu Gly Asp Val Glu Lys Gly Asp Pro Lys Asn
        115                 120                 125
Asp Ser Trp Ile Phe Ala Leu Ala Val Leu Leu Cys Ser Thr Phe Val
    130                 135                 140
Tyr Asn Ser Met Ser Thr Ile Asn His Gln Ala Leu Glu Gln Leu
145                 150                 155

      &lt;210&gt; 99
      &lt;211&gt; 147
      &lt;212&gt; PRT
      &lt;213&gt; Homo sapien

      &lt;400&gt; 99
Met Glu Ser Gly Pro Lys Met Leu Ala Pro Val Cys Leu Val Glu Asn
 1               5                  10                  15
Asn Asn Glu Gln Leu Leu Val Asn Gln Gln Ala Ile Gln Ile Leu Glu
            20                  25                  30
Lys Ile Ser Gln Pro Val Val Val Val Ala Ile Val Gly Leu Tyr Arg
        35                  40                  45
Thr Gly Lys Ser Tyr Leu Met Asn His Leu Ala Gly Gln Asn His Gly
    50                  55                  60
Phe Pro Leu Gly Ser Thr Val Gln Ser Glu Thr Lys Gly Ile Trp Met
65                  70                  75                  80
Trp Cys Val Pro His Pro Ser Lys Pro Asn His Thr Leu Val Leu Leu
                85                  90                  95
Asp Thr Glu Gly Leu Gly Asp Val Glu Lys Gly Asp Pro Lys Asn Asp
            100                 105                 110
Ser Trp Ile Phe Ala Leu Ala Val Leu Leu Cys Ser Thr Phe Val Tyr
        115                 120                 125
Asn Ser Met Ser Thr Ile Asn His Gln Ala Leu Glu Gln Leu His Tyr
    130                 135                 140
Val Thr Asp
145
```

<210> 100
<211> 124
<212> PRT
<213> Homo sapien

<400> 100
Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile Gly Arg
1 5 10 15
Leu Val Thr Arg Ala Ala Phe Asn Ser Gly Lys Val Asp Ile Val Ala
20 25 30
Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met Phe Gln
35 40 45
Tyr Asp Ser Thr His Gly Lys Phe His Gly Thr Val Glu Ala Glu Asn
50 55 60
Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln Glu Arg
65 70 75 80
Asp Pro Ser Lys Ile Lys Trp Gly Asp Ala Gly Ala Glu Tyr Val Val
85 90 95
Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly Ala His Leu
100 105 110
Gln Gly Gly Ala Lys Arg Val Ile Ile Ser Ala Pro
115 120

<210> 101
<211> 127
<212> PRT
<213> Homo sapien

<400> 101
Gln Ser Ala Ala Ser Ser Phe Ala Ser Pro Ala Glu Pro His Arg Ser
1 5 10 15
Asp Thr Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile
20 25 30
Gly Arg Leu Val Thr Arg Ala Ala Phe Asn Ser Gly Lys Val Asp Ile
35 40 45
Val Ala Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met
50 55 60
Phe Gln Tyr Asp Ser Thr His Gly Lys Phe His Gly Thr Val Glu Ala
65 70 75 80
Glu Asn Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln
85 90 95
Glu Arg Asp Pro Ser Lys Ile Lys Trp Gly Asp Thr Gly Ala Glu Tyr
100 105 110
Val Val Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly
115 120 125

<210> 102
<211> 1225
<212> DNA
<213> Homo sapien

<400> 102
atggcggcgc ggtcgtcgtc gggggtggcg gcggcagagg gggcggcggc cctggcggca 60
gcggagacgg cagccgtgac ggtggcagcg gcggcgcggg acctgggcct gggggaatga 120

ggcggccgcg gcgggccagc ggcggagccg tgtagcggag aagctccccc tccctgcttc 180
ccttggccga gccgggggcg cgcgcgcacg cggccgtcca gagcgggctc cccacccctc 240
gactcctgcg acccgcaccg caccccccacc cgggcccgga ggatgatgaa gctcaagtcg 300
aaccagaccc gcacctacga cggcgacggc tacaagaagc gggccgcatg cctgtgtttc 360
cgcagcgaga gcgaggagga ggtgctactc gtgagcagta gtcgccatcc agacagatgg 420
attgtccctg gaggaggcat ggagcccgag gaggagccaa gtgtggcagc agttcgtgaa 480
gtctgtgagg aggctggagt aaaagggaca ttgggaagat tagttggaat ttttgagaac 540
caggagagga agcacaggac gtatgtctat gtgctcattg tcactgaagt gctggaagac 600
tgggaagatt cagttaacat tggaaggaag agggaatggt ttaaaataga agacgccata 660
aaagtgctgc agtatcacaa acccgtgcag gcatcatatt ttgaaacatt gaggcaaggc 720
tactcagcca acaatggcac cccagtcgtg gccaccacat actcggtttc tgctcagagc 780
tcgatgtcag gcatcagatg actgaagact tcctgtaaga gaaatggaaa ttggaaacta 840
gactgaagtg caaatcttcc ctctcaccct ggctctttcc acttctcaca ggcctcctct 900
ttcaaataag gcatggtggg cagcaaagaa agggtgtatt gataatgttg ctgtttggtg 960
ttaagtgatg gggctttttc ttctgttttt attgagggtg ggggttgggt gtgtaatttg 1020
taagtacttt tgtgcatgat ctgtccctcc ctcttcccac ccctgcagtc ctctgaagag 1080
aggccaacag ccttcccctg ccttggattc tgaagtgttc ctgtttgtct tatcctggcc 1140
ctggccagac gttttctttg atttttaatt tttttttttt attaaaagat accagtatga 1200
gaaaaaaaaa aaaaaaaaac tcgag 1225

<210> 103
<211> 741
<212> DNA
<213> Homc sapien

<400> 103
agaaacctca atcggattca gcaaaggaat ggtgttatta tcactacata ccaaatgtta 60
atcaataact ggcagcaact ttcaagcttt aggggccaag agtttgtgtg ggactatgtc 120
atcctcgatg aagcacataa aataaaaacc tcatctacta agtcagcaat atgtgctcgt 180
gctattcctg caagtaatcg cctcctcctc acaggaaccc caatccagaa taatttacaa 240
gaactatggt ccctatttga ttttgcttgt caagggtccc tgctgggaac attaaaaact 300
tttaagatgg agtatgaaaa tcctattact agagcaagag agaaggatgc taccccagga 360
gaaaaagcct tgggatttaa aatatctgaa aacttaatgg caatcataaa accctatttt 420
ctcaggagga ctaaagaaga cgtacagaag aaaaagtcaa gcaacccaga ggccagactt 480
aatgaaaaga atccagatgt tgatgccatt tgtgaaatgc cttccctttc caggagaaat 540
gatttaatta tttggatacg acttgtgcct ttacaagaag aaatatacag gaaatttgtg 600
tctttagatc atatcaagga gttgctaatg gagacgcgct cacctttggc tgagctaggt 660
gtcttaaaga agctgtgtga tcatcctagg ctgctgtctg cacgggcttg ttgtttgcta 720
aatcttggga cattctctgc t 741

<210> 104
<211> 321
<212> DNA
<213> Homo sapien

<400> 104
ttgctctgcg tcatcaaaga caccaaactg ctgtgctata aaagttccaa ggaccagcag 60
cctcagatgg aactgccact ccaaggctgt aacattacgt acatcccgaa agacagcaaa 120
aagaagaagc acgagctgaa gattactcag cagggcacgg acccgcttgt tctcgccgtc 180
cagagcaagg aacaggccga gcagtggctg aaggtgatca aagaagccta cagtggttgt 240
agtggccccg tggattcaga gtgtcctcct ccaccaagct ccccggtgca caaggcagaa 300
ctggagaaga aactgtcttc a 321

<210> 105
<211> 389

<212> DNA
<213> Homo sapien

<400> 105
cagcactggc cacactataa aattcaggtt cagaaaaaca gggtaagtca cagacagcaa 60
cgcttccagc atttattttc tttgcaccca tgggcaattt gagaaaattt acctttagaa 120
cgaactctgt taaaggtaca gacagtacaa tactttttat tcagaaggtt tctgcataaa 180
ggtgatagtc ttttgactta atatattatt gtctcctgcc ttgtgtttct ggaatgaatg 240
aaggtcatta tttagaagat aatctgggtt gtatttgtgt cgtcagattg aattttcatt 300
gcacatgcta cttaatgtct ttaccaaata ataacaaagg gaaagaaaac caaatataga 360
tgtataataa ggaaaagctg gcctataga 389

<210> 106
<211> 446
<212> DNA
<213> Homo sapien

<400> 106
gccacatttg ccctggtcat agtttaaaca ccaggtcctg tgtcacatct ttttggtgcc 60
acaagtatca ctccattgtt cagagagtaa tgtattagtt ctgcccaatt cattcttcac 120
ttttatttct tccatttcat tagcatttat atcagctcaa gaagttaagg ttagaaaatt 180
ttccacttca aattttcagt acagaaatgt gctgtgatgt ttgacaagac tatttcatag 240
taagtgagtt aatgtttatt ggcctctgct ctcctctgtg tcagacctag gaagcctgag 300
gattacttag ttgttctgtc tctgggtcca caggcagaat ttggcccatc caaagactgg 360
ccaagtgcca aaaaaaggcc tgattaggcc ctgaaattca gtgaaattct gcctgaagaa 420
acctcttatt gaatttgaaa accata 446

<210> 107
<211> 467
<212> DNA
<213> Homo sapien

<400> 107
ccgccgctgc cgtcgccttc ctgggattgg agtctcgagc tttcttcgtt cgttcgccgg 60
cgggttcgcg cccttctcgc gcctcggggc tgcgaggctg gggaaggggt tggagggggc 120
tgttgatcgc cgcgtttaag ttgcgctcgg ggcggccatg tcggccggcg aggtcgagcg 180
cctagtgtcg gagctgagcg gcgggaccgg aggggatgag gaggaagagt ggctctatgg 240
cgatgaagat gaagttgaaa ggccagaaga agaaaatgcc agtgctaatc ctccatctgg 300
aattgaagat gaaactgctg aaaatggtgt accaaaaccg aaagtgactg agaccgaaga 360
tgatagtgat agtgacagcg atgatgatga agatgatgtg catgtcacta taggagacat 420
taaaacggga gcaccacagt atgggagtta tggtacagca cctgtaa 467

<210> 108
<211> 491
<212> DNA
<213> Homo sapien

<400> 108
gaaagataca acttccccaa cccaaacccg tttgtggagg acgacatgga taagaatgaa 60
atcgcctctg ttgcgtaccg ttaccgcagg tggaagcttg gagatgatat tgaccttatt 120
gtccgttgtg agcacgatgg cgtcatgact ggagccaacg gggaagtgtc cttcatcaac 180
atcaagacac tcaatgagtg ggattccagg cactgtaatg gcgttgactg gcgtcagaag 240
ctggactctc agcgaggggc tgtcattgcc acggagctga agaacaacag ctacaagttg 300
gcccggtgga cctgctgtgc tttgctggct ggatctgagt acctcaagct tggttatgtg 360
tctcggtacc acgtgaaaga ctcctcacgc cacgtcatcc taggcaccca gcagttcaag 420

cctaatgagt ttgccagcca gatcaacctg agcgtggaga atgcctgagg cattttacgc 480
tgcgtcattg a 491

<210> 109
<211> 489
<212> DNA
<213> Homo sapien

<400> 109
ctcagatagt actgaaccct ttatcaacta tgtttttca gtctgacaac caaggcggct 60
actaagtgac taaggggcag gtagtataca gtgtggataa gcaggacaaa ggggtgattc 120
acatcccagg caggacagag caggagatca tgagatttca tcactcagga tggcttgtga 180
tttattttat tttattcttt ttttttttg agatggagtc tcactcttgc ccaggctgga 240
gtgcagtggt gcgatcttgg ctcactgcaa cctctgcctc ctgggttcaa gcagttctcc 300
tgcctcagcc tcccaagtag ctgggattac aggcgtccgc caccatgccc agccaatttt 360
tgtactttta gtagagatgg ggtttcacca tgttggccag gctggtctcg aactcctgac 420
ctcaggtgat ccactcgcct cggcctccca aagtgctggg attataggca tgcgccacca 480
tgcccgggc 489

<210> 110
<211> 391
<212> DNA
<213> Homo sapien

<400> 110
gcggagtccg ctggctgacc cgagcgctgg tctccgccgg gaaccctggg gcatggagag 60
gtctgagtac ctcggccgcg gcgcacgctg catcgcggag ccaggctgcc gctgtcccag 120
tggagttcca ggagcaccac ctgagtgagg tgcagaatat ggcatctgag gagaagctgg 180
agcaggtgct gagttccatg aaggagaaca aagtggccat cattggaaag attcataccc 240
cgatggagta taagggggag ctagcctcct atgatatgcg gctgaggcgt aagttggact 300
tatttgccaa cgtaatccat gtgaagtcac ttcctgggta tatgactcgg cacaacaatc 360
tagacctggt gatcattcga gagcagacag a 391

<210> 111
<211> 172
<212> PRT
<213> Homo sapien

<400> 111
Met Met Lys Leu Lys Ser Asn Gln Thr Arg Thr Tyr Asp Gly Asp Gly
1 5 10 15
Tyr Lys Lys Arg Ala Ala Cys Leu Cys Phe Arg Ser Glu Ser Glu Glu
20 25 30
Glu Val Leu Leu Val Ser Ser Ser Arg His Pro Asp Arg Trp Ile Val
35 40 45
Pro Gly Gly Gly Met Glu Pro Glu Glu Glu Pro Ser Val Ala Ala Val
50 55 60
Arg Glu Val Cys Glu Glu Ala Gly Val Lys Gly Thr Leu Gly Arg Leu
65 70 75 80
Val Gly Ile Phe Glu Asn Gln Glu Arg Lys His Arg Thr Tyr Val Tyr
85 90 95
Val Leu Ile Val Thr Glu Val Leu Glu Asp Trp Glu Asp Ser Val Asn
100 105 110
Ile Gly Arg Lys Arg Glu Trp Phe Lys Ile Glu Asp Ala Ile Lys Val
115 120 125

Leu Gln Tyr His Lys Pro Val Gln Ala Ser Tyr Phe Glu Thr Leu Arg
130 135 140
Gln Gly Tyr Ser Ala Asn Asn Gly Thr Pro Val Val Ala Thr Thr Tyr
145 150 155 160
Ser Val Ser Ala Gln Ser Ser Met Ser Gly Ile Arg
165 170

<210> 112
<211> 247
<212> PRT
<213> Homo sapien

<400> 112
Arg Asn Leu Asn Arg Ile Gln Gln Arg Asn Gly Val Ile Ile Thr Thr
1 5 10 15
Tyr Gln Met Leu Ile Asn Asn Trp Gln Gln Leu Ser Ser Phe Arg Gly
20 25 30
Gln Glu Phe Val Trp Asp Tyr Val Ile Leu Asp Glu Ala His Lys Ile
35 40 45
Lys Thr Ser Ser Thr Lys Ser Ala Ile Cys Ala Arg Ala Ile Pro Ala
50 55 60
Ser Asn Arg Leu Leu Leu Thr Gly Thr Pro Ile Gln Asn Asn Leu Gln
65 70 75 80
Glu Leu Trp Ser Leu Phe Asp Phe Ala Cys Gln Gly Ser Leu Leu Gly
85 90 95
Thr Leu Lys Thr Phe Lys Met Glu Tyr Glu Asn Pro Ile Thr Arg Ala
100 105 110
Arg Glu Lys Asp Ala Thr Pro Gly Glu Lys Ala Leu Gly Phe Lys Ile
115 120 125
Ser Glu Asn Leu Met Ala Ile Ile Lys Pro Tyr Phe Leu Arg Arg Thr
130 135 140
Lys Glu Asp Val Gln Lys Lys Lys Ser Ser Asn Pro Glu Ala Arg Leu
145 150 155 160
Asn Glu Lys Asn Pro Asp Val Asp Ala Ile Cys Glu Met Pro Ser Leu
165 170 175
Ser Arg Arg Asn Asp Leu Ile Ile Trp Ile Arg Leu Val Pro Leu Gln
180 185 190
Glu Glu Ile Tyr Arg Lys Phe Val Ser Leu Asp His Ile Lys Glu Leu
195 200 205
Leu Met Glu Thr Arg Ser Pro Leu Ala Glu Leu Gly Val Leu Lys Lys
210 215 220
Leu Cys Asp His Pro Arg Leu Leu Ser Ala Arg Ala Cys Cys Leu Leu
225 230 235 240
Asn Leu Gly Thr Phe Ser Ala
245

<210> 113
<211> 107
<212> PRT
<213> Homo sapien

<400> 113
Leu Leu Cys Val Ile Lys Asp Thr Lys Leu Leu Cys Tyr Lys Ser Ser
1 5 10 15
Lys Asp Gln Gln Pro Gln Met Glu Leu Pro Leu Gln Gly Cys Asn Ile

```
            20                  25                  30
Thr Tyr Ile Pro Lys Asp Ser Lys Lys Lys Lys His Glu Leu Lys Ile
        35                  40                  45
Thr Gln Gln Gly Thr Asp Pro Leu Val Leu Ala Val Gln Ser Lys Glu
    50                  55                  60
Gln Ala Glu Gln Trp Leu Lys Val Ile Lys Glu Ala Tyr Ser Gly Cys
65                  70                  75                  80
Ser Gly Pro Val Asp Ser Glu Cys Pro Pro Pro Pro Ser Ser Pro Val
                85                  90                  95
His Lys Ala Glu Leu Glu Lys Lys Leu Ser Ser
            100                 105

      <210> 114
      <211> 155
      <212> PRT
      <213> Homo sapien

      <400> 114
Glu Arg Tyr Asn Phe Pro Asn Pro Asn Pro Phe Val Glu Asp Asp Met
 1               5                  10                  15
Asp Lys Asn Glu Ile Ala Ser Val Ala Tyr Arg Tyr Arg Arg Trp Lys
            20                  25                  30
Leu Gly Asp Asp Ile Asp Leu Ile Val Arg Cys Glu His Asp Gly Val
        35                  40                  45
Met Thr Gly Ala Asn Gly Glu Val Ser Phe Ile Asn Ile Lys Thr Leu
    50                  55                  60
Asn Glu Trp Asp Ser Arg His Cys Asn Gly Val Asp Trp Arg Gln Lys
65                  70                  75                  80
Leu Asp Ser Gln Arg Gly Ala Val Ile Ala Thr Glu Leu Lys Asn Asn
                85                  90                  95
Ser Tyr Lys Leu Ala Arg Trp Thr Cys Cys Ala Leu Leu Ala Gly Ser
            100                 105                 110
Glu Tyr Leu Lys Leu Gly Tyr Val Ser Arg Tyr His Val Lys Asp Ser
        115                 120                 125
Ser Arg His Val Ile Leu Gly Thr Gln Gln Phe Lys Pro Asn Glu Phe
    130                 135                 140
Ala Ser Gln Ile Asn Leu Ser Val Glu Asn Ala
145                 150                 155

      <210> 115
      <211> 129
      <212> PRT
      <213> Homo sapien

      <400> 115
Gly Val Arg Trp Leu Thr Arg Ala Leu Val Ser Ala Gly Asn Pro Gly
 1               5                  10                  15
Ala Trp Arg Gly Leu Ser Thr Ser Ala Ala Ala His Ala Ala Ser Arg
            20                  25                  30
Ser Gln Ala Ala Ala Val Pro Val Glu Phe Gln Glu His His Leu Ser
        35                  40                  45
Glu Val Gln Asn Met Ala Ser Glu Glu Lys Leu Glu Gln Val Leu Ser
    50                  55                  60
Ser Met Lys Glu Asn Lys Val Ala Ile Ile Gly Lys Ile His Thr Pro
65                  70                  75                  80
```

```
Met Glu Tyr Lys Gly Glu Leu Ala Ser Tyr Asp Met Arg Leu Arg Arg
                85                  90                  95
Lys Leu Asp Leu Phe Ala Asn Val Ile His Val Lys Ser Leu Pro Gly
            100                 105                 110
Tyr Met Thr Arg His Asn Asn Leu Asp Leu Val Ile Ile Arg Glu Gln
        115                 120                 125
Thr
```

<210> 116
<211> 550
<212> DNA
<213> Homo sapien

<400> 116

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gaattcggca ccagcctcag agccccccag cccggctacc acccccctgcg gaaaggtacc     60
catctgcatt cctgcccgtc gggacctggt ggacagtcca gcctccttgg cctctagcct    120
tggctcaccg ctgcctagag ccaaggagct catcctgaat gaccttcccg ccagcactcc    180
tgcctccaaa tcctgtgact cctccccgcc ccaggacgct tccaccccca ggcccagctc    240
ggccagtcac ctctgccagc ttgctgccaa gccagcacct tccacggaca gcgtcgccct    300
gaggagcccc ctgactctgt ccagtccctt caccacgtcc ttcagcctgg gctcccacag    360
cactctcaac ggagacctct ccgtgcccag ctcctacgtc agcctccacc tgtcccccca    420
ggtcagcagc tctgtggtgt acggacgctc cccccgtgatg gcatttgagt ctcatcccca    480
tctccgaggg tcatccgtct cttcctccct acccagcatc cctgggggaa agccggccta    540
ctccttccac                                                             550
```

<210> 117
<211> 154
<212> DNA
<213> Homo sapien

<400> 117

```
ttctgaggga aagccgagtg gagtgggcga cccggcggcg gtgacaatga gttttcttgg     60
aggctttttt ggtcccattt gtgagattga tgttgccctt aatgatgggg aaaccaggaa    120
aatggcagaa atgaaaactg aggatggcaa agta                                 154
```

<210> 118
<211> 449
<212> DNA
<213> Homo sapien

<400> 118

```
gaattcggca ccagggcccg cagcccgagt gtcgccgcca tggcttcgcc gcagctctgc     60
cgcgcgctgg tgtcggcgca atgggtggcg gaggcgctgc gggccccgcg cgctgggcag    120
cctctgcagc tgctggacgc ctcctggtac ctgccgaagc tggggcgcga cgcgcgacgc    180
gagttcgagg agcgccacat cccgggcgcc gctttcttcg acatcgacca gtgcagcgac    240
cgcacctcgc cctacgacca catgctgccc ggggccgagc atttcgcgga gtacgcaggc    300
cgcctgggcg tgggcgcggc cacccacgtc gtgatctacg acgccagcga ccagggcctc    360
tactccgccc cgcgcgtctg gtggatgttc cgcgccttcg gccaccacgc cgtgtcactg    420
cttgatggcg gcctccgcca ctggctgcg                                       449
```

<210> 119
<211> 642
<212> DNA
<213> Homo sapien

<400> 119
gaattcggca cgagcagtaa cccgaccgcc gctggtcttc gctggacacc atgaatcaca 60
ctgtccaaac cttcttctct cctgtcaaca gtggccagcc ccccaactat gagatgctca 120
aggaggagca cgaggtggct gtgctggggg cgccccacaa ccctgctccc ccgacgtcca 180
ccgtgatcca catccgcagc gagacctccg tgcccgacca tgtcgtctgg tccctgttca 240
acaccctctt catgaacccc tgctgcctgg gcttcatagc attcgcctac tccgtgaagt 300
ctagggacag gaagatggtt ggcgacgtga ccggggccca ggcctatgcc tccaccgcca 360
agtgcctgaa catctgggcc ctgattctgg gcatcctcat gaccattctg ctcatcgtca 420
tcccagtgct gatcttccag gcctatggat agatcaggag gcatcactga ggccaggagc 480
tctgcccatg acctgtatcc cacgtactcc aacttccatt cctcgccctg cccccggagc 540
cgagtcctgt atcagccctt tatcctcaca cgcttttcta caatggcatt caataaagtg 600
cacgtgtttc tggtgaaaaa aaaaaaaaaa aaaaaactcg ag 642

<210> 120
<211> 603
<212> DNA
<213> Homo sapien

<400> 120
gaattcggca cgagccacaa cagccactac gactgcatcc actggatcca cggccacccc 60
gtcctccacc ccgggaacag ctccccctcc caaagtgctg accagcccgg ccaccacacc 120
catgtccacc atgtccacaa tccacacctc ctctactcca gagaccaccc acacctccac 180
agtgctgacc accacagcca ccatgacaag ggccaccaat tccacggcca caccctcctc 240
cactctgggg acgacccgga tcctcactga gctgaccaca acagccacta caactgcagc 300
cactggatcc acggccaccc tgtcctccac cccagggacc acctggatcc tcacagagcc 360
gagcactata gccaccgtga tggtgcccac cggttccacg gccaccgcct cctccactct 420
gggaacagct cacaccccca aagtggtgac caccatggcc actatgccca cagccactgc 480
ctccacggtt cccagctcgt ccaccgtggg gaccacccgc acccctgcag tgctccccag 540
cagcctgcca accttcagcg tgtccactgt gtcctcctca gtcctcacca ccctgagacc 600
cac 603

<210> 121
<211> 178
<212> PRT
<213> Homo sapien

<400> 121
Ser Glu Pro Pro Ser Pro Ala Thr Thr Pro Cys Gly Lys Val Pro Ile
1 5 10 15
Cys Ile Pro Ala Arg Arg Asp Leu Val Asp Ser Pro Ala Ser Leu Ala
20 25 30
Ser Ser Leu Gly Ser Pro Leu Pro Arg Ala Lys Glu Leu Ile Leu Asn
35 40 45
Asp Leu Pro Ala Ser Thr Pro Ala Ser Lys Ser Cys Asp Ser Ser Pro
50 55 60
Pro Gln Asp Ala Ser Thr Pro Arg Pro Ser Ser Ala Ser His Leu Cys
65 70 75 80
Gln Leu Ala Ala Lys Pro Ala Pro Ser Thr Asp Ser Val Ala Leu Arg
85 90 95
Ser Pro Leu Thr Leu Ser Ser Pro Phe Thr Thr Ser Phe Ser Leu Gly
100 105 110
Ser His Ser Thr Leu Asn Gly Asp Leu Ser Val Pro Ser Ser Tyr Val
115 120 125
Ser Leu His Leu Ser Pro Gln Val Ser Ser Ser Val Val Tyr Gly Arg

130 135 140
Ser Pro Val Met Ala Phe Glu Ser His Pro His Leu Arg Gly Ser Ser
145 150 155 160
Val Ser Ser Ser Leu Pro Ser Ile Pro Gly Gly Lys Pro Ala Tyr Ser
165 170 175
Phe His

<210> 122
<211> 36
<212> PRT
<213> Homo sapien

<400> 122
Met Ser Phe Leu Gly Gly Phe Phe Gly Pro Ile Cys Glu Ile Asp Val
1 5 10 15
Ala Leu Asn Asp Gly Glu Thr Arg Lys Met Ala Glu Met Lys Thr Glu
20 25 30
Asp Gly Lys Val
35

<210> 123
<211> 136
<212> PRT
<213> Homo sapien

<400> 123
Met Ala Ser Pro Gln Leu Cys Arg Ala Leu Val Ser Ala Gln Trp Val
1 5 10 15
Ala Glu Ala Leu Arg Ala Pro Arg Ala Gly Gln Pro Leu Gln Leu Leu
20 25 30
Asp Ala Ser Trp Tyr Leu Pro Lys Leu Gly Arg Asp Ala Arg Arg Glu
35 40 45
Phe Glu Glu Arg His Ile Pro Gly Ala Ala Phe Phe Asp Ile Asp Gln
50 55 60
Cys Ser Asp Arg Thr Ser Pro Tyr Asp His Met Leu Pro Gly Ala Glu
65 70 75 80
His Phe Ala Glu Tyr Ala Gly Arg Leu Gly Val Gly Ala Ala Thr His
85 90 95
Val Val Ile Tyr Asp Ala Ser Asp Gln Gly Leu Tyr Ser Ala Pro Arg
100 105 110
Val Trp Trp Met Phe Arg Ala Phe Gly His His Ala Val Ser Leu Leu
115 120 125
Asp Gly Gly Leu Arg His Trp Leu
130 135

