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METHODS FOR ENHANCING
ANTIBODY-INDUCED CELL LYSIS AND
TREATING CANCER

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ABSTRACT

The invention relates to methods and products for treating
cancer. In particular the invention relates to combinations of
nucleic acids and antibodies for the treatment and prevention
of cancer. The invention also relates to diagnostic methods for
screening cancer cells.

4 Claims, 6 Drawing Sheets
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Fig. 2
Fig. 3
Fig. 4
Fig. 5
METHODS FOR ENHANCING ANTIBODY-INDUCED CELL LYSIS AND TREATING CANCER

PRIORITY

This application claims the benefit of U.S. Provisional Application No. 60/213,346, filed Jun. 22, 2000.

FIELD OF THE INVENTION

The invention relates to the treatment and prevention of cancer using immunostimulatory nucleic acids and antibodies.

BACKGROUND OF THE INVENTION

Cancer is the second leading cause of death, resulting in one out of every four deaths in the United States. In 1997, the estimated total number of new diagnoses for lung, breast, prostate, colorectal and ovarian cancer was approximately two million. Due to the ever increasing aging population in the United States, it is reasonable to expect that rates of cancer incidence will continue to grow.

Cancer is a disease which involves the uncontrolled growth (i.e., division) of cells. Some of the known mechanisms which contribute to the uncontrolled proliferation of cancer cells include growth factor independence, failure to detect genomic mutation, and inappropriate cell signaling. The ability of cancer cells to ignore normal growth controls may result in an increased rate of proliferation. Although the causes of cancer have not been firmly established, there are some factors known to contribute, or at least predispose a subject to cancer. Such factors include particular genetic mutations (e.g., BRCA gene mutation for breast cancer, APC for colon cancer), exposure to suspected cancer-causing agents, or carcinogens (e.g., asbestos, UV radiation) and familial disposition for particular cancers such as breast cancer.

Cancer is currently treated using a variety of modalities including surgery, radiation therapy and chemotherapy. The choice of treatment modality will depend upon the type, location and dissemination of the cancer. For example, surgery and radiation therapy may be more appropriate in the case of solid well-defined tumor masses and less practical in the case of non-solid tumor cancers such as leukemias and lymphomas. One of the advantages of surgery and radiation therapy is the ability to control to some extent the impact of the therapy, and thus to limit the toxicity to normal tissues in the body. However, surgery and radiation therapy are often followed by chemotherapy to guard against any remaining or radio-resistant cancer cells. Chemotherapy is also the most appropriate treatment for disseminated cancers such as leukemia and lymphoma as well as metastases.

More recently, the use of CpG containing nucleic acids has been proposed for the treatment and prevention of cancer. We have found that unmethylated CG dinucleotides within certain sequence contexts (CpG DNA) are recognized by the vertebrate immune system as foreign DNA (bacterial or viral). CpG DNA activates a coordinated set of immune responses that include innate immunity (macrophages, dendritic cells, and natural killer cells), humoral immunity, and cellular immunity. Krieg A M et al., "Pharmacol Ther" 84:113-20 (1999); Krieg A M et al., "Curr Top Microbiol Immunol" 247:1-21 (2000); Wagner H, "Adv Immunol" 73:329-68 (1999).


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SUMMARY OF THE INVENTION

The invention relates in some aspects to methods for treating and preventing cancer using immunostimulatory nucleic acids and antibodies. Thus, in one aspect the invention is a method for treating or preventing cancer. The method involves administering to a subject having or at risk of developing cancer an effective amount to upregulate CD20 expression of a nucleic acid, and an anti-CD20 antibody. The cancer, in some embodiments, is B-cell lymphoma associated with low levels of CD20 expression. The B-cell lymphoma in other embodiments is B-cell chronic lymphocytic leukemia (B-CLL) or a marginal zone lymphoma. In some embodiments the CD20 antibody is C2B8 or Rituximab.