<210> 124
<211> 133
<212> PRT
<213> Homo sapien

<400> 124
Met Asn His Thr Val Gln Thr Phe Phe Ser Pro Val Asn Ser Gly Gln
1 5 10 15
Pro Pro Asn Tyr Glu Met Leu Lys Glu Glu His Glu Val Ala Val Leu

```
            20                      25                      30
Gly Ala Pro His Asn Pro Ala Pro Pro Thr Ser Thr Val Ile His Ile
        35                      40                      45
Arg Ser Glu Thr Ser Val Pro Asp His Val Val Trp Ser Leu Phe Asn
    50                      55                      60
Thr Leu Phe Met Asn Pro Cys Cys Leu Gly Phe Ile Ala Phe Ala Tyr
65                      70                      75                  80
Ser Val Lys Ser Arg Asp Arg Lys Met Val Gly Asp Val Thr Gly Ala
                85                      90                      95
Gln Ala Tyr Ala Ser Thr Ala Lys Cys Leu Asn Ile Trp Ala Leu Ile
            100                     105                     110
Leu Gly Ile Leu Met Thr Ile Leu Leu Ile Val Ile Pro Val Leu Ile
        115                     120                     125
Phe Gln Ala Tyr Gly
    130

      <210> 125
      <211> 195
      <212> PRT
      <213> Homo sapien

      <400> 125
Thr Thr Ala Thr Thr Thr Ala Ser Thr Gly Ser Thr Ala Thr Pro Ser
 1               5                  10                  15
Ser Thr Pro Gly Thr Ala Pro Pro Pro Lys Val Leu Thr Ser Pro Ala
            20                  25                  30
Thr Thr Pro Met Ser Thr Met Ser Thr Ile His Thr Ser Ser Thr Pro
        35                  40                  45
Glu Thr Thr His Thr Ser Thr Val Leu Thr Thr Thr Ala Thr Met Thr
    50                  55                  60
Arg Ala Thr Asn Ser Thr Ala Thr Pro Ser Ser Thr Leu Gly Thr Thr
65                  70                  75                  80
Arg Ile Leu Thr Glu Leu Thr Thr Thr Ala Thr Thr Thr Ala Ala Thr
                85                  90                  95
Gly Ser Thr Ala Thr Leu Ser Ser Thr Pro Gly Thr Thr Trp Ile Leu
            100                 105                 110
Thr Glu Pro Ser Thr Ile Ala Thr Val Met Val Pro Thr Gly Ser Thr
        115                 120                 125
Ala Thr Ala Ser Ser Thr Leu Gly Thr Ala His Thr Pro Lys Val Val
    130                 135                 140
Thr Thr Met Ala Thr Met Pro Thr Ala Thr Ala Ser Thr Val Pro Ser
145                 150                 155                 160
Ser Ser Thr Val Gly Thr Thr Arg Thr Pro Ala Val Leu Pro Ser Ser
                165                 170                 175
Leu Pro Thr Phe Ser Val Ser Thr Val Ser Ser Ser Val Leu Thr Thr
            180                 185                 190
Leu Arg Pro
        195

      <210> 126
      <211> 509
      <212> DNA
      <213> Homo sapien

      <400> 126
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gaattcggca cgagccaagt accccctgag gaatctgcag cctgcatctg agtacaccgt 60
atccctcgtg gccataaagg gcaaccaaga gagccccaaa gccactggag tctttaccac 120
actgcagcct gggagctcta ttccacctta caacaccgag gtgactgaga ccaccattgt 180
gatcacatgg acgcctgctc caagaattgg ttttaagctg ggtgtacgac caagccaggg 240
aggagaggca ccacgagaag tgacttcaga ctcaggaagc atcgttgtgt ccggcttgac 300
tccaggagta gaatacgtct acaccatcca agtcctgaga gatggacagg aaagagatgc 360
gccaattgta aacaaagtgg tgacaccatt gtctccacca acaaacttgc atctggaggc 420
aaaccctgac actggagtgc tcacagtctc ctggagagga gcaccacccc agacattact 480
gggtatagaa ttaccacaac ccctacaaa 509

<210> 127
<211> 500
<212> DNA
<213> Homo sapien

<400> 127
gaattcggca cgagccactg atgtccgggg agtcagccag gagcttgggg aagggaagcg 60
cgcccccggg gccggtcccg gagggctcga tccgcatcta cagcatgagg ttctgcccgt 120
ttgctgagag gacgcgtcta gtcctgaagg ccaagggaat caggcatgaa gtcatcaata 180
tcaacctgaa aaataagcct gagtggttct ttaagaaaaa tccctttggt ctggtgccag 240
ttctggaaaa cagtcagggt cagctgatct acgagtctgc catcacctgt gagtacctgg 300
atgaagcata cccagggaag aagctgttgc cggatgaccc ctatgagaaa gcttgccaga 360
agatgatctt agagttgttt tctaaggtgc catccttggt aggaagcttt attagaagcc 420
aaaataaaga agactatgct ggcctaaaag aagaatttcg taaagaattt accaagctag 480
aggaggttct gactaataag 500

<210> 128
<211> 500
<212> DNA
<213> Homo sapien

<400> 128
agctttcctc tgctgccgct cggtcacgct tgtgcccgaa ggaggaaaca gtgacagacc 60
tggagactgc agttctctat ccttcacaca gctctttcac catgcctgga tcacttcctt 120
tgaatgcaga agcttgctgg ccaaaagatg tgggaattgt tgcccttgag atctattttc 180
cttctcaata tgttgatcaa gcagagttgg aaaaatatga tggtgtagat gctggaaagt 240
ataccattgg cttgggccag gccaagatgg gcttctgcac agatagagaa gatattaact 300
ctctttgcat gactgtggtt cagaatctta tggagagaaa taacctttcc tatgattgca 360
ttgggcggct ggaagttgga acagagacaa tcatcgacaa atcaaagtct gtgaagacta 420
atttgatgca gctgtttgaa gagtctggga atacagatat agaaggaatc gacacaacta 480
atgcatgcta tggaggcaca 500

<210> 129
<211> 497
<212> DNA
<213> Homo sapien

<400> 129
gaattcggca cgagcagagg tctccagagc cttctctctc ctgtgcaaaa tggcaactct 60
taaggaaaaa ctcattgcac cagttgcgga agaagaggca acagttccaa acaataagat 120
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ttctgtgacc gccaattcta agattgtagt ggtaactgca ggagtccgtc agcaagaagg 360
ggagagtcgg ctcaatctgg tgcagagaaa tgttaatgtc ttcaaattca ttattcctca 420

gatcgtcaag tacagtcctg attgcatcat aattgtggtt tccaacccag tggacattct 480
tacgtatgtt acctgga 497

<210> 130
<211> 383
<212> DNA
<213> Homo sapien

<400> 130
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cccaccaacc tttatggaga cttcttcacg ggcgacgcct acgtcatcct gaagacagtg 360
cagcttaaga acggaaaatc ttg 383

<210> 131
<211> 509
<212> DNA
<213> Homo sapien

<400> 131
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caccagggct gcttttaact ctggtaaagt ggatattgtt gccatcaatg accccttcat 180
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ggagcgagat ccctccaaaa tcaagtgggg cgatgctggc gctgagtacg tcgtggagtc 360
cactggccgt cttcaccacc atggagaagg ctggggctca tttgcagggg ggagccaaaa 420
gggtcatcat ctctgccccc tctgctgacg cccccatgtt cgtcatgggt gtgaaccatg 480
agaagtatga caacagcctc aagatcatc 509

<210> 132
<211> 357
<212> DNA
<213> Homo sapien

<400> 132
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gacgatttgt cttctccctg gacacctctg tcagcacggc atatctgcag atcagca 357

<210> 133
<211> 468
<212> DNA
<213> Homo sapien

<400> 133
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gccgcgggga gccccgcttc atctcagtgg gctacgtgga cgacacgcag ttcgtgaggt 180

tcgacagcga cgccgcgagt ccgagagagg agccgcgggc gccgtggata gagcaggagg 240
ggccggagta ttgggaccgg aacacacaga tcttcaagac caacacacag actgaccgag 300
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acgcctacga cggcaaggat tacatcgccc tgaacgagga cctgcgct 468

<210> 134
<211> 214
<212> DNA
<213> Homo sapien

<400> 134
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agtgcctggt tctcttgctc caccaggaac aagccaccat gtctcgccag tcaagtgtgt 120
ccttccggag cgggggcagt cgtagcttca gcaccgcctc tgccatcacc ccgtctgtct 180
cccgcaccag cttcacctcc gtgtcccggt ccgg 214

<210> 135
<211> 355
<212> DNA
<213> Homo sapien

<400> 135
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cgcgccgtgg atttcgctga gcggcacggc tacatcaagg gcatcgtcaa ggacatcatc 180
cacgacccgg gccgcggcgc gcccctcgcc aaggtggtct tccgggatcc gtatcggttt 240
aagaagcgga cggagctgtt cattgccgcc gagggcattc acacgggcca gtttgtgtat 300
tgcggcaaga aggcccagct caacattggc aatgtgctcc ctgtgggcac catgc 355

<210> 136
<211> 242
<212> DNA
<213> Homo sapien

<400> 136
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gcccggattg cagacggagt ctccttcact cagtgctcaa tggtgcccag gctggagtgc 120
agtggtgtga tctcggctcg ctacaacatc cacctcccag cagcctgcct tggcctccca 180
aagtgccgag attgcagctc tctgcccggc cgccacccct gtctgggaag tgaggatgct 240
gt 242

<210> 137
<211> 424
<212> DNA
<213> Homo sapien

<400> 137
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gccaggagca agccgagagc cagccggccg gcgcactccg actccgagca gtctctgtcc 120
ttcgacccga gccccgcgcc ctttccggga cccctgcccc gcgggcagcg ctgccaacct 180
gccggccatg gagaccccgt cccagcggcg cgccacccgc agcggggcgc aggccagctc 240
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caatgatcgc ttggcggtct acatcgaccg tgtgcgctcg ctggaaacgg agaacgcagg 360
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ggcc 424

<210> 138
<211> 448
<212> DNA
<213> Homo sapien

<400> 138
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tgaatggcat gattcagtga gtggcaagaa atttcctgtc tttaatcctg caactgagga 180
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agtcaatgaa tggtggaaaa ctctattcca atgcatatct gaatgattta gcaggctgca 420
tcaaaacatt gcgctactgt gcaggttg 448

<210> 139
<211> 510
<212> DNA
<213> Homo sapien

<400> 139
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gtgccagcgc cggacccgtt tcatctccct ggcgaggcgt gcaagaaggt cttcctggac 180
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ggacttcttc atcgacctgc ggctacccta 510

<210> 140
<211> 360
<212> DNA
<213> Homo sapien

<400> 140
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ctcacacacc ggcctcagcc cgcaccggca gtagaagatg gtgaaagaaa caacttacta 120
cgatgttttg ggggtcaaac ccaatgctac tcaggaagaa ttgaaaaagg cttataggaa 180
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ttctcaagct tacgaagttc tctctgatgc aaagaaaagg gaattatatg acaaaggagg 300
agaacaggca attaaagagg gtggagcagg tggcggtttt ggctccccca tggacatctt 360

<210> 141
<211> 483
<212> DNA
<213> Homo sapien

<400> 141
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acaacatcca gaaagagtct accctgcacc tggtgctccg tctcagaggt gggatgcaga 360
tcttcgtgaa gaccctgact ggtaagacca tcaccctcga ggtggagccc agtgacacca 420
tcgagaatgt caaggcaaag atccaagata aggaaggcat tcctcctgat cagcagaggt 480
tga 483

<210> 142
<211> 500
<212> DNA
<213> Homo sapien

<400> 142
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ccccgacgag atcatcgaca tggtcaagga ggaggtggtg gccaagggcc gcggccgcgg 360
aggcctgcag cagcagaagc agcagaaagg ccgcggcatg ggcggcgctg gccgaggtgt 420
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gcctggcaga caggcgggca 500

<210> 143
<211> 400
<212> DNA
<213> Homo sapien

<400> 143
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ctcagaagaa agcgatcggc cccgaggcag gaaggccggc tccggtgcag ggcgcgccgc 120
ctgcgggctg cttcgggcca gggtcgaccc gagggccagc gcaagcagcg gcaacaggag 180
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cagcatcaca gattataacc ctccgtaaat catctgcatc ccagctccca tcaaaagcca 300
gcctgaagga cccatggaca cgtgactcca gtgttctcaa caacatctta gatcaagttg 360
gtttgcacaa catttgcatc tacttgggac aaagcaagaa 400

<210> 144
<211> 243
<212> DNA
<213> Homo sapien

<400> 144
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gcccggattg cagacggagt ctccttcact cagtgctcaa tggtgcccag gctggagtgc 120
agtggtgtga tctcggctcg ctacaacatc cacctcccag cagcctgcct tggcctccca 180
aagtgccgag attgcagcct ctgcccggcc gtcaccccgt ctgggaagtg aggagcgttt 240
ctg 243

<210> 145
<211> 450
<212> DNA
<213> Homo sapien

<400> 145

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caacaccatc tttgtgcaag gcctgggtga gaatgttaca attgagtctg tggctgatta 300
cttcaagcag attggtatta ttaagacaaa caagaaaacg ggacagccca tgattaattt 360
gtacacagac agggaaactg gcaagctgaa gggagaggca acggtctctt ttgatgaccc 420
accttcagct aaagcagcct attgactggt 450

<210> 146
<211> 451
<212> DNA
<213> Homo sapien

<400> 146
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gcgggagatc gacgcgaaat accaagagat cctgaaggag ctagacgagt gctacgagcg 120
cttcagtcgc gagacagacg gggcgcagaa gcggcggatg ctgcactgtg tgcagcgcgc 180
gctgatccgc accaggagct gggcgacgag aagatccaga tcgtgagcca gatggtggag 240
ctggtggaga accgcacgcg gcaggtggac agccacgtgg agctgttcga ggcgcagcag 300
gagctgggcg acacagcggg caacagcggc aaggctggcg cggacaggcc caaaggcgag 360
gcggcagcgc aggctgacaa gcccaacagc aagcgctcac ggcggcagcg caacaacgag 420
aaccgtgaga acgcgtccag caaccacgac c 451

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

<400> 147
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ctcagaagaa agcgatcggc cccgaggcag gaaggccggc tccggtgcag ggcgcgccgc 120
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cagcatcaca gattataacc ctccgtaaat catctgcatc ccagctccca tcaaaagcca 300
gcctgaagga cccatggaca cgtgactcca gtgttctcaa caacatctta gatcaagttg 360
gtttgcacaa catttgcatc tacttgggac aaagcaagaa 400

<210> 148
<211> 503
<212> DNA
<213> Homo sapien

<400> 148
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cgagtgaagc tgcgcttttt ctaaagaagt ctggcctctc ggacattatc cttgggaaga 180
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ctgcagaggc ccactgggct gtgagggtgg aagaaaaggc caaatttgat gggatttttg 420
aaagcctctt gcccatcaat ggtttgctct ctggagacaa agtcaagcca gtcctcatga 480
actcaaagct gcctcttgat gtc 503

<210> 149

<211> 1061
<212> DNA
<213> Homo sapien

<400> 149
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aggtcctgtt tgcactgtgc tccctgctgc gccacttccc ctatgcccag cggcagttcc 180
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<210> 150
<211> 781
<212> DNA
<213> Homo sapien

<400> 150
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c 781

<210> 151
<211> 3275
<212> DNA
<213> Homo sapien

<400> 151
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<213> Homo sapien

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<212> DNA
<213> Homo sapien

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<213> Homo sapien

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gctcctcgga tgcccttctc cattgggcag gtcacaatgc ccatggttat gcccagtgca 1320
gatccccgct ccttgtcttt cccaatcctg aaccctgccc tttcccagcc cagccagcct 1380
tcctcacccc ttcctggctc ccatggcaga aatagccctg gcttgggttc ccttgtcagc 1440
cctggtgccg aattcggcac gaggtaccac tggtctgtgt gctagaggag ggtgttgcca 1500
tagaaccagt ggccacagtt gtggtggtgg tggtcagcac tgtgggggtg tgggtggtcc 1560
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tccacactgg aggcgtgcgt gccgtccctg ggctgaagga gggggtgact gtgaagcccg 1680
tggttgtggt agtcggcact ttggtagtgt gagctgttcc tggggtggaa gagggggtgg 1740
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cagtctctgg agtggaggag ggtgtggctg tggacatggt ggccgtgggt gtggtggtct 1860
gtgataggcg ggtccaggtg gtgcccaggg aggaggaggg gatggctgta aagctggtag 1920
ctgtgggtgt ggtggctgtg cttctcagtg ctggaagggc ggttgcagtc cctggactgg 1980
agaagggagt ggctttggag ctggtgactg tgggtgtcgt ggccgtggtg ctcacatgtg 2040
gggtgccagc agttgcctgg gtggaggagg cggtggccgt ggatccggtg ggcaccgtca 2100
cgggagtact tcta 2114

<210> 159
<211> 278
<212> DNA
<213> Homo sapien

<400> 159
gaattcggca caggtaactt tgcctggggt atttaaaaaa aaaaaaaaaa aaaaaaaaag 60
tcaaatatct gagtactaat ttcctgaaaa gtatgttccg atagatgaac agatcattaa 120
tgcagaatga gaatcactcc taaaataggt aatggtaaaa attaaattga caattacctc 180
tctctatgca gaaggaaata tcacctatat gacatcatca tcatctattg atacttgctg 240
gcagtgctaa taatggtttt aatgccaatt tgtaagaa 278

<210> 160
<211> 848
<212> DNA
<213> Homo sapien

<400> 160
gaattcggca cgagccccag aggagctcgg cctgcgctgc gccacgatgt ccggggagtc 60
agccaggagc ttggggaagg gaagcgcgcc cccggggccg gtcccggagg gctcgatccg 120
catctacagc atgaggttct gcccgtttgc tgagaggacg cgtctagtcc tgaaggccaa 180
gggaatcagg catgaagtca tcaatatcaa cctgaaaaat aagcctgagt ggttctttaa 240
gaaaaatccc tttggtctgg tgccagttct ggaaaacagt cagggtcagc tgatctacga 300
gtctgccatc acctgtgagt acctggatga agcataccca gggaagaagc tgttgccgga 360
tgacccctat gagaaagctt gccagaagat gatcttagag ttgttttcta aggtgccatc 420
cttggtagga agctttatta gaagccaaaa taaagaagac tatgctggcc taaaagaaga 480
atttcgtaaa gaatttacca agctagagga ggttctgact aataagaaga cgaccttctt 540
tggtggcaat tctatctcta tgattgatta cctcatctgg ccctggtttg aacggctgga 600
agcaatgaag ttaaatgagt gtgtagacca cactccaaaa ctgaaactgt ggatggcagc 660
catgaaggaa gatcccacag tctcagccct gcttactagt gagaaagact ggcaaggttt 720
cctagagctc tacttacaga acagccctga ggcctgtgac tatgggctct gaagggggca 780
ggagtcagca ataaagctat gtctgatatt ttccttcact aaaaaaaaaa aaaaaaaaaa 840
aactcgag 848

<210> 161
<211> 432
<212> DNA
<213> Homo sapien

<400> 161
gaattcggca cgagggcaga ccaagatcct ggaggaggac ctggaacaga tcaagctgtc 60
cttgagagag cgaggccggg agctgaccac tcagaggcag ctgatgcagg aacgggcaga 120
ggaagggaag ggcccaagta aagcacagcg cgggagccta gagcacatga agctgatcct 180
gcgtgataag gagaaggagg tggaatgtca gcaggagcat atccatgaac tccaggagct 240
caaagaccag ctggagcagc agctccaggg cctgcacagg aaggtaggtg agaccagcct 300
cctcctgtcc cagcgagagc aggaaatagt ggtcctgcag cagcaactgc aggaagccag 360
ggaacaaggg gagctgaagg agcagtcact tcagagtcaa ctggatgagg cccagagagc 420
cctagcccag ag 432

<210> 162
<211> 433
<212> DNA
<213> Homo sapien

<400> 162

gattcggcac gagccggagc tgggttgctc ctgctcccgt ctccaagtcc tggtacctcc 60
ttcaagctgg gagagggctc tagtccctgg ttctgaacac tctggggttc tcgggtgcag 120
gccgccatga gcaaacggaa ggcgccgcag gagactctca acgggggaat caccgacatg 180
ctcacagaac tcgcaaactt tgagaagaac gtgagccaag ctatccacaa gtacaatgct 240
tacagaaaag cagcatctgt tatagcaaaa tacccacaca aaataaagag tggagctgaa 300
gctaagaaat tgcctggagt aggaacaaaa attgctgaaa agattgatga gtttttagca 360
actggaaaat tacgtaaact ggaaaagatt cggcaggatg atacgagttc atccatcaat 420
ttcctgactc gag 433

<210> 163
<211> 432
<212> DNA
<213> Homo sapien

<400> 163
gaattcggca ccagatgagg ccaacgaggt gacggacagc gcgtacatgg gctccgagag 60
cacctacagt gagtgtgaga ccttcacgga cgaggacacc agcaccctgg tgcaccctga 120
gctgcaacct gaaggggacg cagacagtgc cggcggctcg gccgtgccct ctgagtgcct 180
ggacgccatg gaggagcccg accatggtgc cctgctgctg ctcccaggca ggcctcaccc 240
ccatggccag tctgtcatca cggtgatcgg gggcgaggag cactttgagg actacggtga 300
aggcagtgag gcggagctgt ccccagagac cctatgcaac gggcagctgg gctgcagtga 360
ccccgctttc ctcacgccca gtccgacaaa gcggctctcc agcaagaagg tggcaaggta 420
cctgcaccag tc 432

<210> 164
<211> 395
<212> DNA
<213> Homo sapien

<400> 164
gacacttgaa tcatgggtga cgttaaaaat tttctgtatg cctggtgtgg caaaaggaag 60
atgaccccat cctatgaaat tagagcagtg ggaacaaaa acaggcagaa attcatgtgt 120
gaggttcagg tggaaggtta taattacact ggcatgggaa attccaccaa taaaaaagat 180
gcacaaagca atgctgccag agactttgtt aactatttgg ttcgaataaa tgaaataaag 240
agtgaagaag ttccagcttt tggggtagca tctccgcccc cacttactga tactcctgac 300
actacagcaa atgctgaagg catcttgttg acatcgaata tgactttgat aataaatacc 360
ggttcctgaa aaaaaaaaa aaaaaaaaac tcgag 395

<210> 165
<211> 503
<212> DNA
<213> Homo sapien

<400> 165
gaattcggca ccaggaacgc tcggtgagag gcggaggagc ggtaactacc ccggttgcgc 60
acagctcggc gctccttccc gctccctcac acaccggcct cagcccgcac cggcagtaga 120
agatggtgaa agaaacaact tactacgatg ttttggggt caaacccaat gctactcagg 180
aagaattgaa aaaggcttat aggaaactgg ccttgaagta ccatcctgat aagaacccaa 240
atgaaggaga gaagtttaaa cagatttctc aagcttacga agttctctct gatgcaaaga 300
aaagggaatt atatgacaaa ggaggagaac aggcaattaa agagggtgga gcaggtggcg 360
gttttggctc ccccatggac atctttgata tgttttttgg aggaggagga aggatgcaga 420
gagaaaggag aggtaaaaat gttgtacatc agctctcagt aaccctagaa gacttatata 480
atggtgcaac aagaaaactg gct 503

<210> 166

<211> 893
<212> DNA
<213> Homo sapien

<400> 166
gaattcggca cgagaggaac ttctcttgac gagaagagag accaaggagg ccaagcaggg 60
gctgggccag aggtgccaac atggggaaac tgaggctcgg ctcggaaggg tgagagtgag 120
actacatctc aaaaaaaaaa aaaaaaaaaa aaaagaaaga aaagaaaaga aaaaagaaag 180
aacggaagta gttgtaggta gtggtatggt ggtatgagtc tgttttctgt tacttataac 240
aacaacaaca acaaaaaacg ctgaaactgg gtaatttata aagaaaagga aaaaaagcag 300
aaaaaaatca ggaagaagag aaaggaaaag aagacaaata aatgaaattt atgtattaca 360
gttctgaagg ctgagacatc ccaggtcaag ggtccacact tggcgagggc tttcttgctg 420
gtggagactc tttgtggagt cctgggacag tgcagaagga tcacgcctcc ctaccgctcc 480
aagcccagcc ctcagccatg gcatgccccc tggatcaggc cattggcctc ctcgtggcca 540
tcttccacaa gtactccggc agggagggtg acaagcacac cctgagcaag aaggagctga 600
aggagctgat ccagaaggag ctcaccattg gctcgaagct gcaggatgct gaaattgcaa 660
ggctgatgga agacttggac cggaacaagg accaggaggt gaacttccag gagtatgtca 720
ccttcctggg ggccttggct ttgatctaca atgaagccct caagggctga aaataaatag 780
ggaagatgga gacaccctct gggggtcctc tctgagtcaa atccagtggt gggtaattgt 840
acaataaatt ttttttggtc aaatttaaaa aaaaaaaaaa aaaaaaactc gag 893

<210> 167
<211> 549
<212> DNA
<213> Homo sapien

<400> 167
gaattcggca cgagcccaga tcccgaggtc cgacagcgcc cggcccagat ccccacgcct 60
gccaggagca agccgagagc cagccggccg gcgcactccg actccgagca gtctctgtcc 120
ttcgacccga gccccgcgcc ctttccggga cccctgcccc gcgggcagcg ctgccaacct 180
gccggccatg gagaccccgt cccagcggcg cgccacccgc agcggggcgc aggccagctc 240
cactccgctg tcgcccaccc gcatcacccg gctgcaggag aaggaggacc tgcaggagct 300
caatgatcgc ttggcggtct acatcgaccg tgtgcgctcg ctggaaacgg agaacgcagg 360
gctgcgcctt cgcatcaccg agtctgaaga ggtggtcagc cgcgaggtgt ccggcatcaa 420
ggccgcctac gaggccgagc tcggggatgc ccgcaagacc cttgactcag tagccaagga 480
gcgcgcccgc ctgcagctgg agctgagcaa agtgcgtgaa gagtttaagg agctgaaagc 540
gcgcaatac 549

<210> 168
<211> 547
<212> DNA
<213> Homo sapien

<400> 168
gaattcggca cgagatggcg gcaggggtcg aagcggcggc ggaggtggcg gcgacggaga 60
tcaaaatgga ggaagagagc ggcgcgcccg gcgtgccgag cggcaacggg gctccgggcc 120
ctaagggtga aggagaacga cctgctcaga atgagaagag gaaggagaaa aacataaaaa 180
gaggaggcaa tcgctttgag ccatatgcca atccaactaa aagatacaga gccttcatta 240
caaacatacc ttttgatgtg aaatggcagt cacttaaaga cctggttaaa gaaaaagttg 300
gtgaggtaac atacgtggag ctcttaatgg acgctgaagg aaagtcaagg ggatgtgctg 360
ttgttgaatt caagatggaa gagagcatga aaaaagctgc ggaagtccta aacaagcata 420
gtctgagcgg aagaccactg aaagtcaaag aagatcctga tggtgaacat gccaggagag 480
caatgcaaaa ggctggaaga cttggaagca cagtatttgt agcaaatctg gattataaag 540
ttggctg 547

<210> 169
<211> 547
<212> DNA
<213> Homo sapien

<400> 169
gaattcggca ccaggagtcc gactgtgctc gctgctcagc gccgcacccg gaagatgagg 60
ctcgccgtgg gagccctgct ggtctgcgcc gtcctggggc tgtgtctggc tgtccctgat 120
aaaactgtga gatggtgtgc agtgtcggag catgaggcca ctaagtgcca gagtttccgc 180
gaccatatga aaagcgtcat tccatccgat ggtcccagtg ttgcttgtgt gaagaaagcc 240
tcctaccttg attgcatcag ggccattgcg gcaaacgaag cggatgctgt gacactggat 300
gcaggtttgg tgtatgatgc ttacctggct cccaataacc tgaagcctgt ggtggcagag 360
ttctatgggt caaaagagga tccacagact ttctattatg ctgttgctgt ggtgaagaag 420
gatagtggct tccagatgaa ccagcttcga ggcaagaagt cctgccacac gggtctaggc 480
aggtccgctg ggtggaacat ccccataggc ttactttact gtgacttacc tgagccacgt 540
aaacctc 547

<210> 170
<211> 838
<212> DNA
<213> Homo sapien

<400> 170
gaattcggca ccagaggagc tcggcctgcg ctgcgccacg atgtccgggg agtcagccag 60
gagcttgggg aagggaagcg cgcccccggg gccggtcccg gagggctcga tccgcatcta 120
cagcatgagg ttctgcccgt ttgctgagag gacgcgtcta gtcctgaagg ccaagggaat 180
caggcatgaa gtcatcaata tcaacctgaa aaataagcct gagtggttct ttaagaaaaa 240
tccctttggt ctggtgccag ttctggaaaa cagtcagggt cagctgatct acgagtctgc 300
catcacctgt gagtacctgg atgaagcata cccagggaag aagctgttgc cggatgaccc 360
ctatgagaaa gcttgccaga agatgatctt agagttgttt tctaaggtgc catccttggt 420
aggaagcttt attagaagcc aaaataaaga agactatgat ggcctaaaag aagaatttcg 480
taaagaattt accaagctag aggaggttct gactaataag aagacgacct tctttggtgg 540
caattctatc tctatgattg attacctcat ctggccctgg tttgaacggc tggaagcaat 600
gaagttaaat gagtgtgtag accacactcc aaaactgaaa ctgtggatgg cagccatgaa 660
ggaagatccc acagtctcag ccctgcttac tagtgagaaa gactggcaag gtttcctaga 720
gctctactta cagaacagcc ctgaggcctg tgactatggg ctctgaaggg ggcaggagtc 780
agcaataaag ctatgtctga tattttcctt cactaaaaaa aaaaaaaaaa aactcgag 838

<210> 171
<211> 547
<212> DNA
<213> Homo sapien

<400> 171
gaattcggca ccagcgggat ttgggtcgca gttcttgttt gtggattgct gtgatcgtca 60
cttgacaatg cagatcttcg tgaagactct gactggtaag accatcaccc tcgaggttga 120
gcccagtgac accatcgaga atgtcaaggc aaagatccaa gataaggaag gcatccctcc 180
tgaccagcag aggctgatct ttgctggaaa acagctggaa gatgggcgca ccctgtctga 240
ctacaacatc cagaaagagt ccaccctgca cctggtgctc cgtctcagag gtgggatgca 300
aatcttcgtg aagacactca ctggcaagac catcaccctt gaggtcgagc ccagtgacac 360
catcgagaac gtcaaagcaa agatccagga caaggaaggc attcctcctg accagcagag 420
gttgatcttt gccggaaagc agctggaaga tgggcgcacc ctgtctgact acaacatcca 480
gaaagagtct accctgcacc tggtgctccg tctcagaggt gggatgcaga tcttcgtgaa 540
gaccctg 547

<210> 172
<211> 608
<212> DNA
<213> Homo sapien

<400> 172
gaattcggca ccagagactt ctccctctga ggcctgcgca cccctcctca tcagcctgtc 60
caccctcatc tacaatggtg ccctgccatg tcagtgcaac cctcaaggtt cactgagttc 120
tgagtgcaac cctcatggtg gtcagtgcct gtgcaagcct ggagtggttg ggcgccgctg 180
tgacctctgt gcccctggct actatggctt tggccccaca ggctgtcaag gcgcttgcct 240
gggctgccgt gatcacacag gggtgagca ctgtgaaagg tgcattgctg gtttccacgg 300
ggacccacgg ctgccatatg gggccagtg ccggccctgt ccctgtcctg aaggccctgg 360
gagccaacgg cactttgcta cttcttgcca ccaggatgaa tattcccagc agattgtgtg 420
ccactgccgg gcaggctata cggggctgcg atgtgaagct tgtgcccctg ggcactttgg 480
ggacccatca aggccaggtg gccggtgcca actgtgtgag tgcagtggga acattgaccc 540
aatggatcct gatgcctgtg acccccacac ggggcaatgc ctgcgctgtt tacaccacac 600
agagggtc 608

<210> 173
<211> 543
<212> DNA
<213> Homo sapien

<400> 173
gaattcggca ccagagatca tccgccagca gggtctggcc tcctacgact acgtgcgccg 60
ccgcctcacg gctgaggacc tgttcgaggc tcggatcatc tctctcgaga cctacaacct 120
gctccgggag ggcaccagga gcctccgtga ggctctcgag gcggagtccg cctggtgcta 180
cctctatggc acgggctccg tggctggtgt ctacctgccc ggttccaggc agacactgag 240
catctaccag gctctcaaga aagggctgct gagtgccgag gtggcccgcc tgctgctgga 300
ggcacaggca gccacaggct tcctgctgga cccggtgaag ggggaacggc tgactgtgga 360
tgaagctgtg cggaagggcc tcgtggggcc cgaactgcac gaccgcctgc tctcggctga 420
gcgggcggtc accggctacc gtgaccccta caccgagcag accatctcgc tcttccaggc 480
catgaagaag gaactgatcc ctactgagga ggccctgcgg ctgtggatgc ccagctggcc 540
acc 543

<210> 174
<211> 548
<212> DNA
<213> Homo sapien

<400> 174
gaattcggca cgagaaatgg cggcaggggt cgaagcggcg gcggaggtgg cggcgacgga 60
gatcaaaatg gaggaagaga gcggcgcgcc cggcgtgccg agcggcaacg gggctccggg 120
ccctaagggt gaaggagaac gacctgctca gaatgagaag aggaaggaga aaaacataaa 180
aagaggaggc aatcgctttg agccatatgc caatccaact aaaagataca gagccttcat 240
tacaaacata ccttttgatg tgaaatggca gtcacttaaa gacctggtta aagaaaaagt 300
tggtgaggta acatacgtgg agctcttaat ggacgctgaa ggaaagtcaa ggggatgtgc 360
tgttgttgaa ttcaagatgg aagagagcat gaaaaaagct gcggaagtcc taaacaagca 420
tagtctgagc ggaagaccac tgaaagtcaa agaagatcct gatggtgaac atgccaggag 480
agcaatgcaa aaggtgatgg ctacgactgg tgggatgggt atgggaccag gtggcccagg 540
aatgatta 548

<210> 175
<211> 604
<212> DNA

<213> Homo sapien

<400> 175
gaattcggca ccagaggacc tccaggacat gttcatcgtc cataccatcg aggagattga 60
gggcctgatc tcagcccatg accagttcaa gtccaccctg ccggacgccg atagggagcg 120
cgaggccatc ctggccatcc acaaggaggc ccagaggatc gctgagagca accacatcaa 180
gctgtcgggc agcaacccct acaccaccgt cacccсgcaa atcatcaact ccaagtggga 240
gaaggtgcag cagctggtgc caaaacggga ccatgccctc ctggaggagc agagcaagca 300
gcagtccaac gagcacctgc gccgccagtt cgccagccag gccaatgttg tggggccctg 360
gatccagacc aagatggagg agatcgggcg catctccatt gagatgaacg ggaccctgga 420
ggaccagctg agccacctga agcagtatga acgcagcatc gtggactaca agcccaacct 480
ggacctgctg gagcagcagc accagcttat ccaggaggcc ctcatcttcg acaacaagca 540
caccaactat accatggagc acatccgcgt gggctgggag cagctgctca ccaccattgc 600
ccgg 604

<210> 176
<211> 486
<212> DNA
<213> Homo sapien

<400> 176
gaattcggca ccagccaagc tcactattga atccacgccg ttcaatgtcg cagaggggaa 60
ggaggttctt ctactcgccc acaacctgcc ccagaatcgt attggttaca gctggtacaa 120
aggcgaaaga gtggatggca acagtctaat tgtaggatat gtaataggaa ctcaacaagc 180
taccccaggg cccgcataca gtggtcgaga gacaatatac cccaatgcat ccctgctgat 240
ccagaacgtc acccagaatg acacaggatt ctataccсta caagtcataa agtcagatct 300
tgtgaatgaa gaagcaaccg gacagttcca tgtataccсg gagctgccca agccctccat 360
ctccagcaac aactccaacc ccgtggagga caaggatgct gtggccttca cctgtgaacc 420
tgaggttcag aacacaacct acctgtggtg ggtaaatggt cagagcctcc cggtcagtcc 480
caaggc 486

<210> 177
<211> 387
<212> DNA
<213> Homo sapien

<400> 177
gaattcggca ccagggacag cagaccagac agtcacagca gccttgacaa aacgttcctg 60
gaactcaagc tcttctccac agaggaggac agagcagaca gcagagacca tggagtctcc 120
ctcggcccct ccccacagat ggtgcatccc ctggcagagg ctcctgctca cagcctcact 180
tctaaccttc tggaacccgc ccaccactgc caagctcact attgaatcca cgccgttcaa 240
tgtcgcagag gggaaggagg tgcttctact tgtccacaat ctgccccagc atctttttgg 300
ctacagctgg tacaaaggtg aaagagtgga tggcaaccgt caaattatag gatatgtaat 360
aggaactcaa caagctaccc cagggcc 387

<210> 178
<211> 440
<212> DNA
<213> Homo sapien

<400> 178
gaattcggca cgaggagaag cagaaaaaca aggaatttag ccagacttta gaaaatgaga 60
aaaatacctt actgagtcag atatcaacaa aggatggtga actaaaaatg cttcaggagg 120
aagtaaccaa aatgaacctg ttaaatcagc aaatccaaga agaactctct agagttacca 180
aactaaagga gacagcagaa gaagagaaag atgatttgga agagaggctt atgaatcaat 240

tagcagaact taatggaagc attgggaatt actgtcagga tgttacagat gcccaaataa 300
aaaatgagct attggaatct gaaatgaaga accttaaaaa gtgtgtgagt gaattggaag 360
aagaaaagca gcagttagtc aaggaaaaaa ctaaggtgga atcagaaata cgaaaggaat 420
atttggagaa aatacaaggt 440

<210> 179
<211> 443
<212> DNA
<213> Homo sapien

<400> 179
gaattcggca ccagcggggg gctacggcgg cggctacggc ggcgtcctga ccgcgtccga 60
cgggctgctg gcgggcaacg agaagctaac catgcagaac ctcaacgacc gcctggcctc 120
ctacctggac aaggtgcgcg ccctggaggc ggccaacggc gagctagagg tgaagatccg 180
cgactggtac cagaagcagg ggcctgggcc ctcccgcgac tacagccact actacacgac 240
catccaggac ctgcgggaca agattcttgg tgccaccatt gagaactcca ggattgtcct 300
gcagatcgac aacgcccgtc tggctgcaga tgacttccga accaagtttg agacggaaca 360
ggctctgcgc atgagcgtgg aggccgacat caacggcctg cgcagggtgc tggatgagct 420
gaccctggcc aggaccgacc tgg 443

<210> 180
<211> 403
<212> DNA
<213> Homo sapien

<400> 180
gaattcggca cgaggttatg agagtcgact tcaatgttcc tatgaagaac aaccagataa 60
caaacaacca gaggattaag gctgctgtcc caagcatcaa attctgcttg gacaatggag 120
ccaagtcggt agtccttatg agccacctag gccggcctga tggtgtgccc atgcctgaca 180
agtactcctt agagccagtt gctgtagaac tcagatctct gctgggcaag gatgttctgt 240
tcttgaagga ctgtgtaggc ccagaagtgg agaaagcctg tgccaaccca gctgctgggt 300
ctgtcatcct gctggagaac ctccgctttc atgtggagga agaagggaag ggaaaagatg 360
cttctgggaa caaggttaaa gccgagccag ccaaaataga agc 403

<210> 181
<211> 493
<212> DNA
<213> Homo sapien

<400> 181
gaattcggca ccagcagagg tctccagagc cttctctctc ctgtgcaaaa tggcaactct 60
taaggaaaaa ctcattgcac cagttgcgga agaagaggca acagttccaa acaataagat 120
cactgtagtg ggtgttggac aagttggtat ggcgtgtgct atcagcattc tgggaaagtc 180
tctggctgat gaacttgctc ttgtggatgt tttggaagat aagcttaaag gagaaatgat 240
ggatctgcag catgggagct tatttcttca gacacctaaa attgtggcag ataaagatta 300
ttctgtgacc gccaattcta agattgtagt ggtaactgca ggagtccgtc agcaagaagg 360
ggagagtcgg ctcaatctgg tgcagagaaa tgttaatgtc ttcaaattca ttattcctca 420
gatcgtcaag tacagtcctg attgcatcat aattgtggtt tccaacccag tggacattct 480
tacgtatgtt acc 493

<210> 182
<211> 209
<212> PRT
<213> Homo sapien

<400> 182

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

<210> 183
<211> 255
<212> PRT
<213> Homo sapien

<400> 183

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

```
145                 150                 155                 160
Arg Leu Gly Ser Thr Val Phe Val Ala Asn Leu Asp Tyr Lys Val Gly
                165                 170                 175
Trp Lys Lys Leu Lys Glu Val Phe Ser Met Ala Gly Val Val Val Arg
            180                 185                 190
Ala Asp Ile Leu Glu Asp Lys Asp Gly Lys Ser Arg Gly Ile Gly Ile
        195                 200                 205
Val Thr Phe Glu Gln Ser Ile Glu Ala Val Gln Ala Ile Ser Met Phe
    210                 215                 220
Asn Gly Gln Leu Leu Phe Asp Arg Pro Met His Val Lys Met Asp Glu
225                 230                 235                 240
Arg Ala Leu Pro Lys Gly Asp Phe Phe Pro Pro Glu Arg His Ser
                245                 250                 255

      <210> 184
      <211> 188
      <212> PRT
      <213> Homo sapien

      <400> 184
Leu Ser Gly Ser Cys Ile Arg Arg Glu Gln Thr Pro Glu Lys Glu Lys
 1               5                   10                  15
Gln Val Val Leu Phe Glu Glu Ala Ser Trp Thr Cys Thr Pro Ala Cys
            20                  25                  30
Gly Asp Glu Pro Arg Thr Val Ile Leu Leu Ser Ser Met Leu Ala Asp
        35                  40                  45
His Arg Leu Lys Leu Glu Asp Tyr Lys Asp Arg Leu Lys Ser Gly Glu
    50                  55                  60
His Leu Asn Pro Asp Gln Leu Glu Ala Val Glu Lys Tyr Glu Glu Val
65                  70                  75                  80
Leu His Asn Leu Glu Phe Ala Lys Glu Leu Gln Lys Thr Phe Ser Gly
                85                  90                  95
Leu Ser Leu Asp Leu Leu Lys Ala Gln Lys Lys Ala Gln Arg Arg Glu
            100                 105                 110
His Met Leu Lys Leu Glu Ala Glu Lys Lys Lys Leu Arg Thr Ile Leu
        115                 120                 125
Gln Val Gln Tyr Val Leu Gln Asn Leu Thr Gln Glu His Val Gln Lys
    130                 135                 140
Asp Phe Lys Gly Gly Leu Asn Gly Ala Val Tyr Leu Pro Ser Lys Glu
145                 150                 155                 160
Leu Asp Tyr Leu Ile Lys Phe Ser Lys Leu Thr Cys Pro Glu Arg Asn
                165                 170                 175
Glu Ser Leu Arg Gln Thr Leu Glu Gly Ser Thr Val
            180                 185

      <210> 185
      <211> 746
      <212> PRT
      <213> Homo sapien

      <400> 185
Asp Lys His Leu Lys Asp Leu Leu Ser Lys Leu Leu Asn Ser Gly Tyr
 1               5                   10                  15
Phe Glu Ser Ile Pro Val Pro Lys Asn Ala Lys Glu Lys Glu Val Pro
            20                  25                  30
```