The invention in other aspects relates to a method for diagnosing lymphoma by isolating a B cell from a subject and identifying a change in cell surface markers when the B cell is contacted with an immunostimulatory nucleic acid, wherein the cell surface marker induced on the B cell is indicative of the type of lymphoma. In some embodiments the subject has a type of lymphoma. In some embodiments the subject is suspected of having a type of lymphoma. The method may optionally include a method for treating cancer by administering to the subject an immunostimulatory nucleic acid and an antibody specific for the cell surface antigens induced on the B cell in order to treat the cancer.

In another aspect the invention is a method for treating or preventing cancer by administering to a subject having or at risk of developing cancer an effective amount to induce expression of a surface antigen on a cancer cell surface, of a nucleic acid, and administering to the subject an antibody selected from the group consisting of an anti-CD22 antibody and an anti-CD19 antibody.

According to another aspect of the invention, a method for treating lymphoma is provided. The method includes the steps of isolating a B cell from a subject having lymphoma, identifying a surface antigen which is not expressed or which is expressed on the surface of the B cell in an amount lower than that of a control B cell, administering to the subject an antibody specific for the identified surface antigen and an immunostimulatory nucleic acid in order to treat the lymphoma, wherein the nucleic acid is administered in an effective amount to upregulate expression of the surface antigen on the lymphoma cell surface.

A method for treating a lymphoma resistant to antibody therapy is provided according to another aspect of the invention. The method includes administering to a subject having a lymphoma resistant to therapy with an antibody specific for a surface antigen, an antibody specific for the surface antigen to which the lymphoma is resistant and a nucleic acid in order to treat the lymphoma, wherein the nucleic acid is administered in an effective amount to upregulate expression of the surface antigen on the lymphoma cell surface.

The surface antigen may be any type of surface antigen which is capable of being expressed on the surface of a cancer cell and which is induced by stimulation with immunostimulatory nucleic acids. In some embodiments the surface antigen is CD20, CD40, CD22, or CD19. In other embodiments the lymphoma is B-CLL or marginal zone lymphoma.
some embodiments the antibody is an anti-CD20 antibody. In some embodiments the anti-CD20 antibody is C2B8. In another embodiment the anti-CD20 antibody is Rituximab.

In some preferred embodiments the antibody is a human IgG1 antibody. In some preferred embodiments the antibody is a murine IgG2a antibody.

In some embodiments the methods also include administering an anti-cancer therapy to the subject.

The invention also includes a method for treating cancer in a human by administering to a human an immunostimulatory nucleic acid and an antibody of IgG1 isotype (an IgG1 isotype antibody as used herein refers to a human or humanized IgG1 unless otherwise specified), which binds to a cell surface antigen of a cancer cell and wherein the nucleic acid and the antibody are administered in an effective amount for killing the cancer cell.

Optionally the nucleic acid and the antibody are administered together. Alternatively the nucleic acid and the antibody may be administered separately.

In some embodiments the method includes the step of administering a cancer therapy. As used herein the term “a cancer therapy” is meant to include a single medicament, a plurality of medicaments of a particular class and a plurality of medicaments of different classes, and includes but is not limited to chemotherapeutic agents, cancer vaccines, biological response modifiers, and hormone therapies.

A chemotherapeutic agent may be selected from the group consisting of methotrexate, vincristine, adriamycin, cisplatin, non-sugar containing chloroethylnitrosoureas, 5-fluorouracil, mitomycin C, bleomycin, doxorubicin, dacarbazine, taxol, fraglyfos, Meglamine GLA, valrubicin, camustine and poliferposan, MIM2100, BAY 12-9566, RAS famesly transferase inhibitor, famesly transferase inhibitor, MMF, MT1/23515, LF24618/1 (lonetoxol), Glamosel (CI-994, TNP-470), Hyctamin/topotecan, PSC412, Valspodaar/ PSC833, Novantrone/Mitoxantrone, Metarub/Stramirum, Batimastat, RT700, BC455-456, CS-8, 9-AC, AG3340, AG3343, Incel/VX-710, VX-853, ZD1001, ISL641, ODN 698, TA 2516/Murmistrin, BB2516/Murmiastin, CDP 845, D2163, D183805, DX8951F, Lenomol DP 2200, FK 317, Picibanil/OK-432, AD 32/Valrubcin, Metustron/strontium derivative, Temodal/Carzolomide, Evacet/lsophamidoxorubicin, Yewtaxan/Paclitaxel, Taxol/Paclitaxel, Xeostar/Cepitaxtane, Furtional/Doxifluridin, Cyclopa/oral paclitaxel, Oral Taxoid, SPU-077/Cisplatin, HMR 1275/Flavopiridol, CP-358 (774)/EGFR, CP-609 (754)/RAS oncogene inhibitor, BMS-182751/oral platinum, UFT (Tegafur/Uracil), Ergamisol/Levamisole, Em luracil/77685/ 5FU enhancer, Campto/Levamisole, Camptosar/Topotecan, Tamodex/RLtruxed, Lasutatin/Chlirubine, Paeox/Paclitaxel, Doxil/lsophamidoxorubicin, Caelyx/loxsophamidoxorubicin, Fludara/Fludaraflacin, Pharnarubicin/Epibrubicin, DepoCyt, ZD1839, LU 70553/Bis-Naphtalidin, LU 10379/Dolastain, Caelyx/lsophamidoxorubicin, Genzara/Gemcitabine, ZD 0473/Aornomed, YM 116, Iodine seeds, CDK4 and CDK2 inhibitors, PARP inhibitors, D4089/Doxifosamide, Illes/Mesnex/lsophamidoxorubicin, Yvomun/Toposide, Parlatin/Carboplatin, Plantolin/lsophamidoxorubicin, Vepsid/Toposide, ZD 9331, Taxotere/Doxetaxel, produgs of guanine arabinoside,

Leomustine (CCNU), Methotrexate (MTX), Mitomycin C (MCCNU), Teniposide (VM-26), and Vindesine sulfate.

In some preferred embodiments the chemotherapeutic agent may be selected from the group consisting of methotrexate, vincristine, adriamycin, cisplatin, mitomycin C, bleomycin, doxorubicin, dacarbazine, taxol, valrubicin, Novantrone/Mitoxantrone, Evacet/lsophamidoxorubicin, Yewtaxan/Paclitaxel, Taxol/Paclitaxel, SPU-077/Cisplatin, HMR 1275/Flavopiridol, BMS-182751/oral platinum, Leustatin/Chlirubine, Paeox/Paclitaxel, Doxil/lsophamidoxorubicin, Caelyx/loxsophamidoxorubicin, Fludara/Fludaraflacin, Pharnarubicin/Epibrubicin, DepoCyt, Caelyx/lsophamidoxorubicin, Genzara/Gemcitabine, Illes/Mesnex/lsophamidoxorubicin, Yvomun/Toposide, Parlatin/Carboplatin, Plantolin/lsophamidoxorubicin, Vepsid/Toposide, Taxotere/Doxetaxel, produgs of guanine arabinoside, nitrosoureas, alkylating agents such as melphalan and cyclophosphamide, Asparaginase, Busulfan, Carboplatin, Chlorambucil, Cyrtanib HCl, Daunorubicin HCl, Etoposide (VP1-23), Hydroxyurea (hydroxyurea), Ifosfamide, Interferon Alpha-2a, Interferon Alpha-2b, Leomustine (CCNU), Methotrexate (MTX), Mitomycin C (MCCNU), Teniposide (VM-26), and Vindesine sulfate.