```
Leu Glu Glu Glu Met Leu Ile Gln Ser Glu Lys Lys Thr Gln Leu Ser
        35                  40                  45
Lys Thr Glu Ser Val Lys Glu Ser Glu Ser Leu Met Glu Phe Ala Gln
    50                  55                  60
Pro Glu Ile Gln Pro Gln Glu Phe Leu Asn Arg Arg Tyr Met Thr Glu
65                  70                  75                  80
Val Asp Tyr Ser Asn Lys Gln Gly Glu Glu Gln Pro Trp Glu Ala Asp
                85                  90                  95
Tyr Ala Arg Lys Pro Asn Leu Pro Lys Arg Trp Asp Met Leu Thr Glu
            100                 105                 110
Pro Asp Gly Gln Glu Lys Lys Gln Glu Ser Phe Lys Ser Trp Glu Ala
        115                 120                 125
Ser Gly Lys His Gln Glu Val Ser Lys Pro Ala Val Ser Leu Glu Gln
    130                 135                 140
Arg Lys Gln Asp Thr Ser Lys Leu Arg Ser Thr Leu Pro Glu Glu Gln
145                 150                 155                 160
Lys Lys Gln Glu Ile Ser Lys Ser Lys Pro Ser Pro Ser Gln Trp Lys
                165                 170                 175
Gln Asp Thr Pro Lys Ser Lys Ala Gly Tyr Val Gln Glu Glu Gln Lys
            180                 185                 190
Lys Gln Glu Thr Pro Lys Leu Trp Pro Val Gln Leu Gln Lys Glu Gln
        195                 200                 205
Asp Pro Lys Lys Gln Thr Pro Lys Ser Trp Thr Pro Ser Met Gln Ser
    210                 215                 220
Glu Gln Asn Thr Thr Lys Ser Trp Thr Thr Pro Met Cys Glu Glu Gln
225                 230                 235                 240
Asp Ser Lys Gln Pro Glu Thr Pro Lys Ser Trp Glu Asn Asn Val Glu
                245                 250                 255
Ser Gln Lys His Ser Leu Thr Ser Gln Ser Gln Ile Ser Pro Lys Ser
            260                 265                 270
Trp Gly Val Ala Thr Ala Ser Leu Ile Pro Asn Asp Gln Leu Leu Pro
        275                 280                 285
Arg Lys Leu Asn Thr Glu Pro Lys Asp Val Pro Lys Pro Val His Gln
    290                 295                 300
Pro Val Gly Ser Ser Ser Thr Leu Pro Lys Asp Pro Val Leu Arg Lys
305                 310                 315                 320
Glu Lys Leu Gln Asp Leu Met Thr Gln Ile Gln Gly Thr Cys Asn Phe
                325                 330                 335
Met Gln Glu Ser Val Leu Asp Phe Asp Lys Pro Ser Ser Ala Ile Pro
            340                 345                 350
Thr Ser Gln Pro Pro Ser Ala Thr Pro Gly Ser Pro Val Ala Ser Lys
        355                 360                 365
Glu Gln Asn Leu Ser Ser Gln Ser Asp Phe Leu Gln Glu Pro Leu Gln
    370                 375                 380
Val Phe Asn Val Asn Ala Pro Leu Pro Pro Arg Lys Glu Gln Glu Ile
385                 390                 395                 400
Lys Glu Ser Pro Tyr Ser Pro Gly Tyr Asn Gln Ser Phe Thr Thr Ala
                405                 410                 415
Ser Thr Gln Thr Pro Pro Gln Cys Gln Leu Pro Ser Ile His Val Glu
            420                 425                 430
Gln Thr Val His Ser Gln Glu Thr Ala Ala Asn Tyr His Pro Asp Gly
        435                 440                 445
Thr Ile Gln Val Ser Asn Gly Ser Leu Ala Phe Tyr Pro Ala Gln Thr
    450                 455                 460
Asn Val Phe Pro Arg Pro Thr Gln Pro Phe Val Asn Ser Arg Gly Ser
```

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

<210> 186
<211> 705
<212> PRT
<213> Homo sapien

<400> 186
Ala Leu Leu Asn Val Arg Gln Pro Pro Ser Thr Thr Thr Phe Val Leu
1 5 10 15
Asn Gln Ile Asn His Leu Pro Pro Leu Gly Ser Thr Ile Val Met Thr
20 25 30
Lys Thr Pro Pro Val Thr Thr Asn Arg Gln Thr Ile Thr Leu Thr Lys
35 40 45
Phe Ile Gln Thr Thr Ala Ser Thr Arg Pro Ser Val Ser Ala Pro Thr
50 55 60
Val Arg Asn Ala Met Thr Ser Ala Pro Ser Lys Asp Gln Val Gln Leu
65 70 75 80
Lys Asp Leu Leu Lys Asn Asn Ser Leu Asn Glu Leu Met Lys Leu Lys
85 90 95
Pro Pro Ala Asn Ile Ala Gln Pro Val Ala Thr Ala Ala Thr Asp Val

```
                100                 105                 110
Ser Asn Gly Thr Val Lys Lys Glu Ser Ser Asn Lys Glu Gly Ala Arg
            115                 120                 125
Met Trp Ile Asn Asp Met Lys Met Arg Ser Phe Ser Pro Thr Met Lys
    130                 135                 140
Val Pro Val Val Lys Glu Asp Asp Glu Pro Glu Glu Glu Asp Glu Glu
145                 150                 155                 160
Glu Met Gly His Ala Glu Thr Tyr Ala Glu Tyr Met Pro Ile Lys Leu
                165                 170                 175
Lys Ile Gly Leu Arg His Pro Asp Ala Val Val Glu Thr Ser Ser Leu
            180                 185                 190
Ser Ser Val Thr Pro Pro Asp Val Trp Tyr Lys Thr Ser Ile Ser Glu
        195                 200                 205
Glu Thr Ile Asp Asn Gly Trp Leu Ser Ala Leu Gln Leu Glu Ala Ile
    210                 215                 220
Thr Tyr Ala Ala Gln Gln His Glu Thr Phe Leu Pro Asn Gly Asp Arg
225                 230                 235                 240
Ala Gly Phe Leu Ile Gly Asp Gly Ala Gly Val Gly Lys Gly Arg Thr
                245                 250                 255
Ile Ala Gly Ile Ile Tyr Glu Asn Tyr Leu Leu Ser Arg Lys Arg Ala
            260                 265                 270
Leu Trp Phe Ser Val Ser Asn Asp Leu Lys Tyr Asp Ala Glu Arg Asp
        275                 280                 285
Leu Arg Asp Ile Gly Ala Lys Asn Ile Leu Val His Ser Leu Asn Lys
    290                 295                 300
Phe Lys Tyr Gly Lys Ile Ser Ser Lys His Asn Gly Ser Val Lys Lys
305                 310                 315                 320
Gly Val Ile Phe Ala Thr Tyr Ser Ser Leu Ile Gly Glu Ser Gln Ser
                325                 330                 335
Gly Gly Lys Tyr Lys Thr Arg Leu Lys Gln Leu Leu His Trp Cys Gly
            340                 345                 350
Asp Asp Phe Asp Gly Val Ile Val Phe Asp Glu Cys His Lys Ala Lys
        355                 360                 365
Asn Leu Cys Pro Val Gly Ser Ser Lys Pro Thr Lys Thr Gly Leu Ala
    370                 375                 380
Val Leu Glu Leu Gln Asn Lys Leu Pro Lys Ala Arg Val Val Tyr Ala
385                 390                 395                 400
Ser Ala Thr Gly Ala Ser Glu Pro Arg Asn Met Ala Tyr Met Asn Arg
                405                 410                 415
Leu Gly Ile Trp Gly Glu Gly Thr Pro Phe Arg Glu Phe Ser Asp Phe
            420                 425                 430
Ile Gln Ala Val Glu Arg Arg Gly Val Gly Ala Met Glu Ile Val Ala
        435                 440                 445
Met Asp Met Lys Leu Arg Gly Met Tyr Ile Ala Arg Gln Leu Ser Phe
    450                 455                 460
Thr Gly Val Thr Phe Lys Ile Glu Glu Val Leu Leu Ser Gln Ser Tyr
465                 470                 475                 480
Val Lys Met Tyr Asn Lys Ala Val Lys Leu Trp Val Ile Ala Arg Glu
                485                 490                 495
Arg Phe Gln Gln Ala Ala Asp Leu Ile Asp Ala Glu Gln Arg Met Lys
            500                 505                 510
Lys Ser Met Trp Gly Gln Phe Trp Ser Ala His Gln Arg Phe Phe Lys
        515                 520                 525
Tyr Leu Cys Ile Ala Ser Lys Val Lys Arg Val Val Gln Leu Ala Arg
    530                 535                 540
```

Glu Glu Ile Lys Asn Gly Lys Cys Val Val Ile Gly Leu Gln Ser Thr
545 550 555 560
Gly Glu Ala Arg Thr Leu Glu Ala Leu Glu Glu Gly Gly Gly Glu Leu
565 570 575
Asn Asp Phe Val Ser Thr Ala Lys Gly Val Leu Gln Ser Leu Ile Glu
580 585 590
Lys His Phe Pro Ala Pro Asp Arg Lys Lys Leu Tyr Ser Leu Leu Gly
595 600 605
Ile Asp Leu Thr Ala Pro Ser Asn Asn Ser Ser Pro Arg Asp Ser Pro
610 615 620
Cys Lys Glu Asn Lys Ile Lys Lys Arg Lys Gly Glu Glu Ile Thr Arg
625 630 635 640
Glu Ala Lys Lys Ala Arg Lys Val Gly Gly Leu Thr Gly Ser Ser Ser
645 650 655
Asp Asp Ser Gly Ser Glu Ser Asp Ala Ser Asp Asn Glu Glu Ser Asp
660 665 670
Tyr Glu Ser Ser Lys Asn Met Ser Ser Gly Asp Asp Asp Asp Phe Asn
675 680 685
Pro Phe Leu Asp Glu Ser Asn Glu Asp Asp Glu Asn Asp Pro Trp Leu
690 695 700
Ile
705

<210> 187
<211> 595
<212> PRT
<213> Homo sapien

<400> 187
Glu Ser Pro Arg His Arg Gly Glu Gly Gly Gly Glu Trp Gly Pro Gly
1 5 10 15
Val Pro Arg Glu Arg Arg Glu Ser Ala Gly Glu Trp Gly Ala Asp Thr
20 25 30
Pro Lys Glu Gly Gly Glu Ser Ala Gly Glu Trp Gly Ala Glu Val Pro
35 40 45
Arg Gly Arg Gly Glu Gly Ala Gly Glu Trp Gly Pro Asp Thr Pro Lys
50 55 60
Glu Arg Gly Gln Gly Val Arg Glu Trp Gly Pro Glu Ile Pro Gln Glu
65 70 75 80
His Gly Glu Ala Thr Arg Asp Trp Ala Leu Glu Ser Pro Arg Ala Leu
85 90 95
Gly Glu Asp Ala Arg Glu Leu Gly Ser Ser Pro His Asp Arg Gly Ala
100 105 110
Ser Pro Arg Asp Leu Ser Gly Glu Ser Pro Cys Thr Gln Arg Ser Gly
115 120 125
Leu Leu Pro Glu Arg Arg Gly Asp Ser Pro Trp Pro Pro Trp Pro Ser
130 135 140
Pro Gln Glu Arg Asp Ala Gly Thr Arg Asp Arg Glu Glu Ser Pro Arg
145 150 155 160
Asp Trp Gly Gly Ala Glu Ser Pro Arg Gly Trp Glu Ala Gly Pro Arg
165 170 175
Glu Trp Gly Pro Ser Pro Ser Gly His Gly Asp Gly Pro Arg Arg Arg
180 185 190
Pro Arg Lys Arg Arg Gly Arg Lys Gly Arg Met Gly Arg Gln His Glu
195 200 205

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

<210> 188
<211> 376
<212> PRT
<213> Homo sapien

<400> 188

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

<210> 189
<211> 160
<212> PRT
<213> Homo sapien

<400> 189

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

<210> 190
<211> 146
<212> PRT
<213> Homo sapien

<400> 190

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

<210> 191
<211> 704
<212> PRT
<213> Homo sapien

<400> 191

Glu Gly Gly Cys Ala Ala Gly Arg Gly Arg Glu Leu Glu Pro Glu Leu
1 5 10 15
Glu Pro Gly Pro Gly Pro Gly Ser Ala Leu Glu Pro Gly Glu Glu Phe
20 25 30
Glu Ile Val Asp Arg Ser Gln Leu Pro Gly Pro Gly Asp Leu Arg Ser
35 40 45
Ala Thr Arg Pro Arg Ala Ala Glu Gly Trp Ser Ala Pro Ile Leu Thr
50 55 60
Leu Ala Arg Arg Ala Thr Gly Asn Leu Ser Ala Ser Cys Gly Ser Ala
65 70 75 80
Leu Arg Ala Ala Ala Gly Leu Gly Gly Gly Asp Ser Gly Asp Gly Thr
85 90 95
Ala Arg Ala Ala Ser Lys Cys Gln Met Met Glu Glu Arg Ala Asn Leu
100 105 110
Met His Met Met Lys Leu Ser Ile Lys Val Leu Leu Gln Ser Ala Leu
115 120 125
Ser Leu Gly Arg Ser Leu Asp Ala Asp His Ala Pro Leu Gln Gln Phe
130 135 140
Phe Val Val Met Glu His Cys Leu Lys His Gly Leu Lys Val Lys Lys
145 150 155 160
Ser Phe Ile Gly Gln Asn Lys Ser Phe Phe Gly Pro Leu Glu Leu Val
165 170 175
Glu Lys Leu Cys Pro Glu Ala Ser Asp Ile Ala Thr Ser Val Arg Asn
180 185 190
Leu Pro Glu Leu Lys Thr Ala Val Gly Arg Gly Arg Ala Trp Leu Tyr
195 200 205
Leu Ala Leu Met Gln Lys Lys Leu Ala Asp Tyr Leu Lys Val Leu Ile
210 215 220
Asp Asn Lys His Leu Leu Ser Glu Phe Tyr Glu Pro Glu Ala Leu Met
225 230 235 240
Met Glu Glu Glu Gly Met Val Ile Val Gly Leu Leu Val Gly Leu Asn
245 250 255
Val Leu Asp Ala Asn Leu Cys Leu Lys Gly Glu Asp Leu Asp Ser Gln
260 265 270
Val Gly Val Ile Asp Phe Ser Leu Tyr Leu Lys Asp Val Gln Asp Leu
275 280 285
Asp Gly Gly Lys Glu His Glu Arg Ile Thr Asp Val Leu Asp Gln Lys
290 295 300
Asn Tyr Val Glu Glu Leu Asn Arg His Leu Ser Cys Thr Val Gly Asp
305 310 315 320
Leu Gln Thr Lys Ile Asp Gly Leu Glu Lys Thr Asn Ser Lys Leu Gln
325 330 335
Glu Glu Leu Ser Ala Ala Thr Asp Arg Ile Cys Ser Leu Gln Glu Glu
340 345 350
Gln Gln Gln Leu Arg Glu Gln Asn Glu Leu Ile Arg Glu Arg Ser Glu
355 360 365
Lys Ser Val Glu Ile Thr Lys Gln Asp Thr Lys Val Glu Leu Glu Thr
370 375 380
Tyr Lys Gln Thr Arg Gln Gly Leu Asp Glu Met Tyr Ser Asp Val Trp
385 390 395 400
Lys Gln Leu Lys Glu Glu Lys Lys Val Arg Leu Glu Leu Glu Lys Glu
405 410 415
Leu Glu Leu Gln Ile Gly Met Lys Thr Glu Met Glu Ile Ala Met Lys
420 425 430

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

<210> 192
<211> 331
<212> PRT
<213> Homo sapien

<400> 192
Arg Ala Gly Ala Ser Ala Met Ala Leu Arg Lys Glu Leu Leu Lys Ser
 1   5   10   15
Ile Trp Tyr Ala Phe Thr Ala Leu Asp Val Glu Lys Ser Gly Lys Val
            20   25   30
Ser Lys Ser Gln Leu Lys Val Leu Ser His Asn Leu Tyr Thr Val Leu
        35   40   45
His Ile Pro His Asp Pro Val Ala Leu Glu Glu His Phe Arg Asp Asp
    50   55   60
Asp Asp Gly Pro Val Ser Ser Gln Gly Tyr Met Pro Tyr Leu Asn Lys
65   70   75   80
Tyr Ile Leu Asp Lys Val Glu Glu Gly Ala Phe Val Lys Glu His Phe
                85   90   95
Asp Glu Leu Cys Trp Thr Leu Thr Ala Lys Lys Asn Tyr Arg Ala Asp
            100   105   110

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

```
      <210> 193
      <211> 475
      <212> PRT
      <213> Homo sapien

      <400> 193
Lys Asn Ser Pro Leu Leu Ser Val Ser Ser Gln Thr Ile Thr Lys Glu
 1               5                  10                  15
Asn Asn Arg Asn Val His Leu Glu His Ser Glu Gln Asn Pro Gly Ser
            20                  25                  30
Ser Ala Gly Asp Thr Ser Ala Ala His Gln Val Val Leu Gly Glu Asn
        35                  40                  45
Leu Ile Ala Thr Ala Leu Cys Leu Ser Gly Ser Gly Ser Gln Ser Asp
    50                  55                  60
Leu Lys Asp Val Ala Ser Thr Ala Gly Glu Glu Gly Asp Thr Ser Leu
65                  70                  75                  80
Arg Glu Ser Leu His Pro Val Thr Arg Ser Leu Lys Ala Gly Cys His
                85                  90                  95
Thr Lys Gln Leu Ala Ser Arg Asn Cys Ser Glu Glu Lys Ser Pro Gln
            100                 105                 110
Thr Ser Ile Leu Lys Glu Gly Asn Arg Asp Thr Ser Leu Asp Phe Arg
        115                 120                 125
Pro Val Val Ser Pro Ala Asn Gly Val Glu Gly Val Arg Val Asp Gln
    130                 135                 140
Asp Asp Asp Gln Asp Ser Ser Ser Leu Lys Leu Ser Gln Asn Ile Ala
145                 150                 155                 160
```

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

<210> 194
<211> 241
<212> PRT
<213> Homo sapien

<400> 194
Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro
1 5 10 15
Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys
20 25 30
Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg
35 40 45
His Glu Val Ile Asn Ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe
50 55 60

Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly
65 70 75 80
Gln Leu Ile Tyr Glu Ser Ala Ile Thr Cys Glu Tyr Leu Asp Glu Ala
85 90 95
Tyr Pro Gly Lys Lys Leu Leu Pro Asp Asp Pro Tyr Glu Lys Ala Cys
100 105 110
Gln Lys Met Ile Leu Glu Leu Phe Ser Lys Val Pro Ser Leu Val Gly
115 120 125
Ser Phe Ile Arg Ser Gln Asn Lys Glu Asp Tyr Ala Gly Leu Lys Glu
130 135 140
Glu Phe Arg Lys Glu Phe Thr Lys Leu Glu Glu Val Leu Thr Asn Lys
145 150 155 160
Lys Thr Thr Phe Phe Gly Gly Asn Ser Ile Ser Met Ile Asp Tyr Leu
165 170 175
Ile Trp Pro Trp Phe Glu Arg Leu Glu Ala Met Lys Leu Asn Glu Cys
180 185 190
Val Asp His Thr Pro Lys Leu Lys Leu Trp Met Ala Ala Met Lys Glu
195 200 205
Asp Pro Thr Val Ser Ala Leu Leu Thr Ser Glu Lys Asp Trp Gln Gly
210 215 220
Phe Leu Glu Leu Tyr Leu Gln Asn Ser Pro Glu Ala Cys Asp Tyr Gly
225 230 235 240
Leu

<210> 195
<211> 138
<212> PRT
<213> Homo sapien

<400> 195
Gln Thr Lys Ile Leu Glu Glu Asp Leu Glu Gln Ile Lys Leu Ser Leu
1 5 10 15
Arg Glu Arg Gly Arg Glu Leu Thr Thr Gln Arg Gln Leu Met Gln Glu
20 25 30
Arg Ala Glu Glu Gly Lys Gly Pro Ser Lys Ala Gln Arg Gly Ser Leu
35 40 45
Glu His Met Lys Leu Ile Leu Arg Asp Lys Glu Lys Glu Val Glu Cys
50 55 60
Gln Gln Glu His Ile His Glu Leu Gln Glu Leu Lys Asp Gln Leu Glu
65 70 75 80
Gln Gln Leu Gln Gly Leu His Arg Lys Val Gly Glu Thr Ser Leu Leu
85 90 95
Leu Ser Gln Arg Glu Gln Glu Ile Val Val Leu Gln Gln Gln Leu Gln
100 105 110
Glu Ala Arg Glu Gln Gly Glu Leu Lys Glu Gln Ser Leu Gln Ser Gln
115 120 125
Leu Asp Glu Ala Gln Arg Ala Leu Ala Gln
130 135

<210> 196
<211> 102
<212> PRT
<213> Homo sapien

<400> 196
Met Ser Lys Arg Lys Ala Pro Gln Glu Thr Leu Asn Gly Gly Ile Thr
1 5 10 15
Asp Met Leu Thr Glu Leu Ala Asn Phe Glu Lys Asn Val Ser Gln Ala
20 25 30
Ile His Lys Tyr Asn Ala Tyr Arg Lys Ala Ala Ser Val Ile Ala Lys
35 40 45
Tyr Pro His Lys Ile Lys Ser Gly Ala Glu Ala Lys Lys Leu Pro Gly
50 55 60
Val Gly Thr Lys Ile Ala Glu Lys Ile Asp Glu Phe Leu Ala Thr Gly
65 70 75 80
Lys Leu Arg Lys Leu Glu Lys Ile Arg Gln Asp Asp Thr Ser Ser Ser
85 90 95
Ile Asn Phe Leu Thr Arg
100

<210> 197
<211> 138
<212> PRT
<213> Homo sapien

<400> 197
Glu Ala Asn Glu Val Thr Asp Ser Ala Tyr Met Gly Ser Glu Ser Thr
1 5 10 15
Tyr Ser Glu Cys Glu Thr Phe Thr Asp Glu Asp Thr Ser Thr Leu Val
20 25 30
His Pro Glu Leu Gln Pro Glu Gly Asp Ala Asp Ser Ala Gly Gly Ser
35 40 45
Ala Val Pro Ser Glu Cys Leu Asp Ala Met Glu Glu Pro Asp His Gly
50 55 60
Ala Leu Leu Leu Leu Pro Gly Arg Pro His Pro His Gly Gln Ser Val
65 70 75 80
Ile Thr Val Ile Gly Gly Glu Glu His Phe Glu Asp Tyr Gly Glu Gly
85 90 95
Ser Glu Ala Glu Leu Ser Pro Glu Thr Leu Cys Asn Gly Gln Leu Gly
100 105 110
Cys Ser Asp Pro Ala Phe Leu Thr Pro Ser Pro Thr Lys Arg Leu Ser
115 120 125
Ser Lys Lys Val Ala Arg Tyr Leu His Gln
130 135

<210> 198
<211> 100
<212> PRT
<213> Homo sapien

<400> 198
Met Gly Asp Val Lys Asn Phe Leu Tyr Ala Trp Cys Gly Lys Arg Lys
1 5 10 15
Met Thr Pro Ser Tyr Glu Ile Arg Ala Val Gly Asn Lys Asn Arg Gln
20 25 30
Lys Phe Met Cys Glu Val Gln Val Glu Gly Tyr Asn Tyr Thr Gly Met
35 40 45
Gly Asn Ser Thr Asn Lys Lys Asp Ala Gln Ser Asn Ala Ala Arg Asp
50 55 60

```
Phe Val Asn Tyr Leu Val Arg Ile Asn Glu Ile Lys Ser Glu Glu Val
65                  70                  75                  80
Pro Ala Phe Gly Val Ala Ser Pro Pro Pro Leu Thr Asp Thr Pro Asp
                85                  90                  95
Thr Thr Ala Asn
            100
```

<210> 199
<211> 127
<212> PRT
<213> Homo sapien

<400> 199

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

<210> 200
<211> 90
<212> PRT
<213> Homo sapien

<400> 200

```
Met Ala Cys Pro Leu Asp Gln Ala Ile Gly Leu Leu Val Ala Ile Phe
 1               5                  10                  15
His Lys Tyr Ser Gly Arg Glu Gly Asp Lys His Thr Leu Ser Lys Lys
            20                  25                  30
Glu Leu Lys Glu Leu Ile Gln Lys Glu Leu Thr Ile Gly Ser Lys Leu
        35                  40                  45
Gln Asp Ala Glu Ile Ala Arg Leu Met Glu Asp Leu Asp Arg Asn Lys
    50                  55                  60
Asp Gln Glu Val Asn Phe Gln Glu Tyr Val Thr Phe Leu Gly Ala Leu
65                  70                  75                  80
Ala Leu Ile Tyr Asn Glu Ala Leu Lys Gly
                85                  90
```

<210> 201
<211> 120
<212> PRT
<213> Homo sapien

<400> 201

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

<210> 202
<211> 177
<212> PRT
<213> Homo sapien

<400> 202
Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Ile
1 5 10 15
Lys Met Glu Glu Glu Ser Gly Ala Pro Gly Val Pro Ser Gly Asn Gly
20 25 30
Ala Pro Gly Pro Lys Gly Glu Gly Glu Arg Pro Ala Gln Asn Glu Lys
35 40 45
Arg Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr
50 55 60
Ala Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe
65 70 75 80
Asp Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly
85 90 95
Glu Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg
100 105 110
Gly Cys Ala Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala
115 120 125
Ala Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val
130 135 140
Lys Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Ala
145 150 155 160
Gly Arg Leu Gly Ser Thr Val Phe Val Ala Asn Leu Asp Tyr Lys Val
165 170 175
Gly

<210> 203
<211> 164
<212> PRT
<213> Homo sapien

<400> 203
Met Arg Leu Ala Val Gly Ala Leu Leu Val Cys Ala Val Leu Gly Leu

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


<210> 204
<211> 241
<212> PRT
<213> Homo sapien

<400> 204
Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro
 1               5                   10                  15
Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys
            20                  25                  30
Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg
        35                  40                  45
His Glu Val Ile Asn Ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe
    50                  55                  60
Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly
65                  70                  75                  80
Gln Leu Ile Tyr Glu Ser Ala Ile Thr Cys Glu Tyr Leu Asp Glu Ala
                85                  90                  95
Tyr Pro Gly Lys Lys Leu Leu Pro Asp Asp Pro Tyr Glu Lys Ala Cys
            100                 105                 110
Gln Lys Met Ile Leu Glu Leu Phe Ser Lys Val Pro Ser Leu Val Gly
        115                 120                 125
Ser Phe Ile Arg Ser Gln Asn Lys Glu Asp Tyr Asp Gly Leu Lys Glu
    130                 135                 140
Glu Phe Arg Lys Glu Phe Thr Lys Leu Glu Glu Val Leu Thr Asn Lys
145                 150                 155                 160
Lys Thr Thr Phe Phe Gly Gly Asn Ser Ile Ser Met Ile Asp Tyr Leu
                165                 170                 175
Ile Trp Pro Trp Phe Glu Arg Leu Glu Ala Met Lys Leu Asn Glu Cys
            180                 185                 190
Val Asp His Thr Pro Lys Leu Lys Leu Trp Met Ala Ala Met Lys Glu
        195                 200                 205
Asp Pro Thr Val Ser Ala Leu Leu Thr Ser Glu Lys Asp Trp Gln Gly
```

```
    210                 215                 220
Phe Leu Glu Leu Tyr Leu Gln Asn Ser Pro Glu Ala Cys Asp Tyr Gly
225                 230                 235                 240
Leu


      <210> 205
      <211> 160
      <212> PRT
      <213> Homo sapien

      <400> 205
Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu
 1               5                  10                  15
Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp
            20                  25                  30
Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys
        35                  40                  45
Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu
    50                  55                  60
Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Met Gln Ile Phe
65                  70                  75                  80
Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser
                85                  90                  95
Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile
            100                 105                 110
Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp
        115                 120                 125
Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His
    130                 135                 140
Leu Val Leu Arg Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu
145                 150                 155                 160

      <210> 206
      <211> 197
      <212> PRT
      <213> Homo sapien

      <400> 206
Thr Ser Pro Ser Glu Ala Cys Ala Pro Leu Leu Ile Ser Leu Ser Thr
 1               5                  10                  15
Leu Ile Tyr Asn Gly Ala Leu Pro Cys Gln Cys Asn Pro Gln Gly Ser
            20                  25                  30
Leu Ser Ser Glu Cys Asn Pro His Gly Gly Gln Cys Leu Cys Lys Pro
        35                  40                  45
Gly Val Val Gly Arg Arg Cys Asp Leu Cys Ala Pro Gly Tyr Tyr Gly
    50                  55                  60
Phe Gly Pro Thr Gly Cys Gln Gly Ala Cys Leu Gly Cys Arg Asp His
65                  70                  75                  80
Thr Gly Gly Glu His Cys Glu Arg Cys Ile Ala Gly Phe His Gly Asp
                85                  90                  95
Pro Arg Leu Pro Tyr Gly Gly Gln Cys Arg Pro Cys Pro Cys Pro Glu
            100                 105                 110
Gly Pro Gly Ser Gln Arg His Phe Ala Thr Ser Cys His Gln Asp Glu
        115                 120                 125
```

```
Tyr Ser Gln Gln Ile Val Cys His Cys Arg Ala Gly Tyr Thr Gly Leu
    130                 135                 140
Arg Cys Glu Ala Cys Ala Pro Gly His Phe Gly Asp Pro Ser Arg Pro
145                 150                 155                 160
Gly Gly Arg Cys Gln Leu Cys Glu Cys Ser Gly Asn Ile Asp Pro Met
                165                 170                 175
Asp Pro Asp Ala Cys Asp Pro His Thr Gly Gln Cys Leu Arg Cys Leu
            180                 185                 190
His His Thr Glu Gly
        195

      <210> 207
      <211> 175
      <212> PRT
      <213> Homo sapien

      <400> 207
Ile Ile Arg Gln Gln Gly Leu Ala Ser Tyr Asp Tyr Val Arg Arg Arg
 1               5                  10                  15
Leu Thr Ala Glu Asp Leu Phe Glu Ala Arg Ile Ile Ser Leu Glu Thr
            20                  25                  30
Tyr Asn Leu Leu Arg Glu Gly Thr Arg Ser Leu Arg Glu Ala Leu Glu
        35                  40                  45
Ala Glu Ser Ala Trp Cys Tyr Leu Tyr Gly Thr Gly Ser Val Ala Gly
    50                  55                  60
Val Tyr Leu Pro Gly Ser Arg Gln Thr Leu Ser Ile Tyr Gln Ala Leu
65                  70                  75                  80
Lys Lys Gly Leu Leu Ser Ala Glu Val Ala Arg Leu Leu Leu Glu Ala
                85                  90                  95
Gln Ala Ala Thr Gly Phe Leu Leu Asp Pro Val Lys Gly Glu Arg Leu
            100                 105                 110
Thr Val Asp Glu Ala Val Arg Lys Gly Leu Val Gly Pro Glu Leu His
        115                 120                 125
Asp Arg Leu Leu Ser Ala Glu Arg Ala Val Thr Gly Tyr Arg Asp Pro
    130                 135                 140
Tyr Thr Glu Gln Thr Ile Ser Leu Phe Gln Ala Met Lys Lys Glu Leu
145                 150                 155                 160
Ile Pro Thr Glu Glu Ala Leu Arg Leu Trp Met Pro Ser Trp Pro
                165                 170                 175

      <210> 208
      <211> 177
      <212> PRT
      <213> Homo sapien

      <400> 208
Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Ile
 1               5                  10                  15
Lys Met Glu Glu Glu Ser Gly Ala Pro Gly Val Pro Ser Gly Asn Gly
            20                  25                  30
Ala Pro Gly Pro Lys Gly Glu Gly Glu Arg Pro Ala Gln Asn Glu Lys
        35                  40                  45
Arg Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr
    50                  55                  60
Ala Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe
```

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

<210> 209
<211> 196
<212> PRT
<213> Homo sapien

<400> 209

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

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

<400> 210

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

<210> 211
<211> 92
<212> PRT
<213> Homo sapien

<400> 211
Met Glu Ser Pro Ser Ala Pro Pro His Arg Trp Cys Ile Pro Trp Gln
1 5 10 15
Arg Leu Leu Leu Thr Ala Ser Leu Leu Thr Phe Trp Asn Pro Pro Thr
20 25 30
Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly
35 40 45
Lys Glu Val Leu Leu Leu Val His Asn Leu Pro Gln His Leu Phe Gly
50 55 60
Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Arg Gln Ile Ile
65 70 75 80
Gly Tyr Val Ile Gly Thr Gln Gln Ala Thr Pro Gly
85 90

<210> 212
<211> 142
<212> PRT
<213> Homo sapien

<400> 212
Glu Lys Gln Lys Asn Lys Glu Phe Ser Gln Thr Leu Glu Asn Glu Lys
1 5 10 15
Asn Thr Leu Leu Ser Gln Ile Ser Thr Lys Asp Gly Glu Leu Lys Met
20 25 30
Leu Gln Glu Glu Val Thr Lys Met Asn Leu Leu Asn Gln Gln Ile Gln
35 40 45
Glu Glu Leu Ser Arg Val Thr Lys Leu Lys Glu Thr Ala Glu Glu Glu
50 55 60
Lys Asp Asp Leu Glu Glu Arg Leu Met Asn Gln Leu Ala Glu Leu Asn

```
65                  70                  75                  80
Gly Ser Ile Gly Asn Tyr Cys Gln Asp Val Thr Asp Ala Gln Ile Lys
                85                  90                  95
Asn Glu Leu Leu Glu Ser Glu Met Lys Asn Leu Lys Lys Cys Val Ser
            100                 105                 110
Glu Leu Glu Glu Glu Lys Gln Gln Leu Val Lys Glu Lys Thr Lys Val
        115                 120                 125
Glu Ser Glu Ile Arg Lys Glu Tyr Leu Glu Lys Ile Gln Gly
    130                 135                 140

      <210> 213
      <211> 142
      <212> PRT
      <213> Homo sapien

      <400> 213
Gly Gly Tyr Gly Gly Gly Tyr Gly Gly Val Leu Thr Ala Ser Asp Gly
 1               5                  10                  15
Leu Leu Ala Gly Asn Glu Lys Leu Thr Met Gln Asn Leu Asn Asp Arg
            20                  25                  30
Leu Ala Ser Tyr Leu Asp Lys Val Arg Ala Leu Glu Ala Ala Asn Gly
        35                  40                  45
Glu Leu Glu Val Lys Ile Arg Asp Trp Tyr Gln Lys Gln Gly Pro Gly
    50                  55                  60
Pro Ser Arg Asp Tyr Ser His Tyr Tyr Thr Thr Ile Gln Asp Leu Arg
65                  70                  75                  80
Asp Lys Ile Leu Gly Ala Thr Ile Glu Asn Ser Arg Ile Val Leu Gln
                85                  90                  95
Ile Asp Asn Ala Arg Leu Ala Ala Asp Asp Phe Arg Thr Lys Phe Glu
            100                 105                 110
Thr Glu Gln Ala Leu Arg Met Ser Val Glu Ala Asp Ile Asn Gly Leu
        115                 120                 125
Arg Arg Val Leu Asp Glu Leu Thr Leu Ala Arg Thr Asp Leu
    130                 135                 140

      <210> 214
      <211> 129
      <212> PRT
      <213> Homo sapien

      <400> 214
Val Met Arg Val Asp Phe Asn Val Pro Met Lys Asn Asn Gln Ile Thr
 1               5                  10                  15
Asn Asn Gln Arg Ile Lys Ala Ala Val Pro Ser Ile Lys Phe Cys Leu
            20                  25                  30
Asp Asn Gly Ala Lys Ser Val Val Leu Met Ser His Leu Gly Arg Pro
        35                  40                  45
Asp Gly Val Pro Met Pro Asp Lys Tyr Ser Leu Glu Pro Val Ala Val
    50                  55                  60
Glu Leu Arg Ser Leu Leu Gly Lys Asp Val Leu Phe Leu Lys Asp Cys
65                  70                  75                  80
Val Gly Pro Glu Val Glu Lys Ala Cys Ala Asn Pro Ala Ala Gly Ser
                85                  90                  95
Val Ile Leu Leu Glu Asn Leu Arg Phe His Val Glu Glu Glu Gly Lys
            100                 105                 110
```