A cancer vaccine may be selected from the group consisting of EGF, Anti-idiotypic cancer vaccines, Gp75 antigen, GMK melanoma vaccine, MGV ganglioside conjugate vaccine, Her2/neu, Ovaex, M-Vax, O-Vax, L-Vax, S thrith-kelter, BL225 (MUC-1), lsophamidoxorubicin, Melunice, peptide antigen vaccines, toxins/antigen vaccines, MVA-based vaccine, PACIS, BCG vaccine, TA-HPV, TA-CIN, DISC-virus and Immucyst/TheraCys. Biological response modifiers include interferon, and lymphokines such as IL-2. Hormone replacement therapy includes tamoxifen alone or in combination with progesterone. In a further embodiment, the cancer therapy is interferon-α (e.g., INTRON®, A, Schering).

The cancer may be selected from the group consisting of basal cell carcinoma, bladder cancer, bone cancer, brain and central nervous system (CNS) cancer, breast cancer, cervical cancer, colon and rectum cancer, connective tissue cancer, esophageal cancer, eye cancer, kidney cancer, larynx cancer, leukemia, liver cancer, lung cancer, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, melanoma, myeloma, oral cavity cancer (e.g., lip, tongue, mouth, and pharynx), ovarian cancer, pancreatic cancer, prostate cancer, rhabdomyosarcoma, skin cancer, stomach cancer, testicular cancer, and uterine cancer. In preferred embodiments, the cancer to be treated may be selected from the group consisting of bone cancer, brain and CNS cancer, connective tissue cancer, esophageal cancer, eye cancer, Hodgkin’s lymphoma, larynx cancer, oral cavity cancer (e.g., lip, tongue, mouth, and pharynx), skin cancer, and testicular cancer.

In another aspect the invention encompasses a kit. The kit includes a package including at least two containers, the first container housing an immunostimulatory nucleic acid, the second container housing an antibody specific for a cell surface antigen, and instructions for screening a cell to determine
whether the immunostimulatory nucleic acid upregulates expression of the cell surface antigen. In one embodiment the antibody is selected from the group consisting of an anti-CD20 antibody, an anti-CD19 antibody, and an anti-CD22 antibody.

The nucleic acids useful according to the invention are immunostimulatory nucleic acids and in some embodiments are immunostimulatory CpG nucleic acids having an unmethylated CpG motif, immunostimulatory T-rich nucleic acids, immunostimulatory poly-G nucleic acids, bacteriophage DNA, yeast DNA, or eukaryotic DNA.

In some embodiments the nucleic acid does not hybridize with genomic DNA or RNA under stringent conditions. In other embodiments the nucleic acid does hybridize with genomic DNA or RNA under stringent conditions.

The nucleic acid may have natural linkages or may include at least one modified backbone internucleotide linkage. In some embodiments the modified backbone is a phosphate backbone modification. In other embodiments the modified backbone is a peptide modified oligonucleotide backbone. The nucleic acid may also include native bases or modified bases. The nucleotide backbone may be chimeric, or the nucleotide backbone is entirely modified.

The immunostimulatory nucleic acid can be any length greater than 6 nucleotides, but in some embodiments is between 8 and 100 nucleotide residues in length. In other embodiments the nucleic acid comprises at least 20 nucleotides, at least 24 nucleotides, at least 27 nucleotides, or at least 30 nucleotides. The nucleic acid may be single-stranded or double-stranded. In some embodiments the nucleic acid is isolated and in other embodiments the nucleic acid may be a synthetic nucleic acid.

The CpG nucleic acid in one embodiment contains at least one unmethylated CpG dinucleotide having a sequence including at least the following formula: 5' XnCnXn 3', wherein C is unmethylated, wherein X is X1, X2, X3, and X4 are nucleotides. In one embodiment the 5' X1C2X3X4 3' sequence of the CpG nucleic acid is a non-palindromic sequence, and in other embodiments it is a palindromic sequence.