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

<210> 215
<211> 148
<212> PRT
<213> Homo sapien

<400> 215
Met Ala Thr Leu Lys Glu Lys Leu Ile Ala Pro Val Ala Glu Glu Glu
1 5 10 15
Ala Thr Val Pro Asn Asn Lys Ile Thr Val Val Gly Val Gly Gln Val
20 25 30
Gly Met Ala Cys Ala Ile Ser Ile Leu Gly Lys Ser Leu Ala Asp Glu
35 40 45
Leu Ala Leu Val Asp Val Leu Glu Asp Lys Leu Lys Gly Glu Met Met
50 55 60
Asp Leu Gln His Gly Ser Leu Phe Leu Gln Thr Pro Lys Ile Val Ala
65 70 75 80
Asp Lys Asp Tyr Ser Val Thr Ala Asn Ser Lys Ile Val Val Val Thr
85 90 95
Ala Gly Val Arg Gln Gln Glu Gly Glu Ser Arg Leu Asn Leu Val Gln
100 105 110
Arg Asn Val Asn Val Phe Lys Phe Ile Ile Pro Gln Ile Val Lys Tyr
115 120 125
Ser Pro Asp Cys Ile Ile Ile Val Val Ser Asn Pro Val Asp Ile Leu
130 135 140
Thr Tyr Val Thr
145

<210> 216
<211> 527
<212> PRT
<213> Homo sapien

<400> 216
Gln Arg Ala Pro Gly Ile Glu Glu Lys Ala Ala Glu Asn Gly Ala Leu
1 5 10 15
Gly Ser Pro Glu Arg Glu Glu Lys Val Leu Glu Asn Gly Glu Leu Thr
20 25 30
Pro Pro Arg Arg Glu Glu Lys Ala Leu Glu Asn Gly Glu Leu Arg Ser
35 40 45
Pro Glu Ala Gly Glu Lys Val Leu Val Asn Gly Gly Leu Thr Pro Pro
50 55 60
Lys Ser Glu Asp Lys Val Ser Glu Asn Gly Gly Leu Arg Phe Pro Arg
65 70 75 80
Asn Thr Glu Arg Pro Pro Glu Thr Gly Pro Trp Arg Ala Pro Gly Pro
85 90 95
Trp Glu Lys Thr Pro Glu Ser Trp Gly Pro Ala Pro Thr Ile Gly Glu
100 105 110
Pro Ala Pro Glu Thr Ser Leu Glu Arg Ala Pro Ala Pro Ser Ala Val
115 120 125
Val Ser Ser Arg Asn Gly Gly Glu Thr Ala Pro Gly Pro Leu Gly Pro

```
    130                 135                 140
Ala Pro Lys Asn Gly Thr Leu Glu Pro Gly Thr Glu Arg Arg Ala Pro
145                 150                 155                 160
Glu Thr Gly Gly Ala Pro Arg Ala Pro Gly Ala Gly Arg Leu Asp Leu
                165                 170                 175
Gly Ser Gly Gly Arg Ala Pro Val Gly Thr Gly Thr Ala Pro Gly Gly
            180                 185                 190
Gly Pro Gly Ser Gly Val Asp Ala Lys Ala Gly Trp Val Asp Asn Thr
        195                 200                 205
Arg Pro Gln Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Glu Ala Gln
    210                 215                 220
Pro Arg Arg Leu Glu Pro Ala Pro Pro Arg Ala Arg Pro Glu Val Ala
225                 230                 235                 240
Pro Glu Gly Glu Pro Gly Ala Pro Asp Ser Arg Ala Gly Gly Asp Thr
                245                 250                 255
Ala Leu Ser Gly Asp Gly Asp Pro Pro Lys Pro Glu Arg Lys Gly Pro
            260                 265                 270
Glu Met Pro Arg Leu Phe Leu Asp Leu Gly Pro Pro Gln Gly Asn Ser
        275                 280                 285
Glu Gln Ile Lys Ala Arg Leu Ser Arg Leu Ser Leu Ala Leu Pro Pro
    290                 295                 300
Leu Thr Leu Thr Pro Phe Pro Gly Pro Gly Pro Arg Arg Pro Pro Trp
305                 310                 315                 320
Glu Gly Ala Asp Ala Gly Ala Ala Gly Gly Glu Ala Gly Gly Ala Gly
                325                 330                 335
Ala Pro Gly Pro Ala Glu Glu Asp Gly Glu Asp Glu Asp Glu Asp Glu
            340                 345                 350
Glu Glu Asp Glu Glu Ala Ala Ala Pro Gly Ala Ala Ala Gly Pro Arg
        355                 360                 365
Gly Pro Gly Arg Ala Arg Ala Ala Pro Val Pro Val Val Val Ser Ser
    370                 375                 380
Ala Asp Ala Asp Ala Ala Arg Pro Leu Arg Gly Leu Leu Lys Ser Pro
385                 390                 395                 400
Arg Gly Ala Asp Glu Pro Glu Asp Ser Glu Leu Glu Arg Lys Arg Lys
                405                 410                 415
Met Val Ser Phe His Gly Asp Val Thr Val Tyr Leu Phe Asp Gln Glu
            420                 425                 430
Thr Pro Thr Asn Glu Leu Ser Val Gln Ala Pro Pro Glu Gly Asp Thr
        435                 440                 445
Asp Pro Ser Thr Pro Pro Ala Pro Pro Thr Pro Pro His Pro Ala Thr
    450                 455                 460
Pro Gly Asp Gly Phe Pro Ser Asn Asp Ser Gly Phe Gly Gly Ser Phe
465                 470                 475                 480
Glu Trp Ala Glu Asp Phe Pro Leu Leu Pro Pro Pro Gly Pro Pro Leu
                485                 490                 495
Cys Phe Ser Arg Phe Ser Val Ser Pro Ala Leu Glu Thr Pro Gly Pro
            500                 505                 510
Pro Ala Arg Ala Pro Asp Ala Arg Pro Ala Gly Pro Val Glu Asn
        515                 520                 525
```

<210> 217
<211> 466
<212> DNA
<213> Homo sapien

<400> 217
gaatggtgcc tgtcctgctg tctctgctgc tgcttctggg tcctgctgtc ccccaggaga 60
accaagatgg tcgttactct ctgacctata tctacactgg gctgtccaag catgttgaag 120
acgtccccgc gtttcaggcc cttggctcac tcaatgacct ccagttcttt agatacaaca 180
gtaaagacag gaagtctcag cccatgggac tctggagaca ggtggaagga atggaggatt 240
ggaagcagga cagccaactt cagaaggcca gggaggacat ctttatggag accctgaaag 300
acatcgtgga gtattacaac gacagtaacg ggtctcacgt attgcaggga aggtttggtt 360
gtgagatcga gaataacaga agcagcggag cattctggaa atattactat gatggaaagg 420
actacattga attcaacaaa gaaatcccag cctgggtccc cttcga 466

<210> 218
<211> 381
<212> DNA
<213> Homo sapien

<400> 218
gagtttcctt cgcaagttca tgtggggtac cttcccaggc tgcctggctg accagctggt 60
tttaaagcgc cggggtaacc agttggagat ctgtgccgtg gtcctgaggc agttgtctcc 120
acacaagtac tacttcctcg tgggctacag tgaaactttg ctgtcctact tttacaaatg 180
tcctgtgcga ctccacctcc aaactgtgcc ctcaaaggtt gtgtataagt acctctagaa 240
caatcccctt ttttccatca agctgtagcc tgcagagaat ggaaacgtgg gaaaggaatg 300
gtatgtgggg gaaatgcatc ccctcagagg actgaggcat agtctctcat ctgctattga 360
ataaagacct tctatcttgt a 381

<210> 219
<211> 1293
<212> DNA
<213> Homo sapien

<400> 219
gaggggaggc gcatggcggg gatggcgctg gcgcgggcct ggaagcagat gtcctggttc 60
tactaccagt acctgctggt cacggcgctc tacatgctgg agccctggga gcggacggtg 120
ttcaattcca tgctggtttc cattgtgggg atggcactat acacaggata cgtcttcatg 180
ccccagcaca tcatggcgat attgcactac tttgaaatcg tacaatgacc aagatgcgac 240
caggatcaga ggttccttgg ggaagaccca ccctacgaag ttggaatgag accatcagat 300
gtgataagaa actcttctag atgtcaacat aaccaacctt ataaagacta aaattcatga 360
gtagaacagg aaaatcatcc tgactcatgt gttgtgttct ttatttttaa ttttcaaaga 420
ggctcttgta tagcagtttt tgtctatttt aacattgtag tcatttgtac tttgatatca 480
gtattttctt aacctttgtg actgtttcaa tattaccccc gtgaaagctt ttcttaatgt 540
aactttgagt acatttaat tgccttctat ttttaaaact caaaatcatt agttgggctt 600
tactgttctt gctattgtat ggcatataca tctgcctgga tatatttcta ctcttgacca 660
aagttttgta aagaacaata taagatttcg ggtaggggta tggggaggga agatatttta 720
ttgagaacta cttaacaaaa gatttatctg taagcttgaa ctcaggagta cagttttagc 780
tatctagact ctaacagctt ttgctttaaa attattaaag tgtttcttaa tgaaaaagaa 840
aagatcttgc taaagttaaa ataaggaaca tttcaccttt taaatattta attcttatgt 900
ggacttattt ccagaaaact ttggtgataa ttcttgagac aaaaggtggt taagtagcat 960
tattatgtaa tgcttatata ccatagagtt tttaatagaa gagaaatcca tttcctccga 1020
gggtcactat taacaatgta cttccttaaa tttagtttaa tgattgtaat gggtgctgca 1080
tttgcacatt gcattaagtt atgatgagac gaattgttgt taaaaattat agcaaaaaga 1140
aatgtaaact tggttaaaat cctttcactc tttgtattgt tttttttaag gtttttattc 1200
cttaaatgta aaatgactac ctaatttttt gatgtaaata cattaaattc aaagagaaaa 1260
aaaatcaaaa aaaaaaaaaa aaaaaaactc gag 1293

<210> 220
<211> 983

<212> DNA
<213> Homo sapien

<400> 220
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caggttattc tgatcctgcc gcctgtcttc cctgtaagag tggagcctcg aggtgtacct     60
taaagtgacc ggaatgttag agatgcaatt tgcagagctg gggcaaggaa gggctccttg    120
tcactgtagt tactttcctt gcagtggcca aatgcccaat aagaaggaat acatgaccac    180
tgctgtgggg agtcagcagg tgcgtgatgc agctggccac actccatcca cggccatgac    240
ataaaacaga caagaagtaa ggctggactg taacacctca aggcctgctc cagtgaccca    300
ctttcttcag agaggctcta ccacacacac aaccaccttc caaatttaca ctcagatcac    360
tacaccatgt ctcccaagtt aaaacatgta tccacctaga ctttaaatgt gctttgtaac    420
tgttgatggc actgtacaga gggccaaagt atttcccatc agatagcatt tttctgaacc    480
catgcctctt gggacgagat cacaggactt gacccatcat caaataggac caggtgacct    540
acagagacat cacaatgatg gcttcctaca gtcaagtcca tttccaataa tgctctcatc    600
taagagaacc catgaacctt atttgaatcc tggttcaaac aaaaacctta aattatttat    660
gagacaatta taaacttgat agattttgat gtgtgaaggt atttatgaat atttttagtc    720
agtgatggta tactgttaag gaaaaggttc atattttagg gacaaaggct gaaacattta    780
tggacagagt gatatgatat ctgggatttg ttttaggatg aagtgggagg gaggaaatga    840
atggaaatag tgttgaaaca gtattggcca cgagtcagct attgtgtgct aagacgctcc    900
tcacaccagt ctactctgta tgtgtttgaa tatctctgta ataaacttaa caaggaaaaa    960
aaaaaaaaaa aaaaaaactc gag                                            983
```

<210> 221
<211> 373
<212> DNA
<213> Homo sapien

<400> 221
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cattttatgg gttaattttt tattaaatag caataagata cttttataac tcaataaaat     60
tattcaatga tacattcgga aaataaatgt ataaaatatg aaaaagtact aaaaagcatt    120
tttcagtact tttaggtaag attaatccaa ctaaacacta gcatatgtta tacagtaata    180
ataaggggaa aatacaataa tgttgagaaa gcaaactcaa agcatagatc aatgaaaaaa    240
ttgagaaatg gacataaatg atttagtatt tttaaagaga gtgaaaaatc attattttat    300
gcttttgtgt agcgttagat gaattaaata acatatgcac atatagcttt gcgatacaaa    360
tttccagacc ata                                                       373
```