In some embodiments X1, X2, are nucleotides selected from the group consisting of: GpT, GpG, CpA, ApT, ApG, CpT, CpA, CpG, TpA, TpT, and TpG; and X3, X4 are nucleotides selected from the group consisting of: TpT, TpA, TpG, CpG, TpC, ApC, CpC, TpA, ApA, and CpA. In other embodiments X1, X2, are GpA or GpT and X3, X4 are TpT. In yet other embodiments X1, X2, both are purines and X3, X4, both are pyrimidines or X1, X2, are GpA and X3, X4, both are pyrimidines. In one embodiment X1 is a T and X2 is a pyrimidine.

In other embodiments the CpG nucleic acid has a sequence selected from the group consisting of SEQ ID Nos: 19, 35-37, 39-42, 91, 92, 101, 108, 111, 135, 141, 151, 274, 277, 280, 286, 319, 350, 363, 368, 375, 495-498, 517, 518, 521, 524, 529, 545, 548, 549, 555, 557, 560-563, 566, 585, 590, 591, 595, 599, 603, 605, 611, 614-616, 650, 676, 679, 682, 684, 702, 703, 707-710, 717-720, 729-732, 752, 755, 770, and 801-803. In some embodiments the T-rich immunostimulatory nucleic acid is a poly-T nucleic acid comprising 5'TTTTTT 3'. In yet other embodiments the poly-T nucleic acid comprises 5' X1X2X3X4X5X6 3' wherein X1, X2, X3, X4, and X5, X6 are nucleotides. In some embodiments X1, X2 is TT and/or X3, X4 is TT. In other embodiments X1, X2, is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC; and/or X3, X4, is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.

The T-rich immunostimulatory nucleic acid may have only a single poly-T motif or it may have a plurality of poly-T nucleic acid motifs. In some embodiments the T-rich immunostimulatory nucleic acid comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 T motifs. In other embodiments it comprises at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 CpG motifs. In some embodiments the plurality of CpG motifs and poly-T motifs are interspersed.

In yet other embodiments at least one of the plurality of poly-T motifs comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, or at least 9 contiguous T nucleotide residues. In other embodiments the plurality of poly-T motifs is at least 3 motifs and wherein at least 3 motifs each comprises at least 3 contiguous T nucleotide residues or the plurality of poly-T motifs is at least 4 motifs and wherein the at least 4 motifs each comprises at least 3 contiguous T nucleotide residues.

The T-rich immunostimulatory nucleic acid may include one or more CpG motifs. In other embodiments the T-rich immunostimulatory nucleic acid is free of one or more CpG dinucleotides.

In other embodiments the T-rich immunostimulatory nucleic acid has poly A, poly-G, and/or poly C motifs. In other embodiments the T-rich immunostimulatory nucleic acid is free of two poly C sequences of at least 3 contiguous C nucleotide residues. Preferably the T-rich immunostimulatory nucleic acid is free of two poly A sequences of at least 3 contiguous A nucleotide residues. In other embodiments the T-rich immunostimulatory nucleic acid comprises a nucleotide composition of greater than 25% C or greater than 25% A. In yet other embodiments the T-rich immunostimulatory nucleic acid is free of poly-C sequences, poly-G sequences or poly-A sequences.

In some cases the T-rich immunostimulatory nucleic acid may be free of poly-T motifs, but rather, comprises a nucleotide composition of greater than 25% T. In other embodiments the T-rich immunostimulatory nucleic acid may have poly-T motifs and also comprises a nucleotide composition of greater than 25% T. In some embodiments the T-rich immunostimulatory nucleic acid comprises a nucleotide composition of greater than 25% T, greater than 30% T, greater than 40% T, greater than 50% T, greater than 60% T, greater than 80% T, or greater than 90% T nucleotide residues.