<210> 222
<211> 544
<212> DNA
<213> Homo sapien

<400> 222
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cagagatgct gctgctacaa aggatcggtg taagcagtta acccaggaaa tgatgacaga     60
gaaagaaaga agcaatgtgg ttataacaag gatgaaagat cgaattggaa cattagaaaa    120
ggaacataat gtatttcaaa acaaaataca tgtcagttat caagagactc aacagatgca    180
gatgaagttt cagcaagttc gtgagcagat ggaggcagag atagctcact tgaagcagga    240
aaatggtata ctgagagatg cagtcagcaa cactacaaat caactggaaa gcaagcagtc    300
tgcagaacta aataaactac gccaggatta tgctaggttg gtgaatgagc tgactgagaa    360
aacaggaaag ctacagcaag aggaagtcca aaagaagaat gctgagcaag cagctactca    420
gttgaaggtt caactacaag aagctgagag aaggtgggaa gaagttcaga gctacatcag    480
gaagagaaca gcggaacatg aggcagcaca gctagattta cagagtaaat ttgtggccaa    540
agaa                                                                 544
```

<210> 223
<211> 316

<212> DNA
<213> Homo sapien

<400> 223
gaggcaaggg atatgcttta gtgcctatta tagttaattc ttcaactcca aagtctaaaa 60
cagttgaatc tgctgaagga aaatctgaag aagtaaatga aacattagtt atacccactg 120
aggaagcaga aatggaagaa agtggacgaa gtgcaactcc tgttaactgt gaacagcctg 180
atatcttggt ttcttctaca ccaataaatg aaggacagac tgtgttagac aaggtggctg 240
agcagtgtga acctgctgaa agtcagccag aagcacttct gagaggaaga tgtttgcaag 300
gtaactctaa cagttg 316

<210> 224
<211> 1583
<212> DNA
<213> Homo sapien

<400> 224
cagaccacgt ctgccctcgc cgctctagcc ctgcgcccca gcccggccgc ggcacctccg 60
cctcgccgcc gctaggtcgg ccggctccgc ccggctgccg cctaggatga atatcatgga 120
cttcaacgtg aagaagctgg cggccgacgc aggcaccttc ctcagtcgcg ccgtgcagtt 180
cacagaagaa aagcttggcc aggctgagaa gacagaattg gatgctcact tagagaacct 240
ccttagcaaa gctgaatgta ccaaaatatg gacagaaaaa ataatgaaac aaactgaagt 300
gttattgcag ccaaatccaa atgccaggat agaagaattt gtttatgaga aactggatag 360
aaaagctcca agtcgtataa acaacccaga acttttggga caatatatga ttgatgcagg 420
gactgagttt ggcccaggaa cagcttatgg taatgccctt attaaatgtg gagaaaccca 480
aaaaagaatt ggaacagcag acagagaact gattcaaacg tcagccttaa attttcttac 540
tcctttaaga aactttatag aaggagatta caaaacaatt gctaaagaaa ggaaactatt 600
gcaaaataag agactggatt tggatgctgc aaaaacgaga ctaaaaaagg caaaagctgc 660
agaaactaga aattcatctg aacaggaatt aagaataact caaagtgaat ttgatcgtca 720
agcagagatt accagacttc tgctagaggg aatcagcagt acacatgccc atcaccttcg 780
ctgtctgaat gactttgtag aagcccagat gacttactat gcacagtgtt accagtatat 840
gttggacctc cagaaacaac tgggaagttt tccatccaat tatcttagta acaacaatca 900
gacttctgtg acacctgtac catcagtttt accaaatgcg attggttctt ctgccatggc 960
ttcaacaagt ggcctagtaa tcacctctcc ttccaacctc agtgacctta aggagtgtag 1020
tggcagcaga aaggccaggg ttctctatga ttatgatgca gcaaacagta ctgaattatc 1080
acttctggca gatgaggtga tcactgtgtt cagtgttgtt ggaatggatt cagactggct 1140
aatgggggaa aggggaaacc agaagggcaa ggtgccaatt acctacttag aactgctcaa 1200
ttaagtaggt ggactatgga aaggttgccc atcatgactt tgtatttata tacaattaac 1260
tctaaataaa gcaggttaag tatcttccat gttaatgtgt taagagactg aaaataccag 1320
ccatcagaaa ctggcctttt tgccaataaa gttgcatggt aaatatttca ttacagaatt 1380
tatgttagag ctttcatgcc aagaatgttt tcttacaaaa ttctcttttt attgaggttt 1440
cactaataag cagcttctac ttttgagcct caacttaaag cagaactgtt ttttactgga 1500
tttttcatta acagcaagct tttttttta tgtaaaataa atctattgtg aattgaaaaa 1560
aaaaaaaaaa aaaaaaactc gag 1583

<210> 225
<211> 491
<212> DNA
<213> Homo sapien

<400> 225
gaacaacatc atcttgaatc actagataga ctcttgacgg aaagcaaagg ggaaatgaaa 60
aaggaaaata tgaagaaaga tgaagcttta aaagcattac agaaccaagt atctgaagaa 120
acaatcaagg ttaggcaact agattcagca ttggaaattt gtaaggaaga acttgtcttg 180
catttgaatc aattggaagg aaataaggaa aagtttgaaa aacagttaaa gaagaaatct 240

gaagaggtat attgtttaca gaaagagcta aagataaaaa atcacagtct tcaagagact 300
tctgagcaaa acgttattct acagcatact cttcagcaac agcagcaaat gttacaacaa 360
gagacaatta gaaatggaga gctagaagat actcaaacta aacttgaaaa acaggtgtca 420
aaactggaac aagaacttca aaaacaaagg gaaagttcag ctgaaaagtt gagaaaaatg 480
gaggagaaat g 491

<210> 226
<211> 483
<212> DNA
<213> Homo sapien

<400> 226
cagccgcacg ccgcggagca ggggctcgga ggtcccggga ttacggtgct cgagcacgct 60
ggtgggaaag gacccgggac ttgaacagtg ttgtgcggcg ccatgcaggt ctccagcctc 120
aatgaggtga agatttacag cctcagctgc ggcaagtccc ttcctgagtg gctttctgat 180
aggaagaaga gagcgctaca gaagaaagat gtagatgtcc gtaggagaat tgaacttatt 240
caggactttg aaatgcctac tgtgtgtacc actattaagg tgtcaaaaga tggacagtac 300
attttagcaa ctggaacata taaacctcgg gttcgatgtt atgacaccta tcaattatcc 360
ttgaagtttg aaaggtgttt agattcagaa gttgtcacct ttgaaatttt gtctgatgac 420
tactcaaaga ttgtcttctt acataatgat agatacattg aatttcattc gcaatcaggt 480
ttt 483

<210> 227
<211> 486
<212> DNA
<213> Homo sapien

<400> 227
gagcctcgct aagctccgac tctgggcggc accgggcgtc ccacgatgcc gaagaacaag 60
aagcggaaca ctccccaccg cggtagcagt gctggcggcg gcgggtcagg agcagccgca 120
gcgacggcgg cgacagcagg tggccagcat cgaaatgttc agccttttag tgatgaagat 180
gcatcaattg aaacagtgag ccattgcagt ggttatagcg atccttccag ttttgctgaa 240
gatggaccag aagtccttga tgaggaagga actcaagaag acctagagta caagttgaag 300
ggattaattg acctaaccct ggataagagt gcgaagacaa ggcaagcagc tcttgaaggt 360
attaaaaatg cactggcttc aaaaatgctg tatgaattta ttctggaaag gagaatgact 420
ttaactgata gcattgaacg ctgcctgaaa aaaggtaaga gtgatgagca acgtgcagct 480
gcagcg 486

<210> 228
<211> 494
<212> DNA
<213> Homo sapien

<400> 228
gaggccagga ctccgggaat gcgagcaggc cccttattct cccagtggcc tcggtctgtc 60
cccacagcgg cccggtcagg gttgcccgag ccccaaggcg gggggcggca ccggggtgct 120
gaaagggaca gaatgctttg acctccaagc tgttttaaat ctagtagata agccagatcc 180
tgtgttgcca taagcccttg gcccacattt aagtgggaat gcagctagct tggatgtctg 240
aaactttgta agcgccttct gtctgaatcc tgaacacagg caccaagact actgaagaag 300
ctcgtcattc ttgtgcaggg atagccacac aagcaaacat gtttgcaaaa cttgaaagaa 360
agaaaattgc agaaagaaga cttgctgttc ttaagaggcc caggaaggtg ctacttagga 420
atcccaccgg cttgtgaagc aagggaatca agtttgcctt caatggggaa cttgacttca 480
ggaaaatgaa cttt 494

<210> 229

<211> 465
<212> DNA
<213> Homo sapien

<400> 229
gtcagagagc tggtataacc tcctgttgga catgcagaac cgactcaata aggtcatcaa 60
aagcgtgggc aagattgagc actccttctg gagatccttt cacactgagc gaaagacaga 120
accagccaca ggcttcatcg atggtgatct gattgaaagt ttcctagata tcagccgccc 180
taagatgcag gaggttgtgg caaacttgca gtatgatgat ggcagtggta tgaagcggga 240
ggcaactgca gatgacctca tcaaagtcgt ggaggaacta actcggatcc attagccaag 300
gacaggatct cttttcctga ccctcctaaa ggcgttgccc tcctatcctc ccttccttgc 360
ccacccttgg tttctttggc atgggaaggt tttccttaac cacttgccct agagccacca 420
gtgaccttgt gtggaaacag ggtttttttt acttaaaaca gttca 465

<210> 230
<211> 495
<212> DNA
<213> Homo sapien

<400> 230
caggggaaag ggtgtttggc cttgaccagc cactgctgac ctcaatctca gacctacaga 60
tggtgaatat ctccctgcga gtgttgtctc gacccaatgc tcaggagctt cctagcatgt 120
accagcgcct agggctggac tacgaggaac gagtgttgcc gtccattgcc aacgaggtgc 180
tcaagagtgt ggtggccaag ttcaatgcct cacagctgat cacccagcgg gcccaggtat 240
ccctgttgat ccgccgggag ctgacagaaa gggccaaagg acttcagcct catcctggat 300
gatgtggcca tcacagactt gagctttagc cgagaagtac acaagctgcc tgtaagaaac 360
ccaaccaagt ggggtgaatt ccaaaaaccc gtgggggtga agggcttctt aagaatgcaa 420
ggaaggagga aaagaattcc atgggggggg ggttccttaa cccaggaaca ggggtttccc 480
ttgaattttt ttcca 495

<210> 231
<211> 498
<212> DNA
<213> Homo sapien

<400> 231
ggcagcttct gagaccaggg ttgctccgtc cgtgctccgc ctcgccatga cttcctacag 60
ctatcgccag tcgtcggcca cgtcgtcctt cggaggcctg ggcggcggct ccgtgcgttt 120
tgggccgggg gtcgcttttc gcgcgcccag cattcacggg ggctccggcg gccgcggcgt 180
atccgtgtcc tccgcccgct ttgtgtcctc gtcctcctcg gggggctacg gcggcggcta 240
cggcggcgtc ctgaccgcgt ccgacgggct gctggcgggc aacgagaagc taaccatgca 300
gaacctcaac gaccgcctgc ctcctacctg gacaaagtgc gcgccctgga agcgggcaac 360
ggcgaactta gaggtgaaag aatcccgcga actggtacca aaaacaaggg gcctggggcc 420
ttccgcgact tacagccaac ttactacacc gaacattcaa gaacttgcgg gaacaaaaat 480
ttttggtgcc acccattt 498

<210> 232
<211> 465
<212> DNA
<213> Homo sapien

<400> 232
caggccggcc gagtaggaaa gctggaggcg cgggtgggga acatgtctga gtcggagctc 60
ggcaggaagt gggaccggtg tctggcggat gcggtcgtga agataggtac tggttttgga 120
ttaggaattg ttttctcact taccttcttt aaaagaagaa tgtggccatt agccttcggt 180

tctggcatgg gattaggaat ggcttattcc aactgtcagc atgatttcca ggctccatat 240
cttctacatg gaaaatatgt caaagagcag gagcagtgac ttcacctgag aacatcccag 300
cgggaggaca agagaaaatc atgtttattc ctcaggaata cttgaagtgc cctggagtaa 360
actgccattc ttctgtaaca atggtatcag taatgcttta aactccagca cctggttatg 420
catttgaaac ccaagtctgg ttcttggttt ggattttctc tctgg 465

<210> 233
<211> 366
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(366)
<223> n = A,T,C or G

<400> 233
cagtaaaaaa ggttatgttt tattaattgc tggacaaccg tgggaaaaca aataagcaat 60
tgacaccacc aaattcttat tacattcaan ataaaanatt tattcacacc acaaaaagat 120
aatcacaaca aaatatacac taacttaaaa aacaaaagat tatagtgaca taaaatgtta 180
tattctcttt ttaagtgggt aaaagtattt tgtttgcttc tacataaatt tctattcatg 240
ananaataac aaatattaaa atacagtgat agtttgcatt tcttctatag aatgaacata 300
gacataaccc tgaagctttt agtttacagg gagtttccat gaagccacaa actaaactaa 360
ttatca 366

<210> 234
<211> 379
<212> DNA
<213> Homo sapien

<400> 234
gagggcagcc ctcctacctg cgcacgtggt gccgccgctg ctgcctcccg ctcgccctga 60
acccagtgcc tgcagccatg gctcccggcc agctcgcctt atttagtgtc tctgacaaaa 120
ccggccttgt ggaatttgca agaaacctga ccgctcttgg tttgaatctg gtcgcttccg 180
gagggactgc aaaagctctc agggatgctg gtctggcagt cacagatgtc tctgagttga 240
cgggatttct gaaatgttgg ggggacgtgt gaaaactttg catcctgcac gatcccatgc 300
tggaatccta gctcctaata ttcagaagat aatgcttgac atgcgccaca cttgattcaa 360
tcttataaca attgttgcc 379

<210> 235
<211> 406
<212> DNA
<213> Homo sapien

<400> 235
caggctgcac catgtacccc accttcagtt taaaagaaaa aaaaaatccc cttcactcct 60
actgggaggt gggacccctt tcattttcag ttttgctcat ctaggaaaaa taaggctttg 120
gtttccagtt taattgtttt tgaccttcta aaatgttttt atgttagcac tgatagttgg 180
cattactgtt gttaagcact gtgttccaga ccgtgtctga cttagtgtaa cctaggagat 240
tttatagttt tattttaatg aaaccctgat tgacgcacag cagtggggag aacagcgtct 300
tttacctgtc accgaagcca ggaagccccg tttgtaagcg tgtgttgtgg tgctttattg 360
tacatcctcc agtggcgttc tttttactct aatgttcttt tggttt 406

<210> 236
<211> 278

<212> DNA
<213> Homo sapien

<400> 236
gagattagca cctgtgaaca atgcgttctc tgatgacact ctgagcatgg accaacgcct 60
tcttaagcta attctgcaaa atcacatatt gaaagtaaaa gttggcctta gcgacctcta 120
caatggacag atactggaaa ccattggagg caaacaactc cgagtctttg tgtatcggac 180
ggctatctgc atagaaaact catgcatggt gagaggaagc aagcagggaa ggaacggtgc 240
cattcacata ttccgagaga tcatccaacc agcagaat 278

<210> 237
<211> 322
<212> DNA
<213> Homo sapien

<400> 237
cagggccgtg gcggaggagg agcgctgcac ggtggagcgt cgggccgacc tcacctacgc 60
ggagttcgtg cagcagtacg tgcgcccctg atcgcggagg tcgcgtcctg ttcaccggcc 120
cgtctgcccc gaccgcccaa ggccgccttc ccctgacctc gcgcgcacgc gtggggctgg 180
ggcggcgagg ctggcggtcc ggcctggccg cgactctgcc cttctttcca gaggttccgg 240
gccctgtgct cccgcgacag gttgctggct tcgtttgggg acagagtggt ccggtgagca 300
ccgccaacac ctactcctac ct 322

<210> 238
<211> 613
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (399)
<223> n=A,T,C or G

<400> 238
gaattcggca ccagccttct tggatcagga ccagtctcca ccccgtttct acagtggaga 60
tcagcctcct tcttatcttg gtgcaagtgt ggataaactc catcaccctt tagaatttgc 120
agacaaatct cccacacctc ctaatttacc tagcgataaa atctaccctc cttctgggtc 180
ccccgaagag aataccagca cagccaccat gacttacatg acaactactc cagcaacagc 240
ccaaatgagc accaaggaag ccagctggga tgtggctgaa caacccacca ctgctgattt 300
tgctgctgcc acacttcagc gcacgcacag aactaatcgt ccccttcccc ctccgccttc 360
ccagagatct gcagagcagc caccagttgt ggggcaggna caagcagcaa ccaatatagg 420
attaaataat tcccacaagg ttcaaggagt agttccagtt ccagagaggc cacctgaacc 480
tcgagccatg gatgaccctg cgtctgcctt catcagtgac agtggtgctg ctgctgctca 540
gtgtcccatg gctacagctg tccagccagg cctgcctgag aaagtgcggg acggtgcccg 600
ggtcccgctg ctg 613

<210> 239
<211> 613
<212> DNA
<213> Homo sapiens

<400> 239
gaattcggca ccaggggaca ctggtgctga gctggatgat gatcagcact ggtctgacag 60
cccgtcggat gctgacagag agctgcgttt gccgtgccca gctgaggggg aagcagagct 120

ggagctgagg gtgtcggaag atgaggagaa gctgcccgcc tcaccgaagc accaagagag 180
aggtccctcc caagccacca gccccatccg gtctccccag gaatcagctc ttctgttcat 240
tccagtccac agcccctcaa cagaggggcc ccaactccca cctgtccctg ccgccaccca 300
ggagaaatca cctgaggagc gccttttccc tgagcctttg ctccccaaag agaagcccaa 360
agctgatgcc ccctcggatc tgaaagctgt gcactctccc atccgatcac agccagtgac 420
cctgccagaa gctaggactc ctgtctcacc agggagcccg cagccccagc cacccgtggc 480
ggcctccacg cccccaccca gcgaggtctc cagagccttc tctctcctgt gcaaaatggc 540
aactcttaag gaaaaactca ttgcaccagt tgcggaagaa gaggcaacag ttccaaacaa 600
taagatcact gta 613

<210> 240
<211> 585
<212> DNA
<213> Homo sapiens

<400> 240
gaattcggca cgaggtgaga tctacgatga actttaagat tggaggtgtg acagaacgca 60
tgccaacccc agttattaaa gcttttggca tcttgaagcg agcggccgct gaagtaaacc 120
aggattatgg tcttgatcca aagattgcta atgcaataat gaaggcagca gatgaggtag 180
ctgaaggtaa attaaatgat cattttcctc tcgtggtatg gcagactgga tcaggaactc 240
agacaaatat gaatgtaaat gaagtcatta gcaatagagc aattgaaatg ttaggaggtg 300
aacttggcag caagatacct gtgcatccca acgatcatgt taataaaagc cagagctcaa 360
atgatacttt tcccacagca atgcacattg ctgctgcaat agaagttcat gaagtactgt 420
taccaggact acagaagtta catgatgctc ttgatgcaaa atccaaagag tttgcacaga 480
tcatcaagat tggacgtact catactcagg atgctgttcc acttactctt gggcaggaat 540
ttagtggtta tgttcaacaa gtaaaatatg caatgacaag aataa 585

<210> 241
<211> 566
<212> DNA
<213> Homo sapiens

<400> 241
gaattcggca ccaggcgagc tgcacctcga ggtgaaggcc tcactgatga acgatgactt 60
cgagaagatc aagaactggc agaaggaagc ctttcacaag cagatgatgg gcggcttcaa 120
ggagaccaag gaagctgagg acggctttcg gaaggcacag aagccctggg ccaagaagct 180
gaaagaggta gaagcagcaa agaaagccca ccatgcagcg tgcaaagagg agaagctggc 240
tatctcacga gaagccaaca gcaaggcaga cccatccctc aaccctgaac agctcaagaa 300
attgcaagac aaaatagaaa agtgcaagca agatgttctt aagaccaaag agaagtatga 360
gaagtccctg aaggaactcg accagggcac accccagtac atggagaaca tggagcaggt 420
gtttgagcag tgccagcagt tcgaggagaa acgccttcgc ttcttccggg aggttctgct 480
ggaggttcag aagcacctag acctgtccaa tgtggctggc tacaaagcca tttaccatga 540
cctggagcag agcatcagag cagctg 566

<210> 242
<211> 556
<212> DNA
<213> Homo sapiens

<400> 242
gaattcggca cgagcaaagg tgaagcagga catgcctccg cccgggggct atgggcccat 60
cgactacaaa cggaacttgc cgcgtcgagg actgtcgggc tacagcatgc tggccatagg 120
gattggaacc ctgatctacg ggcactggag cataatgaag tggaaccgtg agcgcaggcg 180
cctacaaatc gaggacttcg aggctcgcat cgcgctgttg ccactgttac aggcagaaac 240
cgaccggagg accttgcaga tgcttcggga gaacctggag gaggaggcca tcatcatgaa 300

ggacgtgccc gactggaagg tgggggagtc tgtgttccac acaacccgct gggtgccccc 360
cttgatcggg gagctgtacg ggctgcgcac cacagaggag gctctccatg ccagccacgg 420
cttcatgtgg tacacgtagg ccctgtgccc tccggccacc tggatccctg cccctcccca 480
ctgggacgga ataaatgctc tgcagacctg gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 540
aaaaaaaaaa ctcgag 556

<210> 243
<211> 591
<212> DNA
<213> Homo sapiens

<400> 243
gtctatgttt gcagaaatac agatccaaga caaagacagg atgggcactg ctggaaaagt 60
tattaaatgc aaagcagctg tgctttggga gcagaagcaa cccttctcca ttgaggaaat 120
agaagttgcc ccaccaaaga ctaaagaagt tcgcattaag attttggcca caggaatctg 180
tcgcacagat gaccatgtga taaaaggaac aatggtgtcc aagtttccag tgattgtggg 240
acatgaggca actgggattg tagagagcat tggagaagga gtgactacag tgaaaccagg 300
tgacaaagtc atccctctct ttctgccaca atgtagagaa tgcaatgctt gtcgcaaccc 360
agatggcaac ctttgcatta ggagcgatat tactggtcgt ggagtactgg ctgatggcac 420
caccagattt acatgcaagg gcaaaccagt ccaccacttc atgaacacca gtacatttac 480
cgagtacaca gtggtggatg aatcttctgt tgctaagatt gatgatgcag ctcctcctga 540
gaaagtctgt ttaattggct gtgggttttc cactggatat ggcgctgctg t 591

<210> 244
<211> 594
<212> DNA
<213> Homo sapiens

<400> 244
gaattcggca cgagaacaga gtgaactgag catcagtcag aaaaagtcta tgtttgcaga 60
aatacagatc caagacaaag acaggatggg cactgctgga aaagttatta aatgcaaagc 120
agctgtgctt tgggagcaga agcaaccctt ctccattgag gaaatagaag ttgccccacc 180
aaagactaaa gaagttcgca ttaagatttt ggccacagga atctgtcgca cagatgacca 240
tgtgataaaa ggaacaatgg tgtccaagtt tccagtgatt gtgggacatg aggcaactgg 300
gattgtagag agcattggag aaggagtgac tacagtgaaa ccaggtgaca aagtcatccc 360
tctctttctg ccacaatgta gagaatgcaa tgcttgtcgc aacccagatg gcaacctttg 420
cattaggagc gatattactg gtcgtggagt actggctgat ggcaccacca gatttacatg 480
caagggcaaa ccagtccacc acttcatgaa caccagtaca tttaccgagt acacagtggt 540
ggatgaatct tctgttgcta agattgatga tgcagctcct cctgagaaag tctg 594

<210> 245
<211> 615
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (105)
<223> n=A,T,C or G

<400> 245
gtccctttcc tctgctgccg ctcggtcacg cttgtgcccg aaggaggaaa cagtgacaga 60
cctggagact gcagttctct atccttccac agctctttca ccatnctgga tcacttcctt 120
tgaatgcaga agcttgctgg ccaaaagatg tgggaattgt tgcccttgag atctattttc 180
cttctcaata tgttgatcaa gcagagttgg aaaaatatga tggtgtagat gctggaaagt 240

ataccattgg cttgggccag gccaagatgg gcttctgcac agatagagaa gatattaact 300
ctctttgcat gactgtggtt cagaatctta tggagagaaa taacctttcc tatgattgca 360
ttgggcggct ggaagttgga acagagacaa tcatcgacaa atcaaagtct gtgaagacta 420
atttgatgca gctgtttgaa gagtctggga atacagatat agaaggaatc gacacaacta 480
atgcatgcta tggaggcaca gctgctgtct tcaatgcttg ttaactggat tgagtccagc 540
tcttgggatg gacggtatgc cctggtaagt tgcaggagat attgctgtat atgccacagg 600
aaatgctaga cctac 615

<210> 246
<211> 546
<212> DNA
<213> Homo sapiens

<400> 246
gaattcggca ccaggctgcc tcccgctcgc cctgaaccca gtgcctgcag ccatggctcc 60
cggccagctc gccttattta gtgtctctgc aaaaccggcc ttgtgaattt gcaagaaacc 120
tgaccgctct tggtttgaat ctggtcgctt ccggagggac tgcaaaagct ctcagggatg 180
ctggtctggc agtcagagat gtctctgagt tgacgggatt tcctgaaatg ttggggggac 240
gtgtgaaaac tttgcatcct gcagtccatg ctggaatcct agctcgtaat attccagaag 300
ataatgctga catggccaga cttgatttca atcttataag agttgttgcc tgcaatctct 360
atccctttgt aaagacagtg gcttctccag gtgtaactgt tgaggaggct gtggagcaaa 420
ttgacattgg tggagtaacc ttactgagag ctgcagccaa aaaccacgct cgagtgacag 480
tggtgtgtga accagaggac tatgtgggtg ggtgtccacg gagatgcaga gctccgagag 540
taagga 546

<210> 247
<211> 564
<212> DNA
<213> Homo sapiens

<400> 247
gaattcggca ccagagatca cgtgcagtga gatgcagcaa aaagttgaac ttctgagata 60
tgaatctgaa aagcttcaac aggaaaattc tattttgaga aatgaaatta ctactttaaa 120
tgaagaagat agcatttcta acctgaaatt agggacatta aatggatctc aggaagaaat 180
gtggcaaaaa acggaaactg taaaacaaga aaatgctgca gttcagaaga tggttgaaaa 240
tttaaagaaa cagatttcag aattaaaaat caaaaaccaa caattggatt tggaaaatac 300
agaacttagc caaaagaact ctcaaaacca ggaaaaactg caagaactta atcaacgtct 360
aacagaaatg ctatgccaga aggaaaaaga gccaggaaac agtgcattgg aggaacggga 420
acaagagaag tttaatctga aagaagaact ggaacgttgt aaagtgcagt cctccacttt 480
agtgtcttct ctggaggcgg agctctctga agttaaaata cagacccata ttgtgcaaca 540
ggaaaaccac cttctcaaag atga 564

<210> 248
<211> 434
<212> DNA
<213> Homo sapiens

<400> 248
gttcttgttt gtggatcgct gtgatcgtca cttgacaatg cagatcttcg tgaagactct 60
gactggtaag accatcaccc tcgaggttga gcccagtgac accatcgaga atgtcaaggc 120
aaagatccaa gataaggaag gcatccctcc tgaccagcag aggctgatct ttgctggaaa 180
acagctggaa gatgggcgca ccctgtctga ctacaacatc cagaaagagt ccaccctgca 240
cctggtgctc cgtctcagag gtgggatgca aatcttcgtg aagacactca ctggcaagac 300
catcacccctt gaggtggagc ccagtgacac catcgagaac gtcaaagcaa agatccagga 360
caaggaaggc attcctcctg accagcagag gttgatcttt gccggaaagc cagcctggga 420

agatggggcc gcca 434

<210> 249
<211> 416
<212> DNA
<213> Homo sapiens

<400> 249
gcgggcccag gaggcggcgg cggcggcggc ggacgggccc cccgcggcag acggcgagga 60
cggacaggac ccgcacagca agcacctgta cacggccgac atgttcacgc acgggatcca 120
gagcgccgcg cacttcgtca tgttcttcgc gccctggtgt ggacactgcc agcggctgca 180
gccgacttgg aatgacctgg gagacaaata caacagcatg gaagatgcca aagtctatgt 240
ggctaaagtg gactgcacgg cccactccga cgtgtgctcc gcccaggggg tgcgaggata 300
ccccaccta aagcttttca agccaggcca agaagctgtg aagtaccagg gtcctcggga 360
cttccagaca ctggaaaact ggatgctgca gacactgaac gaggagccag tgacac 416

<210> 250
<211> 504
<212> DNA
<213> Homo sapiens

<400> 250
gaattcggca cgaggcgggt aacgttatag tatttgtcag aagttggggt ctccgtgggc 60
attgtgatcc gtcccaggca gtggattagg aggccagaag gagatccctt ccacggtgct 120
aggctgagat ggatcctctc agggcccaac agctggctgc ggagctggag gtggagatga 180
tggccgatat gtacaacaga atgaccagtg cctgccaccg gaagtgtgtg cctcctcact 240
acaaggaagc agagctctcc aagggcgagt ctgtgtgcct ggaccgatgt gtctctaagt 300
acctggacat ccatgagcgg atgggcaaaa agttgacaga gttgtctatg caggatgaag 360
agctgatgaa gagggtgcag cagagctctg ggcctgcatg aggtccctgt cagtatacac 420
cctggggtgt accccacccc ttcccacttt aataaacgtg ctccctgttg ggtgtcatct 480
gtgaagactg ccaggcctag ctct 504

<210> 251
<211> 607
<212> DNA
<213> Homo sapiens

<400> 251
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tactctgctc aaccatatgt taattcatgg tctgtcttgt ccatattgcc gttcaacttt 120
caatgatgtg gaaaagatgg ccgcacacat gcggatggtt cacattgatg aagagatggg 180
acctaaaaca gattctactt tgagttttga tttgacattg cagcagggta gtcacactaa 240
catccatctc ctggtaacta catacaatct gagggatgcc ccagctgaat ctgttgctta 300
ccatgcccaa aataatcctc cagttcctcc aaagccacag ccaaaggttc aggaaaaggc 360
agatatccct gtaaaaagtt cacctcaagc tgcagtgccc tataaaaaag atgttgggaa 420
aaccctttgt cctctttgct tttcaatcct aaaaggaccc atatctgatg cacttgcaca 480
tcacttacga gagaggcacc aagttattca gacggttcat ccagttgaga aaaagctcac 540
ctacaaatgt atccattgcc ttggtgtgta taccagcaac atgaccgcct caactatcac 600
tctgcat 607

<210> 252
<211> 618
<212> DNA
<213> Homo sapiens

<400> 252
gaattcgcac caggggtcct gctggtcttc gcctttcttc tccgcttcta ccccgtcggc 60
cgctgccact ggggtccctg gccccaccga catggcggcg gtgttgagca agtcctggag 120
cgcacggagc tgaacaagct gcccaagtct gtccagaaca aacttgaaaa gttccttgct 180
gatcagcaat ccgagatcga tggcctgaag gggcggcatg agaaatttaa ggtggagagc 240
gaacaacagt attttgaaat agaaaagagg ttgtcccaca gtcaggagag acttgtgaat 300
gaaacccgag agtgtcaaag cttgcggctt gagctagaga aactcaacaa tcaactgaag 360
gcactaactg agaaaaacaa agaacttgaa attgctcagg atcgcaatat tgccattcag 420
agccaattta caagaacaaa ggaagaatta gaagctgaga aaagagactt aattagaacc 480
aatgagagac tatctcaaga acttgaatac ttaacagagg atgttaaacg tctgaatgaa 540
aaacttaaag aaagcaatac aacaaagggt gaacttcagt taaaattgga tgaacttcaa 600
gcttctgatg tttctgtt 618

<210> 253
<211> 1201
<212> DNA
<213> Homo sapiens

<400> 253
gaattcggca ccagggtggc gagcgcggct gctgtgctgg ggcgagcagc ggggaccgtg 60
tgtgagtttg gcatgatttg gtcccctggg attctgcctt agcaagaaag aagttggaaa 120
tacttcctgg aagaaaacta aaacaataca aaagccacag cttattgatt gcatgtcagc 180
ccccttacaa atatggacac atttcctagc ctatttccac ctggaggaga tagtaggctg 240
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aaacataatt atcaggctct gaaaattgaa cacaaaaggt tgcaggaaga atatgtaaaa 360
tcacaaaatg aacttaaacg tgtattaatt gaaaagcaag caagccagga aaaattccaa 420
ctgctccttg aagacttaag gggagaatta gtagagaaag ctagagacat agaaaaaatg 480
aaactgcagg tactaacacc acaaaaattg gaattggtaa aagcccaact acaacaagaa 540
ttagaagctc caatgcgaga acgttttcgg actcttgatg aagaagtgga aaggtacaga 600
gctgagtata acaagctgcg ctacgagtat acatttctca agtcagagtt tgaacaccag 660
aaagaagagt ttactcgggt ttcagaagaa gagaaaatga aatacaagtc agaggttgca 720
cgactggaga aggacaaaga ggagctacat aaccagctgc ttagtgttga tcccacgaga 780
gacagcaaac gaatggagca acttgttcga gaaaaaaccc atttgcttca gaaattgaaa 840
agtttagagg ctgaagtagc agaattaagg gctgagaaag aaaattctgg tgctcaggta 900
gaaaatgtcc aaagaataca ggtgaggcag ttggctgaga tgcaggctac actcagatcc 960
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tcaagcaatg aacagaatac ctgcttaatc agcaaactgc atagagctga ccgagaaatc 1080
agcacactgg ccagtgaagt gaaagagctt aaacatgcaa acaaactaga aataactgac 1140
atcaaactgg aggcagcaag agctaagagt gagctcgaaa gagaaaggaa taagatccaa 1200
a 1201

<210> 254
<211> 560
<212> DNA
<213> Homo sapiens

<400> 254
gaattcggca ccagtttggg gggtgaggtt taattggaaa tggtctctgg ggactgaaaa 60
ctgatgtttt tgcagattac ctcagggaaa cggaggtttg ttgagttaca gacacattaa 120
accaaaggcc gtgggaaaac cctctccag ctccagggga ttggtcagga ccacccacta 180
accagtgcct tccttcttaa cattcacttt tagcagcttg tgtttatttt acatgggcag 240
ttttgatggg aaattgccat gaccacaggg gtttggagtt ctgctttttt tttttcttct 300
tctttttcgg gggactgggg gactcctccc aagatcacat tttagcatct ttctctccta 360
ctccatttag aaaaataagt aacaggtgaa atgtggtctc agtgttaacg ggataattct 420
gctaccggct cctccctgat gattctgaaa tacactactg aacgagctct ggctggtcct 480

ttctatcctg gatgtggttc ttctgtgtag caattccttg atgtccagtt tggaaagatg 540
tactcttctc aacaagaaaa 560

<210> 255
<211> 612
<212> DNA
<213> Homo sapiens

<400> 255
gaattcggca ccaggcgggg cagcagggcc gcggccatgg ggagcttgaa ggaggagctg 60
ctcaaagcca tctggcacgc cttcaccgac tcgaccagga ccacagggca aggtctccaa 120
gtcccagctc aaggtccttt cccataacct gtgcacggtg ctgaaggttc ctcatgaccc 180
agttgccctt gaagagcact tcagggatga tgatgagggt ccagtgtcca accagggcta 240
catgccttat ttaaacaggt tcattttgga aaaggtccaa gacaactttg acaagattga 300
attcaatagg atgtgttgga ccctctgtgt caaaaaaaaa cctcacaaag aatcccctgc 360
tcattacaga agaagatgca tttaaaatat gggttatttt caactttta tctgaggaca 420
agtatccatt aattattgtg tcagaagaga ttgaatacct gcttaagaag cttacagaag 480
ctatgggagg aggttggcag caagaacaat ttgaacatta taaaatcaac tttgatgaca 540
gtaaaaatgg cctttctgca tgggaactta ttgagcttat tggaaatgga cagtttagca 600
aaggcatgga cc 612

<210> 256
<211> 1132
<212> DNA
<213> Homo sapiens

<400> 256
gaattcggca cgaggtctgg gagaggcctc tggagcagga ggcccagtgg ctcttctgac 60
ccaaggcccc gccgtccagc ttctaagtgc cagatgatgg aggagcgtgc caacctgatg 120
cacatgatga aactcagcat caaggtgttg ctccagtcgg ctctgagcct gggccgcagc 180
ctggatgcgg accatgcccc cttgcagcag ttctttgtag tgatggagca ctgcctcaaa 240
catgggctga aagttaagaa gagttttatt ggccaaaata aatcattctt tggtcctttg 300
gagctggtgg agaaactttg tccagaagca tcagatatag cgactagtgt cagaaatctt 360
ccagaattaa agacagctgt gggaagaggc cgagcgtggc tttatcttgc actcatgcaa 420
aagaaactgg cagattatct gaaagtgctt atagacaata aacatctctt aagcgagttc 480
tatgagcctg aggctttaat gatggaggaa gaagggatgg tgattgttgg tctgctggtg 540
ggactcaatg ttctcgatgc caatctctgc ttgaaaggag aagacttgga ttctcaggtt 600
ggagtaatag atttttccct ctaccttaag gatgtgcagg atcttgatgg tggcaaggag 660
catgaaagaa ttactgatgt ccttgatcaa aaaaattatg tggaagaact taaccggcac 720
ttgagctgca cagttgggga tcttcaaacc aagatagatg gcttggaaaa gactaactca 780
aagcttcaag aagagctttc agctgcaaca gaccgaattt gctcacttca agaagaacag 840
cagcagttaa gagaacaaaa tgaattaatt cgagaaagaa gtgaaaagag tgtagagata 900
acaaaacagg ataccaaagt tgagctggag acttacaagc aaactcggca aggtctggat 960
gaaatgtaca gtgatgtgtg gaagcagcta aaagaggaga agaaagtccg gttggaactg 1020
gaaaaagaac tggagttaca aattggaatg aaaaccgaaa tggaaattgc aatgaagtta 1080
ctggaaaagg acacccacga gaagcaggac acactagttg ccctccgcca gc 1132

<210> 257
<211> 519
<212> DNA
<213> Homo sapiens

<400> 257
gaattcgtga cacgaggtgc tcgagatgaa ccccagcgcc cccagctacc ccatggcctc 60
tctgtacgtg ggggacctgc accccgacgt gaccgaggcg atgctctacg agaagttcag 120

cccggccggg cccatcctct ccatccgggt ctgcagggac atgatcaccc gccgctcctt 180
gggctacgcg tacgtgaact tccagcagcc ggcggacgcg gaacgtgctt tggacaccat 240
gaattttgat gttataaagg gcaagccagt acgcatcatg tggtctcagc gtgatccatc 300
acttcgcaaa agtggagtag gcaacatatt cattaaaaat ttggacaaat ccatcgacaa 360
taaagcacta tatgatacgt ttctgcgtt tggtaacatc ctttcatgta aggtggtttg 420
tgatgaaaat ggctccaagg gctatggatt tgtacacttt gaaacacagg aagcagctga 480
aagagctatt gaaaaaatga atgggatgct tctaaatga 519

<210> 258
<211> 596
<212> DNA
<213> Homo sapiens

<400> 258
gctttgccaa agacttagaa gctaagcaga aaatgagctt aacatcctgg tttttggtga 60
gcagtggagg cactcgccac aggctgccac gagaaatgat ttttgttgga agagatgact 120
gtgagctcat gttgcagtct cgtagtgtgg ataagcaaca cgctgtcatc aactatgatg 180
cgtctacgga tgagcattta gtgaaggatt tgggcagcct caatgggact tttgtgaatg 240
atgtaaggat tccggaacag acttatatca ccttgaaact tgaagataag ctgagatttg 300
gatatgatac aaatcttttc actgtagtac aaggagaaat gagggtccct gaagaagctc 360
ttaagcatga gaagtttacc attcagcttc agttgtccca aaaatcttca gaatcagaat 420
tatccaaatc tgcaagtgcc aaaagcatag attcaaaggt agcagacgct gctactgaag 480
tgcagcacaa aactactgaa gcactgaaat ccgaggaaaa agccatggat atttctgcta 540
tgccccgtgg tactccatta tatgggcagc cgtcatggtg gggggatgat gaggtg 596

<210> 259
<211> 595
<212> DNA
<213> Homo sapiens

<400> 259
gaattcggca ccagagaaaa agcttcaagg tatattgagt cagagtcaag ataaatcact 60
tcggagaatt tcagaattaa gagaggagct gcaaatggac cagcaagcaa agaaacatct 120
tcaggacgag tttgatgcat gtttggagga gaaagatcag tatatcagtg ttctccagac 180
tcaggtttct cttctaaagc agcgattaca gaatggccca atgaatgttg atgctcccaa 240
acccctccct cccggggagc tccaggcaga agtgcacggt gacacggaga agatggaggg 300
cgtcggggaa ccagtgggag gtgggacttc cgctaaaacc ctggaaatgc tccagcaaag 360
agtgaaacgt caggagaatc tgcttcagcg ctgtaaggag acaattgggt cccacaagga 420
gcagtgcgca ctgctgctga gtgagaagga ggcactgcag gagcagttgg atgaaaggct 480
gcaggagctg gaaaagatga aggggatggt aataaccgag acgaagcggc aaatgcttga 540
gaccctggaa ctgaaagaag atgaaattgc tcagcttcgt agtcatatca aacag 595

<210> 260
<211> 994
<212> DNA
<213> Homo sapiens

<400> 260
gaattcggca cgaggcgttg cctgccttct tgctgtctat cagcctttct tgcctcttcc 60
ttttcgcctt ccctgttctt ccctttctca aacaaacaag acatggcaaa ccgcagtcta 120
acccagccct ttgaaattat ccatagtttt acagacagct ccaggccatg agccacaatg 180
tccaaaatta ttcttgagca ctgatataaa ttacttagac cttctttgag ggcagaactc 240
agctgttgct ctcatgatgg gcagtgctgg aaagggttct ggtatgtctt caaaatgagt 300
ccacgagttt actgagtgct tacaggtaaa ggaatgaata taagatgtct ttctgatcag 360
aacaggtgtc ccttcacatg agctttacta gactctggga gggaaaagta gccaagtact 420

tctgaaccat tttttaatac ttgttttgtc atggtgaaat tatagcagtt atcccaaaat 480
gttttaatta tcaaaatact gtcttttaaa aaaaaaaaaa agtaacacct tttaaagcat 540
tagatttcac ttgggtttct tttccaaaaa atgctaggta gacaaggcat tgtaaacatg 600
agtttccttt aagaaccatc agaatataaa tttaacatga agaaaactgc tatatctagt 660
agaaataata tctaaagttt aacaactaaa gtaccctcac agaatagcaa ataccttct 720
gttctggaca tgggttcaaa tttgaatatg gaaataattt ccttggaagt ccctagaggc 780
aggtcagagg aagtatgcat taagagggaa aggagagaat ggaaataaaa gtcactataa 840
tgcagattta tgccttattt tttagcattt tttaaatgtt gggtctttca aggtgttttt 900
tgctttttat tagatctata taaataagtt aactagcaat ttagttttgt atttaagcta 960
cacttaatct ttttctttgg tgatatttat ttct 994

<210> 261
<211> 594
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (538)
<223> n=A,T,C or G

<400> 261
gaattcggca ccagtggaga tccagctgaa ccatgccaac cgccaggctg cggaggcaat 60
caggaacctt cggaacaccc agggaatgct gaaggacaca cagctgcacc tggacgatgc 120
tctcagaggc caggacgacc tgaaagagca gctggccatg gttgagcgca gagccaacct 180
gatgcaggct gagatcgagg agctcagggc atccctggaa cagacagaga ggagcaggag 240
agtggccgag caagagctac tggatgccag tgagcgcgtg cagctcctcc acacccagaa 300
caccagcctc atcaacacca agaagaagct ggagacagac atttcccaaa tccagggaga 360
gatggaagac atcgtccagg aagcccgcaa cgcagaagag aaggccaaga aagccatcac 420
tgatgccgcc atgatggcgg aggagctgaa gaaggagcag gacaccagcg cccacctgga 480
gcggatgaag aagaacatgg agcagaccgt gaaggacctg cagcaccgtc tggacgangc 540
tgagcagctt ggcgctgaag ggcgggcaag aagcagatcc agaaactgga ggct 594

<210> 262
<211> 594
<212> DNA
<213> Homo sapiens

<400> 262
gaaaaggtgg ctggagccaa aggcatagtc agggttaatg ctcctttttc tttatcccaa 60
atcagatagt gtttaggctt tttcatcaaa tataaaaacc cagcccagtt catggctcat 120
tcggcagcaa ccctgagacg ctttacagct ctagacccta aaaggtcaaa aggccgtctt 180
atgctcaata tacattttat tacccaatct gccccggaca ttaaataaaa ctccaaaaat 240
taaatccggc cctcaaaccc cacaacagga cttaattgac ctcaccttca aggtgtagaa 300
taataaaaaa aaaaagttgc aattccttgc ctccgctgtg agacaaaccc cagccacatc 360
tccagcacac aagaacttcc aaacgcctga accacagcag ccaggcgttc ctccagaacc 420
tcctccccca ggagcttgct acatgtgccg gaaatctggc cactaggcca aggaatgcct 480
gcagccccgg attcctccta agccgtgtcc catctgtgcg ggaccccact gaaaatcgga 540
ctgttcaact cacctggcag ccactctcag agaccctgga actctggccc aagg 594

<210> 263
<211> 506
<212> DNA
<213> Homo sapiens

<400> 263
gaattcggca cgagcggaaa cttaggggcc acgtgagcca cggccacggc cgcataggca 60
agcaccggaa gcaccccggc ggccgcggta atgctggtgg tctgcatcac caccggatca 120
acttcgacaa ataccaccca ggctactttg ggaaagttgg tatgaagcat taccacttaa 180
agaggaacca gagcttctgc ccaactgtca accttgacaa attgtggact ttggtcagtg 240
aacagacacg ggtgaatgct gctaaaaaca agactggggc tgctcccatc attgatgtgg 300
tgcgatcggg ctactataaa gttctgggaa agggaaagct cccaaagcag cctgtcatcg 360
tgaaggccaa attcttcagc agaagagctg aggagaagat taagagtgtt ggggggggcct 420
gtgtcctggt ggcttgaagc cacatggagg gagtttcatt aaatgctaac tactttttaa 480
aaaaaaaaaa aaaaaaaaaa ctcgag 506

<210> 264
<211> 600
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (32)
<223> n=A,T,C or G

<400> 264
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cggcggcggg gtgtcccgtc ggcggccctg aagtgaccca taaacatgtc ttgtgagagg 120
aaaggcctct cggagctgcg atcggagctc tacttcctca tcgcccggtt cctggaagat 180
ggaccctgtc agcaggcggc tcaggtgctg atccgcgagg tggccgagaa ggagctgctg 240
ccccggcgca ccgactggac cgggaaggag catcccagga cctaccagaa tctggtgaag 300
tattacagac acttagcacc tgatcacttg ctgcaaatat gtcatcgact aggacctctt 360
cttgaacaag aaattcctca aagtgttcct ggagtacaaa ctttattagg agctggaaga 420
cagtctttac tacgcacaaa taaaagctgc aagcatgttg tgtggaaagg atctgctctg 480
gctgcgttgc actgtggaag accacctgag tcaccagtta actatggtag cccacccagc 540
attgcggata ctctgttttc aaggaagctg aatgggaaat acagacttga gcgacttgtt 600

<210> 265
<211> 534
<212> DNA
<213> Homo sapiens

<400> 265
gaattcggca cgagtgagga gcccatcatg gcgacgcccc ctaagcggcg ggcggtggag 60
gccacggggg agaaagtgct gcgctacgag accttcatca gtgacgtgct gcagcgggac 120
ttgcgaaagg tgctggacca tcgagacaag gtatatgagc agctggccaa ataccttcaa 180
ctgagaaatg tcattgagcg actccaggaa gctaagcact cggagttata tatgcaggtg 240
gatttgggct gtaacttctt cgttgacaca gtggtcccag atacttcacg catctatgtg 300
gccctgggat atggtttttt cctggagttg acactggcag aagctctcaa gttcattgat 360
cgtaagagct ctctcctcac agagctcagc aacagcctca ccaaggactc catgaatatc 420
aaagcccata tccacatgtt gctagagggg cttagagaac tacaaggcct gcagaatttc 480
ccagagaagc ctcaccattg acttcttccc cccatcctca gacattaaag agcc 534

<210> 266
<211> 552
<212> DNA
<213> Homo sapiens

<400> 266

gaattcggca ccagggcacc tccgcctcgc cgccgctagg tcggccggct ccgcccggct 60
gccgcctagg atgaatatca tggacttcaa cgtgaagaag ctggcggccg acgcaggcac 120
cttcctcagt cgcgccgtgc agttcacaga agaaaagctt ggccaggctg agaagacaga 180
attggatgct cacttagaga acctccttag caaagctgaa tgtaccaaaa tatggacaga 240
aaaaataatg aaacaaactg aagtgttatt gcagccaaat ccaaatgcca ggatagaaga 300
atttgtttat gagaaactgg atagaaaagc tccaagtcgt ataaacaacc cagaactttt 360
gggacaatat atgattgatg cagggactga gtttggccca ggaacagctt atggtaatgc 420
ccttattaaa tgtggagaaa cccaaaaaag aattggaaca gcagacagag aactgattca 480
aacgtcagcc ttaaattttc ttactccttt aagaaacttt atagaaggag attacaaaac 540
aattgctaaa ga 552

<210> 267
<211> 551
<212> DNA
<213> Homo sapiens

<400> 267
gaagcctacc agccaggtgc cggccccccc acccccggcc cagccccctc ctgcagcggt 60
ggaagcggct cggcagatcg agcgtgaggc ccagcagcag cagcacctgt accgggtgaa 120
catcaacaac agcatgcccc caggacgcac gggcatgggg accccgggga gccagatggc 180
ccccgtgagc ctgaatgtgc cccgacccaa ccaggtgagc gggcccgtca tgcccagcat 240
gcctcccggg cagtggcagc aggcgcccct tccccagcag cagcccatgc caggcttgcc 300
caggcctgtg atatccatgc aggcccaggc ggccgtggct gggccccgga tgcccagcgt 360
gcagccaccc aggagcatct cacccagcgc tctgcaagac ctgctgcgga ccctgaagtc 420
gcccagctcc cctcagcagc aacagcaggt gctgaacatt ctcaaatcaa acccgcagct 480
aatggcagct ttcatcaaac agcgcacagc caagtacgtg gccaatcagc ccggcatgca 540
gccccagcct g 551

<210> 268
<211> 573
<212> DNA
<213> Homo sapiens

<400> 268
gaattcggca ccagggttcc ttgtgggcta gaagaatcct gcaaaaatgt ctctctatcc 60
atctctcgaa gacttgaagg tagacaaagt aattcaggct caaactgctt tttctgcaaa 120
ccctgccaat ccagcaattt tgtcagaagc ttctgctcct atccctcacg atggaaatct 180
ctatcccaga ctgtatccag agctctctca atacatgggg ctgagtttaa atgaagaaga 240
aatacgtgca aatgtggccg tggtttctgg tgcaccactt caggggcagt tggtagcaag 300
accttccagt ataaactata tggtggctcc tgtaactggt aatgatgttg gaattcgtag 360
agcagaaatt aagcaaggga ttcgtgaagt cattttgtgt aaggatcaag atggaaaaat 420
tggactcagg cttaaatcaa tagataatgg tatatttgtt cagctagtcc aggctaattc 480
tccagcctca ttggttggtc tgagatttgg ggaccaagta cttcagatca atggtgaaaa 540
ctgtgcagga tggagctctg ataaagcgca caa 573

<210> 269
<211> 500
<212> DNA
<213> Homo sapiens

<400> 269
gaatcggcac caggaaacct ttattagcag agatagctgg cttggatcag attacgggga 60
atgtggggga gccatgaaga aactaactaa aggggagcct ttggggacca gggggagaca 120
agtcactatt ttgagggaga aagctctgga ttgattctga caggacactt gagtgtgaac 180
tgtccaagct aagcctctgg gtgtgtagag agagccctta cagatagata gcacctttgc 240

tttcagagtg gaaggactag ccactaagga ccagaccaag atgcatgtag gtcactgaca 300
agcacctgat gaagaggagg ggtctcctcc aagtttgtgt ttggaactcc tcctgtgttc 360
aatttcctaa aagccataat ccagcaagct gaactcatga gaaggtctgc ttcatgttga 420
gcatggaaga cagaacacag acggaaactg cagtgatggt gtgaagacac cacggatagg 480
ttaggggcag tgaggaggaa 500

<210> 270
<211> 224
<212> DNA
<213> Homo sapiens

<400> 270
gaattcggca cgagaagact acaatctcca gggaaacctg gggcgtctcg cgcaaacgtc 60
cataactgaa agtagctaag gcacccccagc cggaggaagt gagctctcct ggggcgtggt 120
tgttcgtgat ccttgcatct gttacttagg gtcaaggctt gggtcttgcc ccgcagaccc 180
ttgggacgac ccggccccag cgcagctatg aacctggagc gagt 224

<210> 271
<211> 447
<212> DNA
<213> Homo sapiens

<400> 271
gaattcggca cgaggctggg ccgggcccga gcggatcgcg ggctcgggct gcggggctcc 60
ggctgcgggc gctgggccgc gaggcgcgga gcttgggagc ggagcccagg ccgtgccgcg 120
cggcgccatg aagggcaagg aggagaagga gggcggcgca cggctgggcg ctggcggcgg 180
aagccccgag aagagcccga gcgcgcagga gctcaaggag cagggcaatc gtctgttcgt 240
gggccgaaag tacccggagg cggcggcctg ctacggccgc gcgatcaccc ggaacccgct 300
ggtggccgtg tattacacca accgggcctt gtgctacctg aagatgcagc agcacgagca 360
ggccctggcc gactgccggc gcgccctgga gctggacggg cagtctgtga aggcgcactt 420
cttcctgggg cagtgccagc tggagat 447

<210> 272
<211> 606
<212> DNA
<213> Homo sapiens

<400> 272
gcaactactt atattccttt gatggataat gctgactcaa gtcctgtggt agataagaga 60
gaggttattg atttgcttaa acctgaccaa gtagaaggga tccagaaatc tgggactaaa 120
aaactgaaga ccgaaactga caaagaaaat gctgaagtga agtttaaaga ttttcttctg 180
tccttgaaga ctatgatgtt ttctgaagat gaggctcttt gtgttgtaga cttgctaaag 240
gagaagtctg gtgtaataca agatgcttta aagaagtcaa gtaagggaga attgactacg 300
cttatacatc agcttcaaga aaaggacaag ttactcgctg ctgtgaagga agatgctgct 360
gctacaaagg atcggtgtaa gcagttaacc caggaaatga tgacagagaa agaaagaagc 420
aatgtggtta taacaaggat gaaagatcga attggaacat tagaaaagga acataatgta 480
tttcaaaaca aaatacatgt cagttatcaa gagactcaac agatgcagat gaagtttcag 540
caagttcgtg agcagatgga ggcagagata gctcacttga agcaggaaaa tgggtatact 600
ggagaa 606

<210> 273
<211> 598
<212> DNA
<213> Homo sapiens

<400> 273
gaattcggca ccaggcccgg tcccgcggtc gcagctccag ccgcctcctc cgcgcagccg 60
ccgcctcagc tgctcgctct gtgggtcggt cctctccggc acttgggctc cagtcgcgcc 120
ctccaagccc ttcaggccgc cccagtgtcc tcctccttct ccggccagac ccagccccgc 180
gaagatggtg gaccgcgagc aactggtgca gaaagcccgg ctggccgagc aggcggagcg 240
ctacgacgac atggccgcgg ccatgaagaa cgtgacagag ctgaatgagc cactgtcgaa 300
tgaggaacga aaccttctgt ctgtggccta caagaacgtt gtgggggcac gccgctcttc 360
ctggagggtc atcagtagca ttgagcagaa gacatctgca gacggcaatg agaagaagat 420
tgagatggtc cgtgcgtacc gggagaagat agagaaggag ttggaggctg tgtgccagga 480
tgtgctgagc ctgctggata actacctgat caagaattgc agcgagaccc agtacgagag 540
caaagtgttc tacctgaaga tgaaagggga ctactaccgc tacctggctg aagtggcc 598

<210> 274
<211> 536
<212> DNA
<213> Homo sapiens

<400> 274
gcaccaagag actaaacaag aaagtggatc agggaagaag aaagcttcat caaagaaaca 60
aaagacagaa aatgtcttcg tagatgaacc ccttattcat gcaactactt atattccttt 120
gatggataat gctgactcaa gtcctgtggt agataagaga gaggttattg atttgcttaa 180
acctgaccaa gtagaaggga tccagaaatc tgggactaaa aaactgaaga ccgaaactga 240
caaagaaaat gctgaagtga agtttaaaga ttttcttctg tccttgaaga ctatgatgtt 300
ttctgaagat gaggctcttt gtgttgtaga cttgctaaag gagaagtctg gtgtaataca 360
agatgcttta aagaagtcaa gtaagggaga attgactacg cttatacatc agcttcaaga 420
aaaggacaag ttactcgctg ctgtgaagga agatgctgct gctacaaagg atcggtgtaa 480
gcagttaacc caggaaatga tgacagagaa agaaagaagc aatgtggtta taacaa 536

<210> 275
<211> 494
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (379)
<223> n=A,T,C or G

<400> 275
gaattcggca ccagggtcgc ggttcttgtt tgtggatcgc tgtgatcgtc acttgacaat 60
gcagatcttc gtgaagactc tgactggtaa gaccatcacc ctcgaggttg agcccagtga 120
caccatcgag aatgtcaagg caaagatcca agataaggaa ggcatccctc ctgaccagca 180
gaggctgatc tttgctggaa aacagctgga agatggcgc accctgtctg actacaacat 240
ccagaaagag tccaccctgc acctggtgct ccgtctcaga ggtgggatgc aaatcttcgt 300
gaagacactc actggcaaga ccatcaccct tgaggtggag cccagtgaca ccatcgagaa 360
cgtcaaagca aagatccang acaaggaagg cattcctcct gaccagcaga ggttgatctt 420
tgccggaaag cagctggaag atgggcgcac cctgtctgac tacaacatcc agaaagagtc 480
taccctgcac ctgg 494

<210> 276
<211> 484
<212> DNA
<213> Homo sapiens

<400> 276

ggcttttaac cagaagtcaa acctgttcag acagaaggca gtcacagcag aaaaatcttc 60
agacaaaagg cagtcacagg tgtgcaggga gtgtgggcga ggctttagca ggaagtcaca 120
gctcatcata caccagagga cacacacagg agaaaagcct tatgtctgcg gagagtgtgg 180
gcgaggcttt atagttgagt cagtcctccg caaccacctg agtacacact ccggggagaa 240
accttatgtg tgcagccatt gtgggcgagg ctttagctgc aagccatacc tcatcagaca 300
tcagaggaca cacacaaggg agaaatcgtt tatgtgcaca gtgtgtgggc gaggctttcg 360
tgaaaagtca gagctcatta agcaccagag aattcacacg ggggataagc cttatgtgtg 420
cagagattga ggccgaggct ttgtaaagga gatcatgtct caacacacac cagaggatta 480
catt 484

<210> 277
<211> 513
<212> DNA
<213> Homo sapiens

<400> 277
gcttgaggct gccaatcaga gcttggcaga gctgagagat cagcggcagg gggagcgcct 60
ggaacatgca gcagctttgc gggccctaca agatcaggta tccatccaga gtgcagatgc 120
acaggaacaa gtggaagggc ttttggctga gaacaatgcc ttgaggacta gcctggctgc 180
cctggagcag atccaaacag caaagaccca agaactgaat atgctccggg aacagaccac 240
tgggctggca gctgagttgc agcagcagca ggctgagtac gaggacctta tgggacagaa 300
agatgacctc aactcccagc tccaggagtc attacgggcc aatagtcgac tgctggaaca 360
acttcaagaa atagggcagg agaaggagca gttgacccag gaattacagg aggctcggaa 420
gagtgcggag aagcggaagg ccatgcttgg atgagctagc aatggaaacg ctgcaagaga 480
agtcccacac aaggaagagc ttgggagcag ttc 513

<210> 278
<211> 471
<212> DNA
<213> Homo sapiens

<400> 278
gaattcggca ccagccaagg ccctgtccct ggctcgggcc cttgaagagg ccttggaagc 60
caaagaggaa ctcgagcgga ccaacaaaat gctcaaagcc gaaatggaag acctggtcag 120
ctccaaggat gacgtgggca agaacgtcca tgagctggag aagtccaagc gggccctgga 180
gacccagatg gaggagatga agacgcagct ggaagagctg gaggacgagc tgcaagccac 240
ggaggacgcc aaactgcggc tggaagtcaa catgcaggcg ctcaagggcc agttcgaaag 300
ggatctccaa gcccgggacg agcagaatga ggagaagagg aggcaactgc agagacagct 360
tcacgagtat gagacggaac tggaagacga gcgaaagcaa cgtgccctgg cagctgcagc 420
aaagaagaag ctggaagggg acctgaaaga cctggagctt caggccgact t 471

<210> 279
<211> 497
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (457)
<223> n=A,T,C or G
<221> misc_feature
<222> (471)
<223> n=A,T,C or G

<400> 279

gaattcggca cgaggccaca gaggcggcgg agagatggcc ttcagcggtt cccaggctcc 60
ctacctgagt ccagctgtcc cctttctgg gactattcaa ggaggtctcc aggacggact 120
tcagatcact gtcaatggga ccgttctcag ctccagtgga accaggtttg ctgtgaactt 180
tcagactggc ttcagtggaa atgacattgc cttccacttc aaccctcggt ttgaagatgg 240
agggtacgtg gtgtgcaaca cgaggcagaa cggaagctgg gggcccgagg agaggaagac 300
acacatgcct ttccagaagg ggatgccctt tgacctctgc ttcctggtgc agagctcaga 360
tttcaaggtg atggtgaacg ggatcctctt cgtgcagtac ttccaccgcg tgcccttcca 420
ccgtgtggac accatctccg tcaatggctc tgtgcanctg tcctacatca ncttccagac 480
ccagacagtc atccaca 497

<210> 280
<211> 544
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (451)
<223> n=A,T,C or G

<400> 280
gaattcggca ccagaatagg aacagctccg gtctacagct cccagcgtga gcgacgcaga 60
agacgggtga tttctgcatt tccatctgag gtaccgggtt catctcacta gggagtgcca 120
gacagtgggc gcaggccagt gtgtgtgcgc accgtgcgcg agccgaagca gggcgaggca 180
ttgcctcacc tgggaagcac aaggggtcag ggagttccct ttccgagtca aagaaagggg 240
tgacggacgc acctggaaaa tcgggtcact cccacccgaa tattgtgctt ttcagaccgg 300
cttaagaaac ggcgcaccac gagactatat cccacacctg gctcagaggg tcctacgccc 360
acggaatctc gctgattgct agcacagcag tcttagatca aactgcaagg ggggcaacga 420
ggctggggga ggggcgcccg ccattgccca ngcttgctta ggtaaacaaa gcagccggga 480
agcttgaact gggtggagcc caccacagct caaggaggcc tgcctgcctc tgtagctcca 540
cctc 544

<210> 281
<211> 527
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (456)
<223> n=A,T,C or G

<400> 281
gaattcggca cgaggcctcg ctcagctcca acatggcaaa aatctccagc cctacagaga 60
ctgagcggtg catcgagtcc ctgattgctg tcttccagaa gtatgctgga aaggatggtt 120
ataactacac tctctccaag acagagttcc taagcttcat gaatacagaa ctagctgcct 180
tcacaaagaa ccagaaggac cctggtgtcc ttgaccgcat gatgaagaaa ctggacacca 240
acagtgatgg tcagctagat ttctcagaat ttcttaatct gattggtggc ctagctatgg 300
cttgccatga ctccttcctc aaggctgtcc cttcccagaa gcggacctga ggacccttg 360
gccctggcct tcaaacccac cccctttcct tccagccttt ctgtcatcat ctccacagcc 420
cacccatccc ctgagcacac taaccacctc atgcanggcc cccctgccaa tagtaataaa 480
gcaatgtcct tttttaaaac atgaaaaaaa aaaaaaaaa actcgag 527

<210> 282
<211> 514

<212> DNA
<213> Homo sapiens

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

<400> 282
ggaagactgg agcctttgcg gcggcgctgc ccctcccctg gtccccgcga gctcggaggg 60
cccggctggt gctgcggggg ccccgggagg ttgaaaacta agcatgggga agagctgcaa 120
ggtggtcgtg tgtggccagg cgtctgtggg caaaacttca atcctggagc agcttctgta 180
tgggaaccat gtagtgggtt cggagatgat cgagacgcag gaggacatct acgtgggctc 240
cattgagaca gaccgggggg tgcgagagca ggtgcgtttc tatgacaccc gggggctccg 300
agatggggcc gaactgcccc gacactgctt ctcttgcact gatggctacg tcctggtcta 360
tagcacagat agcagagagt cttttcagcg tgtggagctg ctcaagaagg agattgacaa 420
atccaaggac aagaaggagg tcaccatcgt ggtccttggc aacaagtgtg acttacagga 480
gcagcggcgt gtanacccaa atgtggctca acac 514

<210> 283
<211> 484
<212> DNA
<213> Homo sapiens

<400> 283
gggcgggcgg tggacagtca tggcggcccg gcgcggggct ctcatagtgc tggagggcgt 60
ggaccgcgcc gggaagagca cgcagagccg caagctggtg gaagcgctgt gcgccgcggg 120
ccaccgcgcc gaactgctcc ggttcccgga aagatcaact gaaatcggca aacttctgag 180
ttcctacttg caaaagaaaa gtgacgtgga ggatcactcg gtgcacctgc tttttctgc 240
aaatcgctgg gaacaagtgc cgttaattaa ggaaaagttg agccagggcg tgaccctcgt 300
cgtggacaga tacgcatttt ctggtgtggc cttcaccggt gccaaggaga atttttccct 360
agactggtgt aaacagccag acgtgggcct tcccaaaccc gacctggtcc tgttcctcca 420
gttacagctg gcggatgctg ccaagcgggg agcgtttggc catgagcgct atgagaacgg 480
ggct 484

<210> 284
<211> 514
<212> DNA
<213> Homo sapiens

<400> 284
gaattcggca cgaggcggag gccgcggagg ctcctcggtc cttcagcacc cctcggcccg 60
acgcacccac gcccctcacc ccccgagagc cgaaaatgga cccaagtggg gtcaaagtgc 120
tggaaacagc agaggacatc caggagaggc ggcagcaggt cctagaccga taccaccgct 180
tcaaggaact ctcaaccctt aggcgtcaga agctggaaga ttcctatcga ttccagttct 240
ttcaaagaga tgctgaagag ctggagaaat ggatacagga aaaacttcag attgcatctg 300
atgagaatta taaagaccca accaacttgc agggaaagct tcagaagcat caagcatttg 360
aagctgaagt gcaggccaac tcaggagcca ttgttaagct ggatgaaact ggaaacctga 420
tgatctcaga agggcatttt gcatctgaaa ccatacggac ccgtttgatg gagctgcacc 480
gccagtggga attacttttg gagaagatgc gaga 514

<210> 285
<211> 383
<212> DNA
<213> Homo sapiens

<400> 285
gaattcggca cgaggccggg ctccaccgcg catcctgctc cactctggcg accgcccccg 60
gggccccccgc cgcgggcgcg gcgcccgcca tgggcgagga ggactactat ctggagctgt 120
gcgagcggcc ggtgcagttc gagaaggcga accctgtcaa ctgcgtcttc ttcgatgagg 180
ccaacaagca ggtttttgct gttcgatctg gtggagctac tggcgtggta gttaaaggcc 240
cagatgatag gaatcccatc tcatttagaa tggatgacaa aggagaagtg aagtgcatta 300
agttttcctt agaaaataag atattggctg ttcagaggac ctcaaagact gtggattttt 360
gtaattttat ccctgataat tcc 383

<210> 286
<211> 943
<212> DNA
<213> Homo sapiens

<400> 286
gaattcggca ccagggccgt ggcggaggag gagcgctgca cggtggagcg tcgggccgac 60
ctcacctacg cggagttcgt gcagcagtac gtgcgcccct gatcgcggag gtcgcgtcct 120
gttcaccggc ccgtctgccc cgaccgccca aggccgcctt cccctgacct cgcgcgcacg 180
cgtggggctg gggcggcgag gctggcggtc cggcctggcc gcgactctgc ccttctttcc 240
agaggttccg ggccctgtgc tcccgcgaca ggttgctggc ttcgtttggg gacagagtgg 300
tccggctgag caccgccaac acctactcct accacaaagt ggacttgccc ttccaggagt 360
atgtggagca gctgctgcac ccccaggacc ccacctccct gggcaatggt gaggcagccc 420
taggcggcgg taggggggtgg ggacgcttgg agtctccagg tgccaggatc cctgtccccg 480
ccgtctctgt tggcagacac cctgtacttc ttcggggaca acaacttcac cgagtgggcc 540
tctctctttc ggcactactc cccaccccca tttggcctgc tgggaaccgc tccagcttac 600
agctttggaa tcgcaggagc tggctcgggg gtgcccttcc actggcatgg acccgggtac 660
tcagaagtga tctacggtcg taagcgctgg ttcctttacc cacctgagaa gacgccagag 720
ttccacccca acaagaccac actggcctgg ctccgggaca catacccagc cctgccaccg 780
tctgcacggc ccctggagtg taccatccgg gctggtgagg tgctgtactt ccccgaccgc 840
tggtggcatg ctacgctcaa ccttgacacc agcgtcttca tctccacctt cctcggctag 900
ccaaaacagc tggcaggact gccggtcaca caccagcacg tcc 943

<210> 287
<211> 1143
<212> DNA
<213> Homo sapiens

<400> 287
gaattcggca cgagggaaga acagctgttg gaacaacaag aatatttaga aaaagaaatg 60
gaggaagcaa agaaaatgat atcaggacta caggccttac tgctcaatgg atccttacct 120
gaagatgaac aggagaggcc cttggccctc tgtgaaccag gtgtcaatcc cgaggaacaa 180
ctgattataa tccaaagtcg tctggatcag agtatggagg agaatcagga cttaaagaag 240
gaactgctga aatgtaaaca agaagccaga aacttacagg ggataaagga tgccttgcag 300
cagagattga ctcagcagga cacatctgtt cttcagctca aacaagagct actgagggca 360
aatatggaca aagatgagct gcacaaccag aatgtggatc tgcagaggaa gctagatgag 420
aggaaccggc tcttgggaga atataaaaaa gagctggggc agaaggatcg ccttcttcag 480
cagcaccagg ccaagttaga agaagcactc cggaaactct ctgatgtcag ttaccaccag 540
gtggatctag agcgagagct agaacacaaa gatgtcctct tggctcactg tatgaaaaga 600
gaggcagatg aggcgaccaa ctacaacagt cacaactctc aaagcaatgg ttttctcctt 660
ccaacggcag gaaaaggagc tacttcagtc agcaacagag ggaccagcga cctgcagctt 720
gttcgagatg ctctccgcag cctgcgcaac agcttcagtg gccacgatcc tcagcaccac 780
actattgaca gcttggagca gggcatttct agcctcatgg agcgcctgca tgttatggag 840
acgcagaaga aacaagaaag aaaggttcgg gtcaagtcac ccagaactca agtaggtagt 900
gaataccggg agtcctggcc ccctaactca aagttgcctc actcacagag ctctccaact 960

gtcagcagca cctgtactaa agtgctctat ttcactgacc ggtcacttac gcccttcatg 1020
gtcaatatac caaagaggtt ggaggaggtg acgttaaagg attttaaagc agctattgat 1080
cgggaaggaa atcaccggta tcacttcaaa gcactggatc ctgagtttgg cactgtcaaa 1140
gag 1143

<210> 288
<211> 881
<212> DNA
<213> Homo sapiens

<400> 288
gtgagagcgg gccgaggaga ttggcgacgg tgtcgcccgt gttttcgttg gcgggtgcct 60
gggctggtgg gaacagccgc ccgaaggaag caccatgatt tcggccgcgc agttgttgga 120
tgagttaatg ggccgggacc gaaacctagc cccggacgag aagcgcagca acgtgcggtg 180
ggaccacgag agcgtttgta aatattatct ctgtggtttt tgtcctgcgg aattgttcac 240
aaatacacgt tctgatcttg gtccgtgtga aaaaattcat gatgaaaatc tacgaaaaca 300
gtatgagaag agctctcgtt tcatgaaagt tggctatgag agagattttt tgcgatactt 360
acagagctta cttgcagaag tagaacgtag gatcagacga ggccatgctc gtttggcatt 420
atctcaaaac cagcagtctt ctgggggccgc tggcccaaca ggcaaaaatg aagaaaaaat 480
tcaggttcta acagacaaaa ttgatgtact tctgcaacag attgaagaat tagggtctga 540
aggaaaagta gaagaagccc aggggatgat gaaattagtt gagcaattaa aagaagagag 600
agaactgcta aggtccacaa cgtcgacaat tgaaagcttt gctgcacaag aaaaacaaat 660
ggaagtttgt gaagtatgtg gagccttttt aatagtagga gatgcccagt cccgggtaga 720
tgaccatttg atgggaaaac aacacatggg ctatgccaaa attaaagcta ctgtagaaga 780
attaaaagaa aagttaagga aaagaaccga agaacctgat cgtgatgagc gtctaaaaaa 840
ggagaagcaa gaaagagaaa aaaaaaaaaa aaaaactcga g 881

<210> 289
<211> 987
<212> DNA
<213> Homo sapiens

<400> 289
gaattcggca cgagggactg tggtttccag gaatggtggc gtctcacgct tcttgtgctt 60
tttcctttgg ggcctccgag cggctggggt tgggggactg ggcaggaggc tccctgtaaa 120
catttggact tgggctgggg caggggctgg tgttgggcaa agctgggggt ccaggctgga 180
gaagcagggg cccctccaga cgcagccttg ggagactcag catgtgcccc cctcccctca 240
tcacagaaca agacaatggt taaaaaccag aacagatgcc cagaaggggg taccatggcc 300
attaccagca tctcagacaa gggcaggctt caaacaggga ggcctgtggc aacccctccc 360
ctacgtctgg agctgagggg acagggggag ctgagaacaa agagaggaaa gaggagaaaa 420
gcggcggggg aacaggcggg gagcgtgatc ttcttgcccc catcttcctc aggggttggg 480
gggtacaaag tcggcggtgg cccatcccgc caggccccgc tgcccctcag aagaggccgc 540
agtccttcag gttgttcttg atgatgacat cggtgacggc gtcaaacacg aactgcacgt 600
tcttggtgtc ggtggcgcac gtgaagtgcg tgtagatctc cttggtgtct ttgcgcttat 660
tcaggtcctc aaacttactc tggatgtagc tggctgcctc atcatatttg ttggcccctg 720
tatactcagg gaagcagatg gtcaggggac tgtgtgtgat cttctcctca aacaggtcct 780
tcttgttgag gaagaggatg atggacgtgt ctgtgaacca cttgttgttg cagatgctat 840
cgaatagctt catgctctca tgcatgcggt tcatctcctc gtcctcagct agcaccaagt 900
cataggcgct caaggctacg cagaagatga tggctgtgac gccctcaaag cagtggatcc 960
acttcttccg ctcagaccgc tgaccac 987

<210> 290
<211> 300
<212> DNA

<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(300)
<223> n = A,T,C or G

<400> 290
gattcaagat gtaccccatt gactttgaga aggatgatga cagcaacttt catatggatt 60
tcatcgtggc tgcatccaac ctccgggcag aaaactatga cattccttct gcagaccggc 120
acaagagcaa gctgattgca gggaagatca tcccagccat tgccacgacc acagcagccg 180
tggttggcct tgtgtgtctg gagctgtaca aggttgtgca ggggcaccga canсttgact 240
cctacangaa tgggtgcctc aacttgagcc ctgcctttct ttggtttctc tgaacccctt 300

<210> 291
<211> 352
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(352)
<223> n = A,T,C or G

<400> 291
aaccaagctg ccaccggggg tggatcggat gcggcttgag aggcatctgt ctgccgagga 60
cttctcaagg gtatttgcca tgtcccctga agagtttggc aagctggctc tgtggaagcg 120
gaatgagctc aagaagaagg cctctctctt ctgatggccc ccacctgctc cgggacggcc 180
cccttacccc tgctgcttca gggtttttcc ccggcgggtt gggaggggca ggaggtgggg 240
tggaaatngg gtgggcncct ttcctcaggt agagnggggg gccaaaacct ctgcngtccc 300
cggagngagc tatggacttt cttccccctc acaaggntgg gggcctcctg ct 352

<210> 292
<211> 511
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

<400> 292
cgcggtggct gcgcactcng cctgagaaac tcggcaagcg cgcagtgtcg actccccggt 60
ctatgccagg cgcatctcag ctaatccaaa agtaaatgag aaacttagaa aaagattgcc 120
aattccaaat caacatattt agagaaaatt ggaaaaggag aagcttacta cagctttatt 180
tgaggacttt ttaaagaacg ctgggttcta tctgtgagct gcaaatcttg gagcaaaaac 240
cagagacatt gccagagcaa acaagaacag aaatacaaat ggagaactgg tcaaaagaca 300
taacccacag ttatcttgaa caagaaacta cggggataaa taaaagtacg canccagatg 360
agcaactgac tatgaattct gagaaaagta tgcatcggaa atccactgaa ttagntaatg 420
aaataacatg ngagaacaca gaatggccag ggcagagat caacgaattt tcanatcatc 480
agttcttatc cagatgatga gtctgtttac t 511

<210> 293
<211> 526

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(526)
<223> n = A,T,C or G

<400> 293
gataaaaaga actttaatgg aaggcactgt tgtccaaaat cacataaagg gtaagagccc 60
acacggtacc accctgctct cctacttctc aaacccacat ccaccaccca gacaggaggg 120
tgcanacccc acaggaaatt acctcccgga gcactgactg atatttttcc ttaaaacaaa 180
aaaatggctg tctcagacta ataacagaac atcttaagag ctataccagc tattacagcc 240
tggtaatana agcagctttc taanaattcc caagtttata anaggcccaa naaatgcatt 300
tattctgttg tctattaagc ctccatgaca aggagaaagt tatgagtaaa tccttggttc 360
atcaggagtt aagagctgtg ngcctcatga ggagttaana gctgtgtgca taagcaggtt 420
caagaaacaa actcctgttt gtttgcctct ttgatggttc aaaaacattc agctgctttc 480
acctctanga caaaatgctt aaagaattta ctctcatcac cttggg 526

<210> 294
<211> 601
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(601)
<223> n = A,T,C or G

<400> 294
actttaaaag ccaaatatat ttttaaaaga tcatgcttat aataagtaaa ttacncatta 60
aggaaacatc aaaataaagt agatgaataa aaaggcacac tcgaaaaatt tgagcgcaga 120
aaggacagtt ctttttgttt tgtttctaat gtcggaagaa aaagaaagag atatattaaa 180
atcattgttt tcaagtgaag gtttctgtca gttgaagtag ttagcaatgg cttcttttct 240
cccgtgtcca aagcaggctc ttcctgcgct gacttctgag gaggngttca gtcctctgcc 300
atgtataggc gatacatcaa ggcgacggcc actgcagaga tggcagggat cacccagttg 360
gtccaccaac tggaactaga atcaatagta gtgataagag tttccggagg cttgtttaac 420
tttggtctgt catctggatg gagctcccca atgatgaatg ttttggacat ttccctggca 480
tctgtagant gcccgacatc ctcaaagttc tcagtagcng tcacctccac ttgttccctt 540
aaaacttctt ccccaccagg atgctcttcc agaaatttgg gncaaatcgn acaccttgtg 600
g 601

<210> 295
<211> 262
<212> DNA
<213> Homo sapien

<400> 295
cccttagccc caagggccct gggggcagcc accctcccgc ctgtcggccc gtagatttat 60
caagggtgtt atgggcccag ctttgggggg ccagtcccga tgcactttga ggggtgttgg 120
agaggggact ccccccactcg cacttaactc aacggctctc gggccctggg gctgtttta 180
ccatgtttgt ttttgaagct caggtgtctc acgtctgggc tgcaccaggc gaagagagaa 240
attaaagatt tgaggtttt cc 262

<210> 296

<211> 598
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(598)
<223> n = A,T,C or G

<400> 296
gttagaacaa ctcagcaaaa taaaattcct gtttattgtt ggacaacatt gtttcacaca 60
tacatcaaac aggccaaaaa aaataaacag caacttcata gacaaaaaag gaaaaaaaaa 120
gaaacctttt atctttggcc tttttaacca tctcatacaa accaactact tatagtacag 180
ctaagtacat acacaaaaaa gttactggaa tgctcggaat aagattgttt ttctgttgtc 240
atttttgctt tttttacaag gnttttttc tcctttgaga ttataatgaa catggncaca 300
ccacaagtaa agtcagaagt aggacagana acgctccgaa ggctggtttg gtcatccgan 360
atcattaaaa atggctgacc ctaacaatat gtacaaaaat ataaaatgta aataaaaaat 420
acaaacaaat ttcctttta aagtactttt aagaaaaaaa gcagggcctt ggaagttttg 480
gttctttttt cctcccctgt tgcaaattct catggtttgg gttgggtggn gganancccg 540
tgtcatctgc gggtggcact gccccggngg gcgggcgggc ctctctctcg aangngac 598

<210> 297
<211> 509
<212> DNA
<213> Homo sapien

<400> 297
agaacacagg tgtcgtgaaa actaccccta aaagccaaaa tgggaaagga aaagactcat 60
atcaacattg tcgtcattgg acacgtagat tcgggcaagt ccaccactac tggccatctg 120
atctataaat gcggtggcat cgacaaaaga accattgaaa aatttgagaa ggaggctgct 180
gagatgggaa agggctcctt caagtatgcc tgggtcttgg ataaactgaa agctgagcgt 240
gaacgtggta tcaccattga tatctccttg tggaaatttg agaccagcaa gtactatgtg 300
actatcattg atgccccagg acacagagac tttatcaaaa acatgattac agggacatct 360
caggctgact gtgctgtcct gattgttgct gctggtgttg gtgaatttga agctggtatc 420
tccaagaatg ggcaggaccc gagagcatgc ccttctggct tacacactgg gtgtgaaaca 480
actaattgtc ggtgttaaca aaatggatt 509

<210> 298
<211> 267
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(267)
<223> n = A,T,C or G

<400> 298
gggacggggg aaaggagacg cttcttcctc ttgctgctct tctcgttccc gagatcagcg 60
gcggcggtga ccgcgagtgg gtcggcaccg tctccggctc cgggngcnaa caatgctgac 120
tgatagcgga ggcggnggca cctccttnna ggaggacctg gactctgtgg ctccgcgatc 180
cgccccagct ggggcctcgg agccgcctcc gccgggaggg gtcggtctgg ggatccncac 240
cgngaggctn tttggggagg gcgggcc 267

<210> 299

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

<400> 299
ggcacgaggg ccctcggagc tcgtttccag atcgaggtaa gagggacttt cttaaaggcc 60
tagtctatgg gatggggcgg cggagggaat tttttgagaa ataaaatgaa gctgcagtgt 120
a 121

<210> 300
<211> 533
<212> DNA
<213> Homo sapien

<400> 300
aaggtgcaca gtatttgatg caggctgctg gtcttggtcg tatgaagcca aacacacttg 60
tccttggatt taagaaagat tggttgcaag cagatatgag ggatgtggat atgtatataa 120
acttatttca tgatgctttt gacatacaat atggagtagt ggttattcgc ctaaaagaag 180
gtctggatat atctcatctt caaggacaag aagaattatt gtcatcacaa gagaaatctc 240
ctggcaccaa ggatgtggta gtaagtgtgg aatatagtaa aaagtccgat ttagatactt 300
ccaaaccact cagtgaaaaa ccaattacac acaaagttga ggaagaggat ggcaagactg 360
caactcaacc actgttgaaa aaagaatcca aaggccctat tgtgccttta aatgtagctg 420
accaaaagct tcttgaagct agtacacagt ttcagaaaaa acaaggaaag aatactattg 480
atgtctggtg gcttttttgat gatggaggtt tgaccttatt gataccttac ctt 533

<210> 301
<211> 560
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(560)
<223> n = A,T,C or G

<400> 301
ataaatgatc ccttttattg taagtaatgc gcaacactgg cctggctttg cactgcaagc 60
cctcggtcaa gatatagtca aataactatg gctgcaggtt ccacagttcc acaataacca 120
tggctgcacg atccacaatt cagacacaga catagagctg ggtgggtgg aaggggcagg 180
agggtggcag agtgcggact gtccccagcc ctggcctctc catgcanagt tggcccaggc 240
agacacaccc catggaatga tgagaaagtg acggcacggc cccttcccac agcaagcctg 300
gggctgccag gaactgccct tcanaacctt tgggcccagg tcnccctgaa nccccacaac 360
tttttatctg gaataagtat taaaaaacaa taaattaagc aaacaacntg gnccttgaag 420
gatgttgacc nacatggtcc acagtttttg gcncaaaaaa ataagggctg gtttgctttt 480
tttggaaggc agggtttgtg gnttggcttt caaatnattt tcaaaccatt ccccagggag 540
gganaacccc cggggggggaa 560

<210> 302
<211> 599
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(599)

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

<400> 302
gcaaagttac aaatttattg gtctggaaat aaatacaaat atctcattaa naaactcctc 60
tggaaagact tgtgcacaat agtttcccat ccgtactcag cctctcttgc cccgatcccc 120
gacttttcta ctcaaggcca gggaaggcct ccaaggngat gggcggcagg taacgagtca 180
ttgcctctca cgccacctgg aaggctggac tacttcctcc tcccaactgc ggggtcccan 240
aaatcctcgg gtcccagngg ctgacttaca atattcaatt cactctgacc aaacttccta 300
tganaaaatc cacggngagc caaaatgaaa agtacaaggc agtagtacag gaacctggca 360
gccgcactgg ccgcccanaa acgtcagtgg ngctgcccca ttcggcgaaa ggttagggag 420
caggaaaaga ggaagcagga gagggaagga aagtcccatg gaatatgtat tccanaatcc 480
ttacattttc tcagccaccg ctccccacgt gagttcccac ccccaccccg acaagaagca 540
aagagttctg aggatccaag aacgtgaccg ggtcanacan gttcagctac tgagttcac 599

<210> 303
<211> 591
<212> DNA
<213> Homo sapien

<400> 303
cggagttgta acgctccact gactgataga gcgaccggcc gaccatggcg cccggagtgg 60
cccgcgggcc gacgccgtac tggaggttgc gcctcggtgg cgccgcgctg ctcctgctgc 120
tcatcccggt ggccgccgcg caggagcctc ccggagctgc ttgttctcag aacacaaaca 180
aaacctgtga agagtgcctg aagaacgtct cctgtctttg gtgcaacact aacaaggctt 240
gtctggacta cccagttaca agcgtcttgc caccggcttc cctttgtaaa ttgagctctg 300
cacgctgggg agtttgttgg gtgaactttg aggcgctgat catcaccatg tcggtagtcg 360
ggggaaccct cctcctgggc attgccatct gctgctgctg ctgctgcagg aggaagagga 420
gccggaagcc ggacaggagt gaggagaagg ccatgcgtga gcgggaggag aggcggatac 480
ggcaggagga acggagagca gagatgaaga caagacatga tgaaatcaga aaaaaatatg 540
gcctgtttaa agaagaaaac ccgtatgcta gatttgaaaa caactaaagc g 591

<210> 304
<211> 441
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(441)
<223> n = A,T,C or G

<400> 304
gctggacgga gacctgctgg aggaggagga gctggaggaa gcagaggagg aggaccggtc 60
gtcgctgctg ctgctgtcgc cgcccgcggc caccgcctct cagacccagc agatcccagg 120
cgggtccctg ggtctgtgc tgctgccagc cgccaggttc gatgcccggg aggcggcggc 180
ggcggcgggg gtgctgtacg gaggggacga tgcccagggc atgatggcgg cgatgctgtc 240
ccacgcctac ggccccggcg gttgtggggc ggcggcggcc gccctgaacg gggagcaggc 300
ggccctgctc cggagaaaga gcgtcaacac caccgagtgc gtcccggtgc ccagctccga 360
gcacgtcgcc gagatcgtcg gccgccaggg ttgtaaaatt aaagcactga nagccaagac 420
aaacacgtat atcaagactc c 441

<210> 305
<211> 491
<212> DNA
<213> Homo sapien

<400> 305
tcgccatgcc cccttcttag cactgcaccg ccaggtccat gctgctgcca ccccagacct 60
gggctttgcc tgccacctct gtgggcagag cttccgaggc tgggtggccc tggttctgca 120
tctgcgggcc cattcagctg caaagcggcc catcgcttgt cccaaatgcg agagacgctt 180
ctggcgacga aagcagcttc gagctcatct gcggcggtgc caccctcccg ccccggaggc 240
ccggcccttc atatgcggca actgtggccg gagctttgcc cagtgggacc agctagttgc 300
ccacaagcgg gtgcacgtag ctgaggccct ggaggaggcc gcagccaagg ctctggggcc 360
ccggcccagg ggccgccccg cggtgaccgc cccccggccc ggtggagatg ccgtcgaccg 420
ccccttccag tgtgcctgtt gtggcaagcg cttccggcac aagcccaact tgatcgctca 480
cccgcgcgtg c 491

<210> 306
<211> 547
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(547)
<223> n = A,T,C or G

<400> 306
tctctttctt ttaagacagg aatgtaagcc acaacattta caaatacaat gttttaactc 60
tctacatgta ggaagccaac ctgctccttt ttgatcttct tctttggcac aacctcagtg 120
gatttctctg attcagaacg agttctaatt gatcttctct gttgcttctt ttctactgag 180
cctgtagaac cagatgttgc ttcaggagat gatacactct gcgttggctt ttcatttctc 240
tggtttggtg tagaaattat aagcctgtct tgccccctga cacttatttc tgttttgtta 300
ccaattccct ttgttgaata aacaaattga tcgataaatt tcccatcccc tgtagcattc 360
tgaagagcaa acacttgttc aattttcaca actggagaca tgttacactt ctgcaaatcc 420
aggctcccctt tgtgcatccg taatggaagc tggtaaggat ttccttgctg ccgcagtttt 480
ccaggctatt ttaacaggcg gnggctcttc ctctttccgc acttgtgtgc cgcctctggc 540
tatgtct 547

<210> 307
<211> 571
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(571)
<223> n = A,T,C or G

<400> 307
cgctgcatgt gataatgtca tcatttattt ttaaatggtt ctaaattgca natttaagtt 60
gatttcaaat caaccctatt tttaaattac ttttaatagg aanaaatgaa gcaaggacat 120
acataatcta ctatatttga aggactcaaa caaatacatg tttggctgtg aattctgtac 180
tctcaccaaa acagagataa aaatccacct aaaatacact ttccttcatt tagtgcttgt 240
ggganaaggt caagtattgc actttaaaat tactttcatc taacatttgc cccaactttc 300
cccctgaatt cactatatgt tttcagcaaa catgatttta taaattttaa gtataaaagc 360
aactaggttt tctaattcaa ctttggaagg tttactttac tctacanagc tatttttgta 420
aaacggcata tttacttaca aaattganag ataggggcat ccagctgagg tacatttcct 480
cccttggcgt tgagtttctg gacttgggtc gggggcacag gcttgtgtga ctgccccgtg 540
gcccgataca tggcctggac cccaggatgc g 571

<210> 308
<211> 591
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(591)
<223> n = A,T,C or G

<400> 308
ctccttatgt gtctgcctac ttcattcttc ggcatttcct gcttatccaa gttcaccatt 60
tcaggtcacc actggatatc agttgcctgt atataattat caggcatttc ctgcttatcc 120
aagttcacca tttcaggtca ccactggata tcagttgcct gtatataatt atcaggcatt 180
tcctgcttat ccaagttcac catttcaggt caccactgga tatcagttgc ctgtatataa 240
ttatcaggca tttcctgctt atccaagttc accatttcag gtcaccactg gatatcagtt 300
gcctgtatat aattatcagg catttcctgc ttatccaagt tcaccatttc aggtcaccac 360
tggatatcag ttgcctgtat ataattatca ggcatttcct gcttatccaa gttcaccatt 420
tcaggtcacc actggatatc agttgcctgt atataattat caggcatttc ctgcttatcc 480
aaattcagca gttcaggtca ccactggata tcagttccat gtatacaatt accagatgcc 540
accgcagtgc cctgttgggg gagcaaagga gaaatntgtg gaccgaagca t 591

<210> 309
<211> 591
<212> DNA
<213> Homo sapien

<400> 309
aggggtgca cgtactccca actgtggtcg cgctctcacc ccttctgctg ctctcgtggc 60
cccctcgcga tggcgggcat cctgtttgag gatattttcg atgtgaagga tattgacccg 120
gagggcaaga agtttgaccg aggtaagtaa gtgtctcgac tgcattgtga gagtgaatct 180
ttcaagatgg atctaatctt agatgtaaac attcaaattt accctgtaga cttgggtgac 240
aagtttcggt tggtcatagc tagtaccttg tatgaagatg gtaccctgga tgatggtgaa 300
tacaacccca ctgatgatag gccttccagg gctgaccagt ttgagtatgt aatgtatgga 360
aaagtgtaca ggattgaggg agatgaaact tctactgaag cagcaacacg cctgctgaga 420
ttgagagctg ctgagtggca gtgctccaga atcacgggat ggggccttct gtttcagctc 480
tgcgtacgtg tcctatgggg gcctgctcat gaggctgcag gggatgcca acaacctgca 540
tggattcgag gtggactcca gagtttatct cctgatgaag aagctagcct t 591

<210> 310
<211> 488
<212> DNA
<213> Homo sapien

<400> 310
tggtctcaag cctgaagagg ctccgcccac aagctggccc atgaagttag caatgcctgt 60
ggcttcagtc aattgtcttg agactgtgaa gaggctgaaa gacaccttcc cgggtggaag 120
aaggagttca ctgaaaactt atcttaaact gacccttccc tttgagtgag tcttcattcc 180
tctcccatgt gggaacccag cctccgatgc cccggggact aggggaaaca gttggaggtc 240
cgtgccgtcc ccagcctgcc acgggtgcga ggacagccaa gtcctgagtg actcaagatg 300
cttcacttac atggaagaaa cttctaaaac tctaccgagt ggtttttgta tatactaaag 360
ttctatttag agcttttctg ttttgggcaa gttcgctgct ccttctattt gggcactttg 420
gtttttgtac tgtcttttgt gacggcattg attgaacatt ttttactagt agtcttatga 480
cttttgta 488

<210> 311
<211> 511
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

<400> 311
cccgtttntg nagcaaaana gggggaagat ttataggtag aggcgacaaa cctaccgagc 60
ctggtgatag ctggttgtcc aagatagaat cttagttcaa ctttaaattt gcccacagaa 120
ccctctaaat ccccttgtaa atttaactgt tagtccaaag aggaacagct ctttggacac 180
taggaaaaaa ccttgtagag agagtaaaaa atttaacacc catagtaggc ctaaaagcag 240
ccaccaatta agaaagcgtt caagctcaac acccactacc taaaaaatcc caaacatata 300
actgaactcc tcacacccaa ttggaccaat ctatcaccct atagaagaac taatgttagt 360
ataagtaaca tgaaaacatt ctcctccgca taagcctgcg tcagattaaa acactgaact 420
gacaattaac agcccaatat ctacaatcaa ccaacaagtc attattaccc tcactgtcaa 480
cccaacacag gcatgctcat aaggaaaggt t 511

<210> 312
<211> 591
<212> DNA
<213> Homo sapien

<400> 312
gaacttgcgt tgaaggaagc agaaactgat gaaataaaaa ttttgctgga agaaagcaga 60
gcccagcaga aggagacctt gaaatctctt cttgaacaag agacagaaaa tttgagaaca 120
gaaattagta aactcaacca aaagattcag gataataatg aaaattatca ggtgggctta 180
gcagagctaa gaactttaat gacaattgaa aaagatcagt gtatttccga gttaattagt 240
agacatgaag aagaatctaa tatacttaaa gctgaattaa acaaagtaac atctttgcat 300
aaccaagcat ttgaaataga aaaaaaccta aaagaacaaa taattgaact gcagagtaaa 360
ttggattcag aattgagtgc tcttgaaaga caaaaagatg aaaaaattac ccaacaagaa 420
gagaaatacg aagctattat ccagaacctt gagaaagaca gacaaaaatt ggtcagcagc 480
caggagcaag acagagaaca gttaattcag aagcttaatt gtgaaaaaga tgaagctatt 540
cagactgccc taaaagaatt taaattggag agagaagttg ttgagaaaga g 591

<210> 313
<211> 373
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(373)
<223> n = A,T,C or G

<400> 313
ttgattttta ttctgnattt tattactgaa atangttgtc ctantnatcc caccccacaa 60
taaaaatntn acccangccc cccntttctt tncctnatnc cctnttccac cacaccatcc 120
cggaacaagt gctccaggat tccctgccca ctggccattt tggagtgtgn ccattgggta 180
gcaatgtgga aaccaccaag gcctttgtgg anaaaatgga gggggttgag ggagncccan 240
gaggggctna tttgagggcc tttgccactt gctcataggc gagctcnatc tcctcntnat 300

ctgnacangt ggaagcaaat tcttcccggg cgtnggnant gctnaagnac cgatgcactc 360
cccggaaggn ctn 373

<210> 314
<211> 591
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(591)
<223> n = A,T,C or G

<400> 314
cccgtgccgc cgccgcctcc tgggaagaga ggaagcggga gaggagccca cgtcgcctgt 60
cacccaatat ctccagccgc gcagtcccga agagtgtaag atgttcgcct gcgccaagct 120
cgcctgcacc ccctctctga tccgagctgg atccagagtt gcatacagac caatttctgc 180
atcagtgtta tctcgaccag aggctagtag gactggagag ggctctacgg tatttaatgg 240
ggcccagaat ggtgtgtctc agctaatcca aagggagttt cagaccagtg caatcagcag 300
agacattgat actgctgcca aatttattgg tgcaggtgct gcaacagtag gagtggctgg 360
ttctggtgct ggtattggaa cagtctttgg cagccttatc attggttatg ccagaaaccc 420
ttcgctgaag cagcagctgt tctcatatgc tatcctggga tttgccttgt ctgaagctat 480
gggtctcttt tgtttgatgg ttgctttctt gattttgttt gccatgtaac aaattactgc 540
ttgacatgtt ggcattcata ttaattacng atgtaattct gtgtatctta c 591

<210> 315
<211> 591
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(591)
<223> n = A,T,C or G

<400> 315
aagcccttca ccaacaaaga tgcctatact tgtgcaaatt gcagtgcttt tgtccacaaa 60
ggctgccgag aaagtctagc ctcctgtgca aaggtcaaaa tgaagcagcc caaagggagc 120
cttcaggcac atgacacatc atcactgccc acggtcatta tgagaaacaa gccctcacag 180
cccaaggagc gtcctcggtc cgcagtcctc ctggtggatg aaaccgctac caccccaata 240
tttgccaata gacgatccca gcagagtgtc tcgctctcca aaagtgtctc catacagaac 300
attactggag ttggcaatga tgagaacatg tcaaacacct ggaaattcct gtctcattca 360
acagactcac taaataaaat cagcaaggtc aatgagtcaa cagaatcact tactgatgag 420
ggtacagaca tgaatgaagg acaactactg ggagactttg agattgagtc caaacagctg 480
gaagcagagt cttggagtcg gataatagac agcaagtttc taaaacagcc aaaagaaaga 540
tgtgggtcaa acngcgagaa gtaatatatg agttggatgc agacagagtt t 591

<210> 316
<211> 591
<212> DNA
<213> Homo sapien

<400> 316
gtttttataa gaataaaatt ccattcaagc cagatggtgt ttacattgaa gaagttctaa 60
gtaaatggaa aggagattat gaaaaactgg agcacaacca cacttacatt caatggcttt 120

tccccctgag agaacaaggc ttgaacttct atgccaaaga actaactaca tatgaaattg 180
aggaattcaa aaaaacaaaa gaagcaatta gaagattcct cctggcttat aaaatgatgc 240
tagaattttt tggaataaaa ctgactgata aaactggaaa tgttgctcgg gctgttaact 300
ggcaggaaag atttcagcat ctgaatgagt cccagcacaa ctatttaaga atcactcgta 360
ttcttaaaag ccttggtgag cttggatatg aaagttttaa atctcctctt gtaaaattta 420
ttcttcatga agctcttgtg gagaatacta ttcccaatat taagcagagt gctctagagt 480
attttgttta tacaattaga gacagaagag aaaggagaaa gctcctgcgg ttcgcccaga 540
aacactacac gccttcagag aactttatct ggggacccgc ctcgaaaaga a 591

<210> 317
<211> 323
<212> DNA
<213> Homo sapien

<400> 317
ccaagctacg gaagcaagtg gaagagattt ttaatttgaa atttgctcaa gctcttggac 60
tcaccgaggc agtaaaagta ccatatcctg tgtttgaatc aaacccggag ttcttctatg 120
tggaaggctt gccagagggg attcccttcc gaagccctac ctggtttgga attccacgac 180
ttgaaaggat cgtccacggg agtaataaaa tcaagttcgt tgttaaaaaa cctgaactag 240
ttatttccta cttgcctcct gggatggcta gtaaaataaa cactaaagct ttgcagtccc 300
ccaaaagacc acgaagtcct ggg 323

<210> 318
<211> 591
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(591)
<223> n = A,T,C or G

<400> 318
gatggcgtac ttggcttgga gactggcgcg gcgttcgtgt ccgagttctc tgcaggtcac 60
tagtttcccg gtagttcagc tgcacatgaa tagaacagca atgagagcca gtcagaagga 120
ctttgaaaat tcaatgaatc aagtgaaact cttgaaaaag gatccaggaa acgaagtgaa 180
gctaaaactc tacgcgctat ataagcaggc cactgaagga ccttgtaaca tgcccaaacc 240
aggtgtattt gacttgatca acaaggccaa atgggacgca tggaatgccc ttggcagcct 300
gcccaaggaa gctgccaggc agaactatgt ggatttggtg tccagtttga gtccttcatt 360
ggaatcctct agtcaggtgg agcctggaac agacaggaaa tcaactgggt ttgaaactct 420
ggtggtgacc tccgaagatg gcatcacaaa gatcatgttc aaccggccca aaaagaaaaa 480
tgccataaac actgagatgt atcatgaaat tatgcgtgca cttaaagctg ccagcaanga 540
tgactcaatc atcacttgtt ttaacaggaa atggtgacta ttacagtagn g 591

<210> 319
<211> 591
<212> DNA
<213> Homo sapien

<400> 319
gaattcggca cgaggttgct gctaagcgaa cgccctttgg agcttacgga ggccttctga 60
aagacttcac tgctactgac ttgtctgaat ttgctgccaa ggctgccttg tctgctggca 120
aagtctcacc tgaaacagtt gacagtgtga ttatgggcaa tgtcctgcag agttcttcag 180
atgctatata tttggcaagg catgttggtt tgcgtgtggg aatcccaaag gagaccccag 240
ctctcacgat taataggctc tgtggttctg gttttcagtc cattgtgaat ggatgtcagg 300

aaatttgtgt taaagaagct gaagttgttt tatgtggagg aaccgaaagc atgagccaag 360
ctccctactg tgtcagaaat gtgcgttttg gaaccaagct tggatcagat atcaagctgg 420
aagattcttt atgggtatca ttaacagatc agcatgtcca gctccccatg gcaatgactg 480
cagagaatct tgctgtaaaa cacaaaataa gcagagaaga atgtgacaaa tatgccctgc 540
agtcacagca gagatggaaa gctgctaatg atgctggcta ctttaatgat g 591

<210> 320
<211> 591
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(591)
<223> n = A,T,C or G

<400> 320
ggctccggcg tctgcagggg tcgccgagct aacccgtggc taggcgagtg ggcggggcg 60
gccggcacca tgtcgaggca ggcgaaccgt ggcaccgaga gcaagaaaat gagctctgag 120
ctcttcaccc tgacctatgg tgccctggtc acccagctat gtaaggacta tgaaaatgat 180
gaagatgtga ataaacagct ggacaaaatg ggctttaaca ttggagtccg gctgattgaa 240
gatttcttgg ctcggtcaaa tgttgggagg tgccatgact ttcgggaaac tgcggatgtc 300
attgccaagg tggcgttcaa gatgtacttg ggcatcactc caagcattac taattggagc 360
ccagctggtg atgaattctc cctcattttg gaaaataacc ccttggtgga ctttgtggaa 420
cttcctgata accactcatc ccttatttat tccaatctct tgtgtggggt gttgcgggga 480
gctttggaga tggtccagat ggctngngga ggcccaagtt tgtccaggac accctnaaag 540