In some embodiments the poly-G nucleic acid comprises: 5' X1X2X3X4X5X6 3' wherein X1, X2, X3, X4, and X5, X6 are nucleotides. In embodiments at least one of X1 and X2 are a G or both of X3 and X4 are a G. In other embodiments the poly-G nucleic acid comprises the following formula: 5' GGGNGGGG 3' wherein N represents between 0 and 20 nucleotides. In other embodiments the poly-G nucleic acid comprises the following formula: 5' GGGNGGGGNGGGG 3' (SEQ ID NO:849) wherein N represents between 0 and 20 nucleotides.

The poly-G immunostimulatory nucleic acid may include one or more CpG motifs or T-rich motifs. In other embodiments the poly-G nucleic acid is free of one or more CpG dinucleotides or poly-T motifs.

Each of the limitations of the invention can encompass various embodiments of the invention. It is, therefore, anticipated that each of the limitations of the invention involving any one element or combinations of elements can be included in each aspect of the invention.

**BRIEF DESCRIPTION OF THE DRAWINGS**

Fig. 1 depicts data from flow cytometry which demonstrates the induction of a morphologic change in marginal
zone lymphoma cells upon CpG oligonucleotide stimulation. Malignant B cells from a patient with marginal zone lymphoma were stimulated with no oligonucleotide (A and D), control oligonucleotide (ODN 2017, SEQ ID NO: 168, B and E) or CpG oligonucleotide (ODN 2006, SEQ ID NO: 729, C and F) and analyzed by flow cytometry. A, B, and C illustrate forward scatter (FSC; x-axis) vs. side scatter (SSC; y-axis), D, E and F illustrate CD19 expression (x-axis) against FSC (y-axis).

FIG. 2 depicts data from flow cytometry which demonstrates the change in expression of surface antigens on marginal zone lymphoma cells upon CpG oligodeoxynucleotide (ODN) treatment. Flow cytometric analysis of surface antigen expression on malignant B cells from a patient with marginal zone lymphoma was performed using either CpG or non-CpG oligonucleotide. Thin curves indicate incubation with medium alone, dotted curves indicate incubation with control oligonucleotide, and bold curves indicate incubation with CpG oligonucleotide.

FIG. 3 is a set of bar graphs depicting changes in expression of surface antigens on primary cells representing different B-cell malignancies and cells of a benign follicular hyperplasia on treatment with, from left to right in each panel: negative control, no oligonucleotide, control oligonucleotide (ODN 2017, SEQ ID NO: 168), or CpG oligonucleotide (ODN 2006, SEQ ID NO: 729). Each panel represents one experiment.

FIG. 4 is a set of graphs depicting the observation that the effect of CpG oligonucleotide on CD20 (top) and CD40 (bottom) is dependent on the baseline level of expression of CD20 and CD40. Cells from lymph node biopsies, peripheral blood or pleural fluid from patients with different B-cell malignancies were incubated with or without CpG oligonucleotide, and expression of CD20 and CD40 was measured by flow cytometry.

FIG. 5 depicts data from flow cytometry which demonstrates the effect of CpG oligonucleotide-induced proliferation of malignant and normal B cells. Peripheral blood mononuclear cells from patients with B-CLL (left) or marginal zone lymphoma with circulating malignant cells (right), were incubated with CpG oligonucleotide (bottom) or medium alone (top) and evaluated by two-color flow cytometry. CFSE fluorescence (x-axis) and expression of CD5 (B-CLL) or CD19 (marginal zone lymphoma) (y-axis) were evaluated.

FIG. 6 is a graph depicting the survival of mice injected on Day 0 with tumor cells in response to CpG stimulation in combination with murine IgG2a and murine IgG1 anti-tumor antibodies. Treatments are shown as filled squares, untreated controls; filled circles, murine IgG1; filled triangles, murine IgG1 plus CpG; filled diamonds, murine IgG2a; and open squares, murine IgG2a plus CpG.

**DETAILED DESCRIPTION**

Present cancer treatments are often ineffective as well as being associated with a high degree of patient morbidity. The invention provides methods and products for the more effective treatment of cancer using a combination of immunostimulatory nucleic acids, antibodies, and optionally cancer therapies.