gagacgggng tgacagaaat ccggatgaga ttcatcaggc ggattganga c 591

<210> 321
<211> 260
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(260)
<223> n = A,T,C or G

<400> 321
ctgcttggct ccacacgtgg gccgccgtag gtattccgac cggtaattcc tcctattggt 60
gtgcagcagc cacattgaag gatagagtgg cagcagaggc caaggatcgt gagttgatgg 120
agtttgctgc tgaaaatgaa gggaagtctg gggaggtctc ccacagcgta gctgaggggg 180
tgcggctaag tccagagcct ggcagggagg gagtaaggga cttagcaggg gcggaggagt 240
tctgcggngg anaggagggg 260

<210> 322
<211> 559
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(559)
<223> n = A,T,C or G

<400> 322
ttccacatga catggagtgt gaagctggat gagcacatca ttccactggg aagcatggca 60
nttaacagca tctcaaaact gactnanctc acccagtctt ccatgtattc acttcctaat 120
gcacccactc tggcanacct gnaggacnat acacatgaag ncantgatga tcagccagan 180
aancctcact ttgactctcg canngtgata tttgagctgg attcatgcaa tggnagtggg 240
aaagtttgcc ttgtctacaa aagtgggaaa ccagnattag cagaanacac tgagatctgg 300
ttcctgnaca nancgttata ctggcatttt ctcacanaca cctttactgc ctattaccgc 360
ctgctcatca cccacctggg cctgccccag tggcaatatg ccttcccagc tatggcatta 420
gcccacaggc caagcaatgg ttcagcatgt ataaacctat cacctacaac acaaacctgc 480
tcacagaaga naccgactcc tttgtgaata agctagatcc canctnagtg tttaagagca 540
agaacaagat cgttatccc 559

<210> 323
<211> 492
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(492)
<223> n = A,T,C or G

<400> 323
cctgtctccc agccgtacca gcgagggctc ggccggcagc gccgggctgg ggggcggcgg 60
cgccggcgcc ggagccgggg tgggtgcagg cggcggcggg ggcagcggcg cgagcagcgg 120
cggcggggcc gggggctgc aacccagcag ccgcgctggc ggcggccggc cctccagccc 180
cagcccgtcg gtggtgagcg agaaggagaa ggaagagttg gagcggctgc agaaagagga 240
ggaggagagg aagaagaggc tgcagctgta tgtgttcgtg atgcgctgca tcgcctaccc 300
ctttaatgcc aagcagccca ccgacatggc tcgccggcag cagaagatca gcaaacagca 360
gctgcagaca gtcaaggacc ggtttcaggc tttcctcaat ggggaaaccc anatcatggc 420
tgacgaagcc ttcatgaacc gctgtngcag agttactatg aggtgttcct gaagaccacc 480
cgtgtggccg ca 492

<210> 324
<211> 474
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(474)
<223> n = A,T,C or G

<400> 324
aatttcagca acatacttct caatttcttc aggatttaaa atcttgaggg attgatctcg 60
cctcatgaca gcaagttcaa tgtttttgcc acctgactga accacttcca ggagtgcctt 120
gatcaccagc ttaatggtca natcatctgt ttcaatggct tcgtcagtat agttcttctc 180
cagnaactca cgcactgact tggcaccccg gcctatggca ttggccttcc aggcatggta 240
tgtgcccgag ggtcagtct gatagagcct aggagtgcca tcaaagtcga aacccacgat 300
gagggcagag atgccaaacg gcctgcgccc attgctctgc gtataacgct gcttcanact 360
ggcgatgtag cgggtgatgt actccacagt gaccgggtcc tccacagtca gccggtggct 420
ctggcactcc acccgggccc tgttgatgac tatccttgca tcggcggtga ggcc 474

<210> 325
<211> 532

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(532)
<223> n = A,T,C or G

<400> 325
gaggagacag gacagagcgt ctggagaggc aggaggacac cgagttcccc gtgttggcct 60
ccaggtcctg tgcttgcgga gccgtccggc ggctgggatc gagccccgac aatgggcaac 120
gcgcaggagc ggccgtcaga gactatcgac cgcgagcgga aacgcctggt cgagacgctg 180
caggcggact cgggactgct gttggacgcg ctgctggcgc ggggcgtgct caccgggcca 240
gagtacgagg cattggatgc actgcctgat gccgagcgca gggtgcgccg cctactgctg 300
ctggtgcagg gcaagggcga ggccgcctgc caggagctgc tacgctgtgc ccagcgtacc 360
gcgggcgcgc cggaccccgc ttgggactgg cagcacgtgg gtccgggcta ccgggaccgc 420
agctatgacc ctccatgccc aggccactgg acgccggagg cacccggctc ggggaccaca 480
tgccccgggt tgcccagact tcagaccctg acgaggncgg gggccctgag gg 532

<210> 326
<211> 322
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(322)
<223> n = A,T,C or G

<400> 326
caaaattaac atttttatta aatcaagtta aaaaaaatgt tcagtgtana aaagtcaaca 60
agggttttaa caaaaccaaa atataccttt ttatacaata tatgtatata ttagcagcaa 120
actacttctg anattctctt tcttttatgt tcttctagtt attttaaaga aagcataaac 180
aatgtatatt agtatggaat gtcagcaaat ccactcttag tcctttattc tgtgatttgg 240
gccttctaca aaatactttg tgattctcac taatgaatat taagaacata cccaatttta 300
actaaaaagt agtgaaacag tg 322

<210> 327
<211> 387
<212> DNA
<213> Homo sapien

<400> 327
aaaaccgtgt actattagcc atggtcaacc ccaccgtgtt cttcgacatt gccgtcgacg 60
gcgagccctt gggccgcgtc tcctttgagc tgtttgcaga caaggtccca aagacagcag 120
aaaattttcg tgctctgagc actggagaga aaggatttgg ttataagggt tcctgctttc 180
acagaattat tccagggttt atgtgtcagg gtggtgactt cacacgccat aatggcactg 240
gtggcaagtc catctatggg gagaaatttg aagatgagaa cttcatccta aagcatacgg 300
gtcctggcat cttgtccatg gcaaatgctg gacccaacac aaatggttcc cagtttttca 360
tctgcactgc caagactgag tggttgg 387

<210> 328
<211> 502
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(502)
<223> n = A,T,C or G

<400> 328
agcagcccgg cgcggccgcc gcgccggcgg gcggcaaggc tccgggccag catgggggct 60
tcgtggtgac tgtcaagcaa gagcgcggcg agggtccacg cgcgggcgag aaggggtccc 120
acgaggagga gccggtgaag aaacgcggct ggcccaaggg caagaagcgg aagaagattc 180
tgccgaatgg gcccaaggca ccggtcacgg gctacgtgcg cttcctgaac gagcggcgcg 240
agcagatccg cacgcgccac ccggatctgc cctttcccga gatcaccaag atgctgggcg 300
ccgagtggag caagctgcag ccaacggaaa agcagcggta cctggatgag gccnagagag 360
agaagcagca gtacatgaag gagctgcggg cgtaccagca gtctgaagcc tataagatgt 420
gcacggagaa gatccaggag aagaagatca agaaagaaga ctcgagctct gggctcatga 480
acactcttct gaatggacac aa 502

<210> 329
<211> 463
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

<400> 329
caagttgcac attttaattt acaattttta ccaataaaaa ggattagttt acaaaaaggg 60
aagtccttta tacaaaataa ggacaatttg taaaganaat ccactgtcat gttttgcctt 120
gtcaagtcaa aactcaaata gcttgttttg gtaaaattat tccagaaaca taatccagac 180
aaaatcaata acgtcatcag cttcctaacc atgtttaana ggaataactt catgaacatt 240
ttgccctgaa ctgaanagtt ctaaatactt gtaaaccttt aggaaaaaat gactgctcgc 300
aggcagcttg actggtaaga gggtacacca nagactccgg gtcactcact gtcagaatat 360
tcttatacat acaatgagtc tccacgcctg tacaatgagt gtcgtgcaac ataattggag 420
taatggcctc taaaatttta caagtaaact ttattgnggc ccc 463

<210> 330
<211> 500
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(500)
<223> n = A,T,C or G

<400> 330
taattataga tctacaaaat atgaaatgta ttccaagaat gcagaaaaac catctagaag 60
caaaaggact ataaaacaaa aacagagaag aaaattcatg gctaaaccag ctgaagaaca 120
gcttgatgtg ggacagtcta aagatgaaaa catacataca tcacatatta cccaagacga 180
atttcaaaga aattcagaca gaaatatgga agagcatgaa gagatgggaa atgattgtgt 240
ttccaaaaaa acagatgcca cctgtgggaa gcaagaaaag tagcactaga aaagataagg 300
aagaatctaa aaagaagcgc ttttccagtg agtccaagaa caaacttgtn cctgaagaag 360
tgacttcaac tgtcacgaaa agtcgaanaa tttccangcg tccatctgat tggtgggtgg 420

taaaancaga ggagagtcct gtttatagca attcttcagt aagaaatgaa ttaccaantg 480
catcacaatn ntgcccggaa 500

<210> 331
<211> 494
<212> DNA
<213> Homo sapien

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

<400> 331
tctctctctc tctcaaaatt acagtgttca ttgtcattga cctcagcagc aaatttgact 60
tgaattcact taggatcgca ggaatcaggg gaaagtgatt ttaaaggtgg tttctccagc 120
acattttaag aaaagggacc aaaagttatt ttagcttcct caatagattg catgttgctt 180
attaggataa taaattaata ttaaatgcaa tatatgtctt gnctttatta tggcatctat 240
ttaggagttg ttcaaatcac tgcagtaggg ctctgcaaat aaaataatgn aacctattat 300
catggatcta atgnactgna actttatcag tgaaaggnaa aatctcaaat aacaagtaca 360
aacattggac aattacctat aaagatttgt aaaaggaaaa tttttccata gatttcattc 420
ttggcatttt gtaaagacga ccctgcagnc ccctgtttgn aacttttttta ataaaataga 480
catctgttta cttg 494

<210> 332
<211> 538
<212> DNA
<213> Homo sapien

<400> 332
aaagaacaaa tggaacgcga tggttgttct gaacaagagt ctcaaccgtg tgcatttatt 60
gggataggaa atagtgacca agaaatgcag cagctaaact tggaaggaaa gaactattgc 120
acagccaaaa cattgtatat atctgactca gacaagcgaa agcacttcat gttgtctgta 180
aagatgttct atggcaacag tgatgacatt ggtgtgttcc tcagcaagcg gataaaagtc 240
atctccaaac cttccaaaaa gaagcagtca ttgaaaaatg ctgacttatg cattgcctca 300
ggaacaaagg tggctctgtt taatcgacta cgatcccaga cagttagtac cagatacttg 360
catgtagaag gaggtaattt tcatgccagt tcacagcagt ggggagcctt ttttattcat 420
ctcttggatg atgatgaatc agaaggagaa gaattcacag tccgagatgg ctacatccat 480
tatggacaaa cagtcaaact tgtgtgctca gttactggca tggcactccc aagattga 538

<210> 333
<211> 499
<212> DNA
<213> Homo sapien

<400> 333
ctcagcctgc gggactgctc ggctcggctt ctaggcggtt ttgatgaaca cctggcttta 60
ttcttgcaat gaagaaaggt tctcaacaaa aaatattctc caaagcaaag ataccatcat 120
catctcactc tcctatccca tcatctatgt ccaatatgag atctaggtca ctttcacctt 180
tgattggatc agagactcta cctttttcatt ctggaggaca gtggtgtgag caagttgaga 240
ttgcagatga aaacaatatg cttttggact atcaagacca taaaggagct gattcacatg 300
caggagttag atatattaca gaggccctca ttaaaaaact tactaaacag gataatttgg 360
ctttgataaa atctctgaac ctttcacttt ctaaagacgg tggcaagaaa tttaagtata 420
ttgagaattt ggaaaaatgt gttaaacttg aagtactgaa tctcagctat aatctaatag 480
ggaagattga aaagtcgga 499

<210> 334
<211> 561
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(561)
<223> n = A,T,C or G

<400> 334
ttcccggtag ttcagctgca catgaataga acagcaatga gagccagtca gaaggacttt 60
gaaaattcaa tgaatcaagt gaaactcttg aaaaaggatc caggaaacga agtgaagcta 120
aaactctacg cgctatataa gcaggccact gaaggacctt gtaacatgcc caaaccaggt 180
gtatttgact tgatcaacaa ggccaaatgg gacgcatgga atgcccttgg cagcctgccc 240
aaggaagctg ccaggcagaa ctatgtggat ttggtgtcca gtttgagtcc ttcattggaa 300
tcctctagtc aggtggagcc tggaacagac aggaaatcaa ctgggtttga aactctggtg 360
gtgacctccg aagatggcat cacaaagatc atgttcaacc cggcccaaaa agaaaaatgc 420
cataaacact gagatgtatc atgaaattat gcgtgcactt aaagctgcca gcaaggatga 480
ctcaatcatc actgttttaa cangaaatgg tgactattac agtagtggga atgatctgac 540
taacttcnct gatattcccc c 561

<210> 335
<211> 551
<212> DNA
<213> Homo sapien

<400> 335
aagctggtca tggctgggga gaccaccaac tcccgcggcc agcggctgcc ccagaaggga 60
gacgtggaga tgctgtgcgg cgggccgccc tgccagggct tcagcggcat gaaccgcttc 120
aattcgcgca cctactccaa gttcaaaaac tctctggtgg tttccttcct cagctactgc 180
gactactacc ggccccggtt cttcctcctg gagaatgtca ggaactttgt ctccttcaag 240
cgctccatgg tcctgaagct caccctccgc tgcctggtcc gcatgggcta tcagtgcacc 300
ttcggcgtgc tgcaggccgg tcagtacggc gtggcccaga ctaggaggcg ggccatcatc 360
ctggccgcgg cccctggaga gaagctccct ctgttcccgg agccactgca cgtgtttgct 420
ccccgggcct gccagctgag cgtggtgggt ggatgacaag aagtttgtga gcaacataac 480
caggttgagc tcgggtcctt tccggaccat acggtgcgag aaacgatgtc cgacctgccg 540
gaagtgcgga a 551

<210> 336
<211> 540
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(540)
<223> n = A,T,C or G

<400> 336
aggtctatgt ctactgaagg caataaacga ggaatgatcc agcttattgt tgcaaggaga 60
ataagcaagt gcaatgagct gaagtcacct gggagccccc ctggacctga gctgcccatt 120
gaaacagcgt tggatgatag agaacgaaga atttcccatt ccctctacag tgggattgag 180
gggcttgatg aatcgcccag cagaaatgct gccctcagta ggataatggg taaataccag 240

ctgtccccta cagtgaatat gccccaagat gacactgtca ttatagaaga tgacaggttg 300
ccagtgcttc ctccacatct ctctgaccag tcctcttcca gctcccatga tgatgtgggg 360
tttgtgacgg cagatgctgg tacttgggcc aaggctgcaa tcagtgattc agccgactgc 420
tctttgagtc cagatgttga tccagttctt gcttttcaac gaaaaaggat ttggacgtca 480
gaagtatgtc agaaaaacgc accaaagcaa ttttcanatg ccagtcaatt ggatttcgtt 540

<210> 337
<211> 422
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(422)
<223> n = A,T,C or G

<400> 337
gcagcaggaa cagttacagc agcagcagca acagcagctg ttgcaacagc agcaggaaca 60
attgcagcag caacaactgc agcctcctcc cctggagccc gaggaggagg aagaggtgga 120
gctggagctc atgccggtgg acctggggtc agagcaggag ctggagcagc agcggcagga 180
gttggagcgg cagcaggagc tggaacggca gcaggagcag cggcagctgc agctcaaact 240
gcaggaggag ctgcagcagc tggagcaaca gctggagcag cagcagcagc agctggagca 300
gcaggaggtg cagctggagc tgaccccggt ggagctaggc gcccagcagc aggaggtgca 360
gctggagctg acccccgtgc agccggagct gcagctggaa ctggtgccan cccagggggc 420
gg 422

<210> 338
<211> 601
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(601)
<223> n = A,T,C or G

<400> 338
catcttacga acgctctatg atgtcttatg agcggtctat gatgtcccct atggctgaac 60
gctctatgat gtcagcctac gagcgctcta tgatgtcagc ctacgagcgc tctatgatgt 120
cccctatggc tgagcgctct atgatgtcag cttatgaacg ctccatgatg tcagcttatg 180
aacgctccat gatgtcccca atggctgatc gatctatgat gtccatgggt gctgaccggt 240
ctatgatgtc gtcatactct gctgctgacc ggtctatgat gtcatcgtac tctgcagctg 300
accgatctat gatgtcatct tatactgctg atcgttcaat gatgtctatg gctgctgatt 360
cttacaccga ttcttacact gacacatata cagaggcata tatggtgcca cctttgcctc 420
ctgaagagcc cccaacaatg ccaccgttgc cacctgagga gccaccaatg acaccaccat 480
tgcctnctga ggaaccaccc agagggtcca gcattgccca cttgagcagt cagcattaac 540
cagcttgaaa atacttggcc ctacanangg tgccatcatt accatctgaa gagctgtatc 600
g 601

<210> 339
<211> 440
<212> DNA
<213> Homo sapien

<220>

<221> misc_feature
<222> (1)...(440)
<223> n = A,T,C or G

<400> 339
agagggagga ggcccaactg gtgatgctgc tgctgctgct gctgccgccg ccgccgcctc 60
tattgctgat actctagtgg ggctggaagg gtggttccta ttcgcaccat cgccaaccag 120
agacagaggg aaaaaaaaaa ccggcagcca ctgctgatgt tgggttcgga ggctgcatcc 180
gactcggtca caaggaaaat ggattcagtt tgcatctctc cctcctttaa acagcttctc 240
cgggtctcag catggtatca aagcttgaaa gagagaagac tcaagaagcg aagaggattc 300
gtgagctgga gcagcgcaag cacacggtgc tggtgacaga actcaaagcc aagctccatg 360
aggagaagat gaaggagctg caggctgtga gggagaacct tatcaagcag cacgacagga 420
aatgtcaang acggtgaagg 440

<210> 340
<211> 450
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(450)
<223> n = A,T,C or G

<400> 340
gatttccagg ggcggatatt gagtgtcgac ccagaggaag aaagggagga gggcccgcct 60
aggattcctc aggccgacca gtggaagtct tcaaacaaga gcctggtgga ggctctgggg 120
ctggaagccg agggtgcagt tcctgagaca cagactttga ccggatggag taaggggttc 180
attggcatgc acagggaaat gcaagtcaac cccatttcaa agcggatggg gcccatgact 240
gtggtcagga tggacgcttc agtccagcca ggcccttttc ggaccctgct ccagtttctt 300
tatacgggac aactggatga aaaggaaaag gatttggtgg gcctggctca gatcgcagag 360
gtcctcgaga tgttcgattt gaggatgatg gtggaaaaca tcatgaacaa ggaagccttc 420
atgaaccagg agattacgaa nncctttcac 450

<210> 341
<211> 451
<212> DNA
<213> Homo sapien

<400> 341
aacagctatt aaaacagaaa atggatgaac ttcataagaa gttgcatcag gtggtggaga 60
catcccatga ggatctgccc gcttcccagg aaaggtccga ggttaatcca gcacgtatgg 120
ggccaagtgt aggctcccag caggaactga gagcgccatg tcttccagta acctatcagc 180
agacaccagt gaacatggaa aagaacccaa gagaggcacc tcctgttgtt cctcctttgg 240
caaatgctat ttctgcagct ttggtgtccc cagccaccag ccagagcatt gctcctcctg 300
ttcctttgaa agcccagaca gtaacagact ccatgtttgc agtggccagc aaagatgctg 360
gatgtgtgaa taagagtact catgaattca agccacagag tggagcagag atcaaagaag 420
ggtgtgaaac acataaggtt gccaacacaa g 451

<210> 342
<211> 498
<212> DNA
<213> Homo sapien

<220>

<221> misc_feature
<222> (1)...(498)
<223> n = A,T,C or G

<400> 342
ctcaagcagg ctattgaaga ggaaggaggc gatccagata atattgaatt aactgtttca 60
actgatactc caaacaagaa accaactaaa ggcaaaggta aaaaacatga agcagatgag 120
ttgagtggag atgcttctgt gggaagatga tgcttttatc aaggactgtg aattggagaa 180
tcaagaggca catgagcaag atggaaatga tgaactaaag gactctgaag aatttggtga 240
aaatgaagaa gaaaatgtgc attccaagga gttactctct gcagaagaaa acaagagagc 300
tcatgaatta atagaggcag aaggaataga agatatagaa aaagaggaca tcgaaagtca 360
ggaaattgaa gctcaagaag gtgaagatga tacctttcta acagcccaag atggtgagga 420
agaagaaaat gagaaagata tagcagggtt ctggtgatgg cncacaagaa gtatntaaac 480
ctcttccttc aaaaaggg 498

<210> 343
<211> 491
<212> DNA
<213> Homo sapien

<400> 343
ccgaccccta ctcggcggcg caactccaca accagtacgg ccccatgaat atgaacatgg 60
gtatgaacat ggcagcagcc gcggcccacc accaccacca ccaccaccac caccccggtg 120
cctttttccg ctatatgcgg cagcagtgca tcaagcagga gctaatctgc aagtggatcg 180
accccgagca actgagcaat cccaagaaga gctgcaacaa aactttcagc accatgcacg 240
agctggtgac acacgtctcg gtggagcacg tcggcggccc ggagcagagc aaccacgtct 300
gcttctggga ggagtgtccg cgcgagggca agcccttcaa ggccaaatac aaactggtca 360
accacatccg cgtgcacaca ggcgagaaac ccttccctgc ccttccgggt gtggcaaagt 420
cttcgcgcgc tccgagaacc tcaagatcca caaaaggacc acacagggga gaagccgtcc 480
agtggagttg a 491

<210> 344
<211> 412
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(412)
<223> n = A,T,C or G

<400> 344
gtgcgctgtc ttcccgcttg cgtcagggac ctgcccgact cagtggccgc catggcatca 60
gatgaaggca aactttttgt tggagggctg agttttgaca ccaatgagca gtcgctggag 120
caggtcttct caaagtacgg acagatctct gaagtggtgg ttgtgaaaga cagggagacc 180
cagagatctc ggggatttgg gtttgtcacc tttgagaaca ttgacgacgc taaggatgcc 240
atgatggcca tgaatgggaa gtctgtagat ggacggcaga tccgagtaga ccaggcaggc 300
aagtcgtcan acaaccgatc ccgtgggtac cgtggtggct ctgccggggg ccggggcttc 360
ttccgtgggg gcccgangac ggggcccgtg ggttctctaa aagaagaggg ga 412

<210> 345
<211> 498
<212> DNA
<213> Homo sapien

<400> 345
aactagtctc gggccatcct ttctgcgcac ccggtgtcgc tgggctgcac cccgggcggg 60
gacgtccgcc gggcacggga gggggccaag atgccgatca ataaatcaga gaagccagaa 120
agctgcgata atgtgaaggt tgttgttagg tgccggcccc tcaatgagag agagaaatca 180
atgtgctaca aacaggctgt cagtgtggat gagatgaggg gaactatcac tgtacataag 240
actgattctt ccaatgaacc tccaaagaca tttacttttg atactgtttt tggaccagag 300
agtaaacaac ttgatgttta taacttaact gcaagaccta ttattgattc tgtacttgaa 360
ggctacaatg ggactatttt tgcatatgga caaaccggaa caggcaaaac ttttaccatg 420
gaaaggtgtc gagctattcc tgaacttaga ggaataattc cccaatttct ttgctcacaa 480
tatttgggcc atatttgc 498

<210> 346
<211> 427
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(427)
<223> n = A,T,C or G

<400> 346
agatggcggt cgccgtgaga actttgcagg aacagctgga aaaggccaaa gagagtctta 60
agaacgtgga tgagaacatt cgcaagctca ccgggcggga tccgaatgac gtgaggccca 120
tccaagccag attgctggcc ctttctggtc ctggtggagg tagaggacgt ggtagtttat 180
tactgaggcg tggattctca gatagtggag gaggaccccc agccaaacag agagaccttg 240
aaggggcagt cagtaggctg ggcggggagc gtcggaccag aagagaatca cgccaggaaa 300
gcgacccgga ggatgatgat gttaaaaagc cagcattgca gtcttcannt gtagctacct 360
cccaaagagc gccccacgta gagaccttat ccagggatca aaattttgga tgaaaaaggg 420
gaaagcc 427

<210> 347
<211> 280
<212> DNA
<213> Homo sapien

<400> 347
cacagaaagt tctccgctcc cagacatggg tccctcggct tcctgcctcg gaagcgcagc 60
agcaggcatc gtgggaaggt gaagagcttc cctaaggatg acccgtccaa gccggtccac 120
ctcacagcct tcctgggata caaggctggc atgactcaca tcgtgcggga agtcgacagg 180
ccgggatcca aggtgaacaa gaaggaggtg gtggaggctg tgaccattgt agagacacca 240
cccatggtgg ttgtgggcat tgtgggctac gtggaaaccc 280

<210> 348
<211> 411
<212> DNA
<213> Homo sapien

<400> 348
caactatgat gtgcctgaaa aatgggcacg attctatact gcagaagtag ttcttgcatt 60
ggatgcaatc cattccatgg gttttattca cagagatgtg aagcctgata acatgctgct 120
ggataaatct ggacatttga agttagcaga ttttggtact tgtatgaaga tgaataagga 180
aggcatggta cgatgtgata cagcggttgg aacacctgat tatatttccc ctgaagtatt 240
aaaatcccaa ggtggtgatg gttattatgg aagagaatgt gactggtggt cggttggggt 300
atttttatac gaaatgcttg taggtgatac accttttat gcagattctt tggttggaac 360

ttacagtaaa attatgaacc attaaaatt cacttacctt tcctgatgat a 411

<210> 349
<211> 408
<212> DNA
<213> Homo sapien

<400> 349
gatgggcatc tctcgggaca actggcacaa gcgccgcaaa accgggggca agagaaagcc 60
ctaccacaag aagcggaagt atgagttggg gcgcccagct gccaacacca agattggccc 120
ccgccgcatc cacacagtcc gtgtgcgggg aggtaacaag aaataccgtg ccctgaggtt 180
ggacgtgggg aatttctcct ggggctcaga gtgttgtact cgtaaaacaa ggatcatcga 240
tgttgtctac aatgcatcta ataacgagct ggttcgtacc aagaccctgg tgaagaattg 300
catcgtgctc atcgacagca caccgtaccg acagtggtac gagtcccact atgcgctgcc 360
cctgggccgc aagaagggag ccaaactgac ttctgaggaa gaagaaaa 408

<210> 350
<211> 409
<212> DNA
<213> Homo sapien

<400> 350
ggttccccca gctctgggta cccggctctg catcgcgtcg ccatgatggg ccatcgtcca 60
gtgctcgtgc tcagccagaa cacaaagcgt gaatccggaa gaaaagttca atctggaaac 120
atcaatgctg ccaagactat tgcagatatc atccgaacat gtttgggacc caagtccatg 180
atgaagatgc ttttggaccc aatgggaggc attgtgatga ccaatgatgg caatgccatt 240
cttcgagaga ttcaagtcca gcatccagcg gccaagtcca tgatcgaaat tagccggacc 300
caggatgaag aggttggaga tgggaccaca tcagtaatta ttcttgcagg ggaaatgctg 360
tctgtagctg agcacttcct ggagcagcag atgcacccaa caggtgggg 409

<210> 351
<211> 226
<212> DNA
<213> Homo sapien

<400> 351
aatcccaaac atataactga actcctcaca cccaattgga ccaatctatc accctataga 60
agaactaatg ttagtataag taacatgaaa acattctcct ccgcataagc ctgcgtcaga 120
ttaaaacact gaactgacaa ttaacagccc aatatctaca atcaaccaac aagtcattat 180
taccctcact gtcaacccaa cacaggcatg ctcataagga aaggtt 226

<210> 352
<211> 410
<212> DNA
<213> Homo sapien

<400> 352
gcggaggggc tggctgggca ggaggggttg gcggggcagc agggccgcgg ccatggggag 60
cttgaaggag gagctgctca aagccatctg gcacgccttc accgcactcg accaggacca 120
cagcggcaag gtctccaagt cccagctcaa ggtcctttcc cataacctgt gcacggtgct 180
gaaggttcct catgacccag ttgcccttga agagcacttc agggatgatg atgagggtcc 240
agtgtccaac cagggctaca tgccttattt aaacaggttc attttggaaa aggtccaaga 300
caactttgac aagattgaat tcaataggat gtgttggacc ctctgtgtca aaaaaaacct 360
cacaaagaat cccctgctca ttacagaaga agatgcattt aaaatatggg 410

<210> 353
<211> 380
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

<400> 353
gagtttattt agaaagtatc atagtgtaaa caaacaaatt gtaccacttt gattttcttg 60
gaatacaaga ctcgtgatgc aaagctgaag ttgtgtgtac aagactcttg acagttgtgc 120
ttctctagga ggntgggttt ttttaaaaaa agaattatct gngaaccata cgtgattaat 180
aaagatttcc tttaaggcan aggctggtcn agatgctgct gttatcttct gcctcagaca 240
gacagtataa gnggtcttgt ttctaagatt cctaccacca gttactttgg gccaagtatc 300
cacatcccct tgcgtatggg aggngggtga anagtgttgg atgcaaagng gttattatgg 360
gaagnagctc natggtaaaa 380

<210> 354
<211> 379
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(379)
<223> n = A,T,C or G

<400> 354
caacacatct ttattaaaca cctgaagtta ctgggaggag gccatgatgc tggacacact 60
gtcaaagtca atcttctcca caatgttctt gggtttaatg ctctcttctt ggctacagan 120
gaanatctgc cccgactngt cggcactcca gccgtatttg ctcatccaca cctttagctg 180
gctgtccgac aganccccga gcatntcggc cagcagccan cggncaatgt gctggtaagt 240
gatacccaca acatggcaga taaactttcg gacanagtct tcaaagccag ttataccttc 300
caagaggtcc atgttttcat ccagggcttg ccanaagcct ggaaatggca ggtctccaac 360
aggtccccca ggtacaaaa 379

<210> 355
<211> 499
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(499)
<223> n = A,T,C or G

<400> 355
gtccagagct gctggtgctc ccgttcccca gaccctaccc ctatccccag tggagccgga 60
gtgcgggcgc gccccaccac cgccctcacc atggtgctgt tggcagcagc ggtctgcaca 120
aaagcaggaa aggctattgt ttctcgacag tttgtggaaa tgacccgaac tcggattgag 180
ggcttattag cagcttttcc aaagctcatg aacactggaa aacaacatac gtttgttgaa 240
acagagagtg taagatatgt ctaccagcct atggagaaac tgtatatggt actgatcact 300
accaaaaaca gcaacatttt agaagatttg gagaccctaa ggctcttctc aagagtgatc 360

cctgaatatt gcgagcctta gaagagaatg aaatatctga gcactgnttt gatttgattt 420
ttgcttttga tgaaaatgtc gcactgggat acccgggang aatgttaact tggcacagat 480
canaaccttt cacagaaaa 499

<210> 356
<211> 511
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

<400> 356
gggcttctgc tgagggggca ggcggagctt gaggaaaccg cagataagtt tttttctctt 60
tgaaagatag agattaatac aactacttaa aaaatatagt caataggtta ctaagatatt 120
gcttagcgtt aagtttttaa cgtaatttta atagcttaag attttaagag aaaatatgaa 180
gacttagaag agtagcatga ggaaggaaaa gataaaaggt ttctaaaaca tgacggaggt 240
tgagatgaag cttcttcatg gagtaaaaaa tgtatttaaa agaaaattga gagaaaggac 300
tacagagccc cgaattaata ccaatagaag ggcaatgctt ttagattaaa atgaaggtga 360
cttaaacagc ttaaagttta ntttaaaagt tgtaggtgat taaaataatt tgaaggcgat 420
cttttaaaaa gagattaaac ccgaaggtga ttaaaagacc ttgaaatcca tgacgccagg 480
gagaattgcc gtcatttaaa gcctagttaa c 511

<210> 357
<211> 511
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

<400> 357
gatacttcac atttccctag ggacgggagc ccgaggggtc cgttcggccc tcttcctctc 60
gctgggccga cacccccgctg taggaccgta acccttagtc ccaatgcctc cgtaagcgga 120
gttgagtggg tgcctgtggt tggagctgtg gaggtgtccc cggtggcgag cgcggccaga 180
actgcggtca cttaagtttt ccgtgtgcgg gttgcaagga gcgtgcgtgc gtctggtata 240
atttggcttc ctgagattct gcttacaaga aaggagtggg aaataccctt ggaaagaaaa 300
ctaaaacagt aagaaaacca aaacttattt ttacatggnt gtcagcacat ttaccgatat 360
ggacactttt cccaataatt tcctcctggt ggagacagtg gattgacagg ttctcagtcg 420
gaattccaga aaaatgttaa ttgatgaaaa gggtacnatg tgagcatcat aaagntaatt 480
attaanacac tgaaggctga acacacaagg g 511

<210> 358
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 358
acggatgaag atgatgacct tcaagaaaat gaagacaata aacaacataa agaaagcttg 60
aaaagagtga cctttgcttt accagatgat gcggaaactg aagatacagg tgttttaaat 120
gtaaagaaaa attctgatga agttaaatcc tcctttgaaa aaagacagga aaagatgaat 180
gaaaaaattg catctttaga aaaagagttg ttagaaaaaa agcccgtggc agcttcaggg 240
ggaagtgaca gcacagaaga ggccagagaa cacctcctgg aggagaccct acctttgcca 300
tctgcccgat ggccctgtga ttacagagga accccttca ctggagattt ctttaacnga 360
ngatagagat cngnttggga tatgtntcct taagaaaacc t 401

<210> 359
<211> 511
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

<400> 359
gcgatgcccg cgcgcccagg acgcctcctc ccgctgctgg cccggccggc ggccctgact 60
gcgctgctgc tgctgctgct gggccatggc ggcggcgggc gctggggcgc ccgggcccag 120
gaggcggcgg cggcggcggc ggacgggccc cccgcggcag acggcgagga cggacaggac 180
ccgcacagca agcacctgta cacggccgac atgttcacgc acgggatcca gagcgcccgc 240
gcacttcgtc atgttcttcg cgccctggtg tggacacttg ccagcggctt gcagccgant 300
ttggaatgac cttgggangа acaaatacaa cagcatggaa agaatgccaa aagtctatgt 360
ggnttaaagt ggacttgcac nggccacttc gactngtgct cccccaaggg gngggaagat 420
acccacctta aaactttca accaagccaa aaactttgaa aaccaggtct cggattcaaa 480
atggaaaact gatgttcaac ctgaacaaga a 511

<210> 360
<211> 511
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

<400> 360
tactgggaga ctttgagatt gagtccaaac agctggaagc agagtcttgg agtcggataa 60
tagacagcaa gtttctaaaa cagcaaaaga aagatgtggt caaacggcaa gaagtaatat 120
atgagttgat gcagacagag tttcatcatg tcccgactct caagatcatg agtggtgtgt 180
cnagccnggg gatgatggcg gatctgnttt ttgagcanca gatggtagaa aaagctggtt 240
ccctgtttgg atgagcttga tcagtatccc atacccattc tttccagagg attcttggag 300
ccggaaagaa nggagtcttc ttggtgggat aaaaagtgaa aaagaacttt ctcttcaana 360
aggatagggg gatgtgcttt gtaaaatcan tttttcaggg ngganaatgc cnnaaccgtt 420
ttaaagaaaa acatnttggg naagtttttg tgggccaaca ttacccggtc ttgtaaacct 480
accttcaaag aacctttttg cccagggtta a 511

<210> 361
<211> 411
<212> DNA

<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(411)
<223> n = A,T,C or G

<400> 361
gctcagcggc ccgatcccac ggaagcgcgc tcggaggggt gggacccggc cggaccggag 60
atggcgccgc cagcgggcgg ggcggcggcg gcggcctcgg acttgggctc cgccgcagtg 120
ctcttggctg tgcacgccgc ggtgaggccg ctgggcgccg ggccagacgc cgaagcacaa 180
cttgcggagg ctgcagctta acgcggaccc tgagaagcct ggcgcttncn gctggaactt 240
cttggcgcgg gacctggggc ggtaatttga gtggccctga gtcatttcta caccatccag 300
gcccaccaca cgactaagct cacaagaagg ctgaactnnc tgattctnaa cctagaanta 360
cgtgcatcta tcagtgccng aagaaatgac aacataccac tggcaactct g 411

<210> 362
<211> 511
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

<400> 362
cgggggaccg ggctgccttg gcccctcagc gctcgcgtct tttccggcag ttggaacgct 60
tcctgttgtc ctcacccgta accgcctgtt gccccctgtc tcagagtccc tcacgcgtcc 120
cctcccgtct ttggctcgtt ggctgccgcc gccggggctt cgccagcctt caagtcgaga 180
ctactggccg aaggggcgtc tgcggctctc cgccgtcccc agccctgcct ctccctgggc 240
tctgccatgg caatgacagg ctcaacacct tgctcatcca tgagtaacca cacaaaggaa 300
agggtgacaa tgaccaaaag tgacactgga gaatttttat agcaacctta tcgctcacat 360
gaagaacgag aaatgagaca aaagaagtta gaaaaagggg atggaagaag aaggcctaaa 420
aaaatgaagg agaaaaccaa cttccgaaga tcaaccacat tgcttcggaa anggaaacaa 480
aantttcttt cgtttgaaan aaaaacaaan a 511

<210> 363
<211> 401
<212> DNA
<213> Homo sapien

<400> 363
caggatctgg ggagaaagag ccccatccct tctctctctg ccaccatttc ggacaccccg 60
cagggactcg ttttgggatt cgcactgact tcaaggaagg acgcgaaccc ttctctgacc 120
ccagctcggg cggccacctg tctttgccgc ggtgaccctt ctctcatgac cctgcggtgc 180
cttgagccct ccgggaatgg cggggaaggg acgcggagcc agtgggggac cgcggggtcg 240
gcggaggagc catccccgca ggcggcgcgt ctggcgaagg ccctgcggga gctcggtcag 300
acaggatggt actggggaag tatgactgtt aatgaagcca aagagaaatt aaaagaggca 360
ccagaaggaa ctttcttgat tagagatagc tcgcattcag a 401

<210> 364
<211> 401
<212> DNA

<213> Homo sapien

<400> 364
agtcaaaggt ttcttttccc tttttaccat ggtttctaca aaaataacct tcaggaaaaa 60
gaaaatcagg aaaaaaattt tttttcaata atcttattcc ctatattaaa ttagatttga 120
agaggattaa cgttgtttta gtttgggtcc agatcagcct tatacaacat ttctaaactc 180
atttgtactt ttaaaaaatt taaacacaga cttctaaaat tacttgatgt aagtaattta 240
aatcacttat gaccaagtta ttaaccttat gaatcagaag tctgaccctt gtaggaaatt 300
atattcacat ataaagtaca tcagatcttt gccatatatt gatggttatt atgcataaac 360
acattgagtt gtgttggaag cagatttata aacctgcatg t 401

<210> 365
<211> 361
<212> DNA
<213> Homo sapien

<400> 365
atctggagtt gcacaaatag ttctttagaa cataaaacta aatggattta tacataacag 60
ttacattcag catttaagag aggcagtaca aaaatgtgtt ctgcttttat ctgatataaa 120
ttgcatgtaa taccatgatt taaacaatat cagttatatt aactaatgcc atgagatata 180
tcttactcag aacgtctgat gtttcccata atagacagaa aaaatgcagt tgtatgagca 240
actgagtttc ttttcatctt caaattcatt tgtgatggtg ggaagatcta aggacaatcc 300
ttccattgaa gaagtaggaa aaacagttca gcactgttct gaactcatca aaaatgaaat 360
t 361

<210> 366
<211> 401
<212> DNA
<213> Homo sapien

<400> 366
cgggagcagc agaggtctag cagccgggcg ccgcgggccg ggggcctgag gaggccacag 60
gacgggcgtc ttcccggcta gtggagcccg gcgcggggcc cgctgcggcc gcaccgtgag 120
gggaggaggc cgaggaggac gcagcgccgg ctgccggcgg gaggaagcgc tccaccaggg 180
cccccgacgg cactcgttta accacatccg cgcctctgct ggaaacgctt gctggcgcct 240
gtcaccggtt ccctccattt tgaaagggaa aaaggctctc cccacccatt cccctgcccc 300
taggagctgg agccggagga gccgcgctca tggcgttcag cccgtggcag atcctgtccc 360
ccgtgcagtg ggcgaaatgg acgtggtctg cggtacgcgg c 401

<210> 367
<211> 401
<212> DNA
<213> Homo sapien

<400> 367
catggagtcg ggcaagatgg cgcctcccaa gaacgctccg agagatgcct tggtgatggc 60
acagatcctg aaggatatgg gaatcacaga gtatgaacca agggttataa atcaaatgtt 120
ggaatttgct ttccgttatg tgactacaat tctggatgat gcaaaaattt attcgagcca 180
tgctaagaaa cctaatgttg atgcagatga tgtgagactg gcaatccagt gtcgtgctga 240
ccaatctttt acctctcctc ccccaagaga ttttttactg gatatcgcaa ggcagaaaaa 300
tcaaacccct ttgccactga ttaagccata tgcaggacct agactgccac ctgatagata 360
ctgcttaaca gctccaaact ataggctgaa gtccttaatt a 401

<210> 368
<211> 401

<212> DNA
<213> Homo sapien

<400> 368
cggagcggta ggagcagcaa tttatccgtg tgcagcccca aactggaaag aagatgctaa 60
ttaaagtgaa gacgctgacc ggaaaggaga ttgagattga cattgaacct acagacaagg 120
tggagcgaat caaggagcgt gtggaggaga aagagggaat ccccccacaa cagcagaggc 180
tcatctacag tggcaagcag atgaatgatg agaagacagc agctgattac aagattttag 240
gtggttcagt ccttcacctg gtgttggctc tgagaggagg aggtggtctt aggcagtgat 300
ggaccctcca ttttacctct ttaccctgtc gctcataatg aggcatcata tatcctctca 360
ctctctggga caccatagcc ctgccccctc ccctggatgc c 401

<210> 369
<211> 174
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(174)
<223> n = A,T,C or G

<400> 369
gcgagnnggg cgccaagcgc ggggccggag cggccttccc ggagtccttt gcgcggcacc 60
tggcgacaaa atggctgccc gagggagacg ggcggagcct cagggccggg aggctccggg 120
ccccgcgggc ggtggcggtg gcgggagccg ttgggctgag tcgggatcgg ggac 174

<210> 370
<211> 375
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(375)
<223> n = A,T,C or G

<400> 370
tgcttttcca actttattta gaaaaacaaa tccaggtccc agtgccccct gtaccctccc 60
cgaccccagc cataatttaa ataacttana gacagagttg gagggagggg acagganagg 120
ttggggtcac ggtggaagga ggaaganagc ccactacagc cgccgcagcg cccgcttctt 180
gtccgtcttt ttcttggccg ccagcttctt atcgcgctcg ccagcatgct tnttggccat 240
gggaccctca gcccctcccg ggccccctgg ggccccaggg tcggtggagg aagcttcagt 300
gccactggcc agggcccgac cggcttcggc cctgccgctg ggcccgccgg cgccccgtg 360
gatctctgtg agcag 375

<210> 371
<211> 375
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(375)
<223> n = A,T,C or G

<400> 371
taaattctaa aaaatatttt aatacttgaa aacttctaaa acaaaaggta aggtaacatg 60
ttctttcaaa agtgaatttc acatgcaaac cattaattat atttatttta ctgngagata 120
aaagcaaaac ataacattcg gagaaagaga ccagtaactg acctatttat tttatattat 180
attaatgnga atcctcatta gaaatgtgat aacgttattg cacaaacaaa accgtgggca 240
gaaacatccc agcaatgcag gggcgcccat accgggttac aagggatgtc cagcatgtgt 300
ttccctggaa cactcanagt ctgcactttt cctgcaaatg ggaccatgtc tgattattta 360
ttatgaaaga acact 375

<210> 372
<211> 164
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(164)
<223> n = A,T,C or G

<400> 372
cgctctgtnt cctcaacctc tacctggcgg aggttatatg taaagtcaga tgtgccactg 60
aacttgacag acacaaaatt ctactgcatt tgggctttat aatggcaagc ctgctctttt 120
tagtggtgaa cttgacttgc gcaatgctag ttcatggaga tgtc 164

<210> 373
<211> 401
<212> DNA
<213> Homo sapien

<400> 373
gcgctgttcg cctttgccta cctgcagctg tggcggctgc tcctgtaccg cgagcggcgg 60
ctgagttacc agagcctctg cctcttcctc tgtctcctgt gggcagcgct caggaccacc 120
ctcttctccg ccgccttctc gctcagcggc tccctgccct tgctccggcc gccccgctcac 180
ctgcacttct tcccccactg gctgctctac tgcttcccct cctgtctcca gttctccacg 240
ctctgtctcc tcaacctcta cctggcggag gttatatgta aagtcagatg tgccactgaa 300
cttgacagac acaaaattct actgcatttg ggctttataa tggcaagcct gctcttttta 360
gtggtgaact tgacttgcgc aatgctagtt catggagatg t 401

<210> 374
<211> 401
<212> DNA
<213> Homo sapien

<400> 374
ggaatgatac cattcagatt gatttggaga ctggcaagat tactgatttc atcaagttcg 60
acactggtaa cctgtgtatg gtgactggag gtgctaacct aggaagaatt ggtgtgatca 120
ccaacagaga gaggcaccct ggatcttttg acgtggttca cgtgaaagat gccaatggca 180
acagctttgc cactcgactt tccaacattt ttgttattgg caagggcaac aaaccatgga 240
tttctcttcc ccgaggaaag ggtatccgcc tcaccattgc tgaagagaga gacaaaagac 300
tggcggccaa acagagcagt gggtgaaatg ggtccctggg tgacatgtca gatctttgta 360
cgtaattaaa aatattgtgg caggattaat agcaaaaaaa a 401

<210> 375
<211> 401

<212> DNA
<213> Homo sapien

<400> 375
gagcggagtc cgctggctga cccgagcgct ggtctccgcc gggaaccctg gggcatggag 60
aggtctgagt acctcggccg cggcgcacgc tgcatcgcgg agccaggccg aggacgtgag 120
ggtggagggc tcctttcccg tgaccatgct tccgggagac ggtgtggggc ctgagctgat 180
gcacgccgtc aaggaggtgt tcaaggctgc cgctgtccca gtggagttcc aggagcacca 240
cctgagtgag gtgcagaata tggcatctga ggagaagctg gagcaggtgc tgagttccat 300
gaaggagaac aaagtggcca tcattggaaa gattcatacc ccgatggagt ataaggggga 360
gctagcctcc tatgatatgc ggctgaggcg taagttggac t 401

<210> 376
<211> 284
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(284)
<223> n = A,T,C or G

<400> 376
ggaacaaggt cgtgaaaaaa aaggtcttgg tgaggtgccg ccatttcatc tgtcctcatt 60
ctctgcgcct ttcgcagagc ttccancagc tggtatgttg ggccagagca tccggaggtt 120
cacaacctct gtggtccgta ggagccacta tgaggagggc cctgggaaga atttgccatt 180
ttcagtggaa aacaagtggt cgttactagc taagatgtgt ttgtactttg gatctgcatt 240
tgctacaccc ttccttgtan taagacacca actgcttaaa acat 284

<210> 377
<211> 401
<212> DNA
<213> Homo sapien

<400> 377
atttatgtta ttgcactctc ggtgtgattt atcgtatgta tctgataggt tttatgaatt 60
gttttgagtt gtaaactcct ataccctta ttaaaatgga cctaattaag tgatttatgc 120
tttgtgcaat ttcttaaatc agatctctct aggattgaag ggatccatag gtatctttca 180
cttagtgtga agcctagtag tatactttta tattcctgaa gagagaccag cattaacata 240
aagagagaag tcttaggaaa aaatataccт aagaattatt tttaaaattc atactgtgaa 300
ggagaatctg cctgcctatt tcctctccaa atttcagaaa ataacacaga gtgctatttg 360
cctgaacttt aatgagcttg actttgttat gattcaggga g 401

<210> 378
<211> 401
<212> DNA
<213> Homo sapien

<400> 378
ccagaacaca ggtgtcgtga aaactacccc taaaagccaa aatgggaaag gaaaagactc 60
atatcaacat tgtcgtcatt ggacacgtag attcgggcaa gtccaccact actggccatc 120
tgatctataa atgcggtggc atcgacaaaa gaaccattga aaaatttgag aaggaggctg 180
ctgagatggg aaagggctcc ttcaagtatg cctgggtctt ggataaactg aaagctgagc 240
gtgaacgtgg tatcaccatt gatatctcct tgtggaaatt tgagaccagc aagtactatg 300
tgactatcat tgatgcccca ggacacagag actttatcaa aaacatgatt acagggacat 360

ctcaggctga ctgtgctgtc ctgattgttg ctgctggtgt t 401

<210> 379
<211> 401
<212> DNA
<213> Homo sapien

<400> 379
tcagatatca ggtggcttct tcaaatgatt tttaagtatc tcgatgatga tgaagaacaa 60
agacatcaat caggattcag gaagacagct tttgcggaaa atgcttaaag ggaagcatca 120
aggattggtg ttgatatttg aaagtttaag agtggtatac ttttattcag tcaacacatg 180
acaaatgtaa aaggcactca tttgttgttc ctggaagaag cctggcagca ttccattcag 240
acatctgccc tttcatcgtc ccacttttta cttattgcag tcctttcagt ctgaatattt 300
cctcctgacg catcttctgc cgtccgaaat gactccctgc tcccagatcc tgtagccctt 360
attattgaca cctttcattt agaaatttag cacatgtcac a 401

<210> 380
<211> 401
<212> DNA
<213> Homo sapien

<400> 380
cctgactctc tgaggctcat tttgcagttg ttgaaattgt ccccgcagtt ttcaatcatg 60
tctgaaccaa tcagagtcct tgtgactgga gcagctggtc aaattgcata ttcactgctg 120
tacagtattg gaaatggatc tgtctttggt aaagatcagc ctataattct tgtgctgttg 180
gatatcaccc ccatgatggg tgtcctggac ggtgtcctaa tggaactgca agactgtgcc 240
cttcccctcc tgaaagatgt catcgcaaca gataaagaag acgttgcctt caaagacctg 300
gatgtggcca ttcttgtggg ctccatgcca agaagggaag gcatggagag aaaagattta 360
ctgaaagcaa atgtgaaaat cttcaaatcc cagggtgcag c 401

<210> 381
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 381
ggggcttcgc tggcagtctg aacggcaagc ttgagcaacg cggtaaaaat attgcttcgg 60
tgggtgacgc ggtacagctg tccaagggcn ttngtaacgg gaatgccgaa gcgtgggaaa 120
aagggagcgg tggcggaaga cggggatgag ctcaggacag agccagaggc caagaagagt 180
aagacggccg caaagaaaaa tgacaaagag gcagcaggag agggcccagc cctgtatgag 240
gacccccag atcagaaaac ctcacccagt ggcaaacctg ccacactcaa gatctgctct 300
tggaatgtgg atgggcttcg agcctggatt aagaagaaag gattagattg ggtaaaggaa 360
gaagccccag atatactgtg ccttcaagag accaaatgtt c 401

<210> 382
<211> 491
<212> DNA
<213> Homo sapien

<400> 382

```
gagcagcccc cggcggctga aagccggggc agaagtgctg gtctcggtcg ggattccggg     60
cttggtccca ccgaggcggc gactgcggta ggagggaaga ggttttggac gcgctggcct    120
cccgccgctg tgcattgcag cattatttca gttcaaaatg aactatatgc ctggcaccgc    180
cagcctcatc gaggacattg acaaaaagca cttggttctg cttcgagatg gaaggacact    240
tataggcttt ttaagaagca ttgatcaatt tgcaaactta gtgctacatc agactgtgga    300
gcgtattcat gtgggcaaaa aatacggtga tattcctcga gggatttttg tggtcagagg    360
agaaaatgtg gtcctactag gagaaataga cttggaaaag gagagtgaca caccccctcca    420
gcaagtatcc attgaagaaa ttctagaaga acaaagggtg gaacagcaga ccaagctgga    480
agcagagaag t                                                         491
```

<210> 383
<211> 491
<212> DNA
<213> Homo sapien

<400> 383

```
gagtccatct cagcgcctgg aaaatgcagt gaaaaaacct gaagataaaa aggaagtttt     60
cagacccctc aagcctgctg gcgaagtgga tctgaccgca ctggccaaag agcttcgagc    120
agtggaagat gtacggccac ctcacaaagt aacggactac tcctcatcca gtgaggagtc    180
ggggacgacg gatgaggagg acgacgatgt ggagcaggaa ggggctgacg agtccacctc    240
aggaccagag gacaccagag cagcgtcatc tctgaatttg agcaatggtg aaacggaatc    300
tgtgaaaacc atgattgtcc atgatgatgt agaaagtgag ccggccatga ccccatccaa    360
ggagggcact ctaatcgtcc gccagagtac agttgaccaa aagcgtgcca gccatcatga    420
gagcaatggc tttgccggtc gcattcacct cttgccagat ctcttacagc aaagccattc    480
ctcctccact t                                                         491
```

<210> 384
<211> 491
<212> DNA
<213> Homo sapien

<400> 384

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gagcctaatc tcaggtggtc cacccgagac cccttgagca ccaaccctag tcccccgcgc     60
ggccccttat tcgctccgac aaggtacaaa aaggctctgg acggcggcgt ggtaggagga    120
cgggagcggg ggcgggaagt tccctgaagg agcgagacag ggagggacag ggcagaggag    180
gagaggaagg cgatgcgacg gacaggcgca cccgctcagg ctgactctcg gggcgaggt     240
cgagccaggg gcggctgccc tgggggcgag gcgacgctgt ctcaacctcc acctcgcggc    300
ggaacccgag gacaggagcc tcagatgaaa gaaacaatca tgaaccagga aaaactcgcc    360
aaactgcagg cacaagtgcg cattggtggg aaaggaactg ctcgcagaaa gaagaaggtg    420
gttcatagaa cagccacagc agatgacaaa aaacttcagt tctccttaaa gaagttaggg    480
gtaaacaata t                                                         491
```

<210> 385
<211> 483
<212> DNA
<213> Homo sapien

<400> 385

```
agccgctgcg aagggagccg ccgccatgtc tgcgcatctg caatggatgg tcgtgcggaa     60
ctgctccagt ttcctgatca agaggaataa gcagacctac agcactgagc ccaataactt    120
gaaggcccgc aattccttcc gctacaacgg actgattcac cgcaagactg tgggcgtgga    180
gccggcagcc gacggcaaag gtgtcgtggt ggtcattaag cggagatccg gccagcggaa    240
gcctgccacc tcctatgtgc ggaccaccat caacaagaat gctcgcgcca cgctcagcag    300
catcagacac atgatccgca agaacaagta ccgccccgac ctgcgcatgg cagccatccg    360
cagggccagc gccatcctgc gcagccagaa gcctgtgatg gtgaagagga agcggacccg    420
```

ccccaccaag agctcctgag ccccctgccc ccagagcaat aaagtcagct ggctttctca 480
cct 483

<210> 386
<211> 491
<212> DNA
<213> Homo sapien

<400> 386
aggtggaagg aaaaaacata aatgaagtta atgcacttct tttcctagcc caaaagtcac 60
tgtgattata tttttttaat gaagtttaga aaaaaagctg ttgtcttctc aattgtaaaa 120
ttagtttcaa aatgctgctt ctcttatcat tagtctagta attgttgaac ttttctgcaa 180
actgcatttt acaaaattga aacttggaag ctgtattaac ttttatagtt aaacattgta 240
ttaaataaac tatactataa taaacagttt ggttttgtat tttttaaatt gtattatcca 300
gccttttaaa aattaaaagc taaataatga aaataaacca attaaaacat acttttactc 360
tcagatatac aggtatttac attatgaaaa aactgaacaa agttttaaca atactgagct 420
ttaagaattt agccagcagg gaaaatttcc aggtttgaga atgttctaat gtaaatattt 480
aatcataata c 491

<210> 387
<211> 491
<212> DNA
<213> Homo sapien

<400> 387
ccacaccacc gtgtcccaag tccagccccc tccctccaag gcatcagcac ctgaaccccc 60
tgcagaagaa gaagtggcaa ctggtacaac ctcagcctct gatgacctgg aagccctggg 120
tacactgagc ctggggacca cagaggagaa ggcagcagct gaggcggctg tgcccaggac 180
cattggggcc gagctgatgg agctggtgcg gagaaacact ggcctgagcc acgaattatg 240
ccgggtggcc atcggcatca tagtgggtca catccaggcc tcggtgccgg ccagctcacc 300
agtcatggag caggtcctcc tctcactcgt agagggcaag gacctcagca tggccctgcc 360
ctcagggcag gtctgccacg accagcagag gctggaggtg atctttgcag acctggctcg 420
ccggaaggac gacgcccagc agcgcagttg ggcactatat gaggatgagg gtgtcatccg 480
ctgctaccta g 491

<210> 388
<211> 491
<212> DNA
<213> Homo sapien

<400> 388
gagactatca aactcctgag ccaacaactt aatatgacta gcttacacaa tagcttttat 60
agtaaagata cctctttacg gactccactt atgactccct aaagcccatg tcgaagcccc 120
catcgctggg tcaatagtac ttgccgcagt actcttgaaa ctaggcggct atggtataat 180
acgcctcaca ctcattctca accccctgac aaaacacata gcctacccct tccttgtact 240
atccctatga ggcataatta taacaagctc catctgccta cgacaaacag acctaaaatc 300
gctcattgca tactcttcaa tcagccacat agccctcgta gtaacagcca ttctcatcca 360
aaccccctga agcttcaccg gcgcagtcat tctcataatc gcccacggac ttacatcctc 420
attactattc tgcctagcaa actcaaacta cgaacgcact cacagtcgca tcataatcct 480
ctctcaagga c 491

<210> 389
<211> 511
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

<400> 389
tactgatatc tctttaatac tttcatcatt caagtttgtt canaacatta caagaggcat       60
gaaagaaaaa ataattccat ttttaaaact ctgtctgtcc aaagtataac atatgaaacc      120
atgccattat ctnttaggaa acaaaagcat tcaaaattaa tttggtatta aagttcaaga      180
ttcanactaa cctcaaagta cggcatgtgc agtgtttaag tgcaanaagt attttcattc      240
caattatttt acananatgc tggagtgacg tgtgcaattt gaaatattca aatcctttaa      300
ggnttctgaa ctaagtgttt aaatgaaaac tgaaatgctg catagtttca gtggctttca      360
atttcctgtt tgatctcaga aatatatgga tgatctttgc cgtgagctac ttccatgatt      420
gcaatggcct tcttcagggc tttctcccct gcggctttgt gttccaggcc catgtagagt      480
ctccctagct tcaaccacat ggaggccacg t                                     511
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patsnap

专利名称(译)	用于治疗和诊断肺癌的化合物及其使用方法		
公开(公告)号	EP1187915A2	公开(公告)日	2002-03-20
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[标]申请(专利权)人(译)	科里克萨有限公司		
申请(专利权)人(译)	Corixa公司CORPORATION		
当前申请(专利权)人(译)	Corixa公司CORPORATION		
[标]发明人	REED STEVEN G LODES MICHAEL J MOHAMATH RAODOH SECRIST HEATHER		
发明人	REED, STEVEN, G. LODES, MICHAEL, J. MOHAMATH, RAODOH SECRIST, HEATHER		
IPC分类号	G01N33/53 A61K31/7088 A61K38/00 A61K39/00 A61K39/39 A61K39/395 A61K45/00 A61K48/00 A61P35/00 C07K14/47 C07K14/82 C07K16/32 C07K19/00 C12N1/15 C12N1/19 C12N1/21 C12N5/10 C12N15/09 C12N15/12 C12P21/08 C12Q1/02 C12Q1/68 G01N33/566 G01N33/574 G01N33/577 G01N33/58 A61K35/14 A61K38/17 C07K16/18		
CPC分类号	C07K14/47 A61K38/00 A61K39/00		
优先权	09/476235 1999-12-30 US 09/370838 1999-08-09 US 09/518809 2000-03-03 US 09/285323 1999-04-02 US		
外部链接	Espacenet		

摘要(译)

公开了用于治疗和诊断癌症（例如肺癌）的组合物和方法。组合物可包含一种或多种肺肿瘤蛋白，其免疫原性部分或编码这些部分的多核苷酸。或者，治疗组合物可包含表达肺肿瘤蛋白的抗原呈递细胞，或对表达这种蛋白的细胞特异的T细胞。此类组合物可用于例如预防和治疗诸如肺癌的疾病。还提供了基于在样品中检测肺肿瘤蛋白或编码这种蛋白的mRNA的诊断方法。