The invention is based, in part, on the surprising discovery that administration to a subject of immunostimulatory nucleic acids induces the expression of cell surface antigens including CD20, CD19, and CD22 on the surface of a cancer cell and that the induction of these antigens leads to enhanced antibody-dependent cellular cytotoxicity (ADCC). It was previously believed that CpG oligonucleotides enhanced ADCC by influencing the effector cell (e.g., by activating natural killer (NK) cells). Now it has been discovered according to the invention that immunostimulatory nucleic acids actually cause the induction of specific antigens CD20, CD19, and CD22, each of which can be targeted by specific antibody therapies. The discovery that immunostimulatory nucleic acids are capable of upregulating expression of certain target antigens on the surface of cancer cells, supports the development of therapies using immunostimulatory nucleic acids in combination with specific antibodies which interact with these cell surface antigens. Thus, in one aspect, the invention provides a method for treating or preventing cancer which involves the administration to a subject of a combination of an immunostimulatory nucleic acid and an antibody which specifically interacts with CD20, CD19, and CD22 in an effective amount to prevent or treat the cancer.

Additionally, it was discovered that the increased expression of these and other cell surface antigens varies widely depending upon the histological state of the tumor cell studied. The effect of immunostimulatory nucleic acids on different types of primary malignant B cells and reactive follicular hyperplasia was extensively examined. All B-cell lymphoma cells tested increased in size and granularity, upregulated activation markers (CD80, CD86, CD40, CD54, CD69), and upregulated antigen presentation molecules (class I major histocompatibility complex (MHC I), class II major histocompatibility complex (MHC II)) in response to immunostimulatory nucleic acids. A control poly-C oligodeoxynucleotide (ODN) showed only minor effects. The extent of phenotypic change induced by immunostimulatory nucleic acids differed from sample to sample. Immunostimulatory nucleic acids, but not control nucleic acids, increased the expression of co-stimulatory molecules (e.g., CD40, CD80, CD86, CD54) on malignant B cells without altering the phenotype of B cells derived from reactive follicular hyperplasia. Immunostimulatory nucleic acids also enhanced expression of both class I and class II MHC in most samples. CD20 expression was increased in response to immunostimulatory nucleic acids, most notably in B-CLL and marginal zone lymphoma.

Furthermore, an inverse correlation was found between baseline expression of specific cell surface antigens and their expression after exposure to immunostimulatory nucleic acids. Thus the most significant increase in expression of these molecules was found in those samples that had the lowest (or no) baseline levels. These data indicate that immunostimulatory nucleic acids may reverse low expression of co-stimulatory molecules on malignant B cells that correspond to a low level of activation, while their effects on cells that are already in an activated state are less profound.

Thus, the invention relates to methods for identifying an appropriate therapy for a lymphoma patient, and for treating the patient using that therapy. The method can be accomplished by isolating a B cell from a lymphoma patient and comparing the surface antigens expressed on the malignant B cell with those expressed on normal B cells. The antigens which are expressed in low levels or not at all on the malignant B cell can be identified. The subject can then be treated using a combination of an immunostimulating nucleic acid and an antibody which specifically recognizes the antigen(s) which are expressed in low levels or not at all on the malignant B cell.

The invention is also useful for treating cancers which are resistant to monoclonal antibody therapy. It has been discovered according to the invention, that immunostimulatory nucleic acids can reverse the resistance of tumor cells and render tumor cells which were previously non-responsive or
A cancer cell is a cell that divides and reproduces abnormally due to a loss of normal growth control. Cancer cells almost always arise from at least one genetic mutation. In some instances, it is possible to distinguish cancer cells from their normal counterparts based on profiles of expressed genes and proteins, as well as to the level of their expression. Genes commonly affected in cancer cells include oncogenes, such as ras, neu/HER2/erbB, myb, myc and abl, as well as tumor suppressor genes such as p53, Rb, DCC, RET and WT. Cancer-related mutations in some of these genes leads to a decrease in their expression or a complete deletion. In others, mutations cause an increase in expression or the expression of an activated variant of the normal counterpart.

The term “tumor” is usually equated with neoplasm, which literally means “new growth” and is used interchangeably with “cancer.” A “neoplastic disorder” is any disorder associated with cell proliferation, specifically with a neoplasm. A “neoplasm” is an abnormal mass of tissue that persists and proliferates after withdrawal of the carcinogenic factor that initiated its appearance. There are two types of neoplasms, benign and malignant. Nearly all benign tumors are encapsulated and are noninvasive; in contrast, malignant tumors are almost never encapsulated but invade adjacent tissue by infiltrative destructive growth. This infiltrative growth can be followed by tumor cells implanting at sites discontinuous with the original tumor. The method of the invasion can be used to treat neoplastic disorders in humans, including but not limited to: sarcoma, carcinoma, fibroma, glioma, leukemia, lymphoma, melanoma, myeloma, neuroblastoma, retinoblastoma, and rhabdomyosarcoma, as well as each of the other tumors described herein.

“Cancer” as used herein refers to an uncontrolled growth of cells which interferes with the normal functioning of the bodily organs and systems. Cancers which migrate from their original location and seed vital organs can eventually lead to the death of the subject through the functional deterioration of the affected organs. Hemopoietic cancers, such as leukemia, are able to out-compete the normal hemopoietic compartments in a subject, thereby leading to hemopoietic failure (in the form of anemia, thrombocytopenia and neutropenia), ultimately causing death.

A metastasis is a region of cancer cells, distinct from the primary tumor location, resulting from the dissemination of cancer cells from the primary tumor to other parts of the body. At the time of diagnosis of the primary tumor mass, the subject may be monitored for the presence of metastases. Metastases are most often detected through the sole or combined use of magnetic resonance imaging (MRI) scans, computed tomography (CT) scans, blood and platelet counts, liver function studies, chest X-rays and bone scans in addition to the monitoring of specific symptoms.

Cancers include, but are not limited to: basal cell carcinoma, biliary tract cancer; bladder cancer; bone cancer; brain and CNS cancer; breast cancer; cervical cancer; choriocarcinoma; colon and rectum cancer; connective tissue cancer; cancer of the digestive system; endometrial cancer; esophageal cancer; eye cancer; cancer of the head and neck; gastric cancer; intra-epithelial neoplasm; kidney cancer; larynx cancer; leukemia; liver cancer; lung cancer (e.g., small cell and non-small cell); lymphoma including Hodgkin’s and non-Hodgkin’s lymphomas; melanoma; myeloma; neuroblastoma; oral cavity cancer (e.g., lip, tongue, mouth, and pharynx); ovarian cancer; pancreatic cancer; prostate cancer; retinoblastoma; rhabdomyosarcoma; rectal cancer; renal cancer; cancer of the respiratory system; sarcoma; skin cancer; stom-
ach cancer; testicular cancer; thyroid cancer; uterine cancer; cancer of the urinary system, as well as other carcinomas and sarcomas.

The immunostimulatory nucleic acids and antibodies are useful for treating or preventing cancer in a subject. A “subject” unless otherwise specified shall mean a human or ver- tebrate mammal including but not limited to a dog, cat, horse, cow, pig, sheep, goat, or primate, e.g., monkey. Thus the invention can be used to treat cancer and tumors in human and non human subjects. Cancer is one of the leading causes of death in companion animals (i.e., cats and dogs). Cancer usually strikes older animals which, in the case of house pets, have become integrated into the family. Forty-five percent of dogs older than 10 years of age are likely to succumb to the disease. The most common treatment options include surgery, chemotherapy and radiation therapy. Other treatment modalities which have been used with some success are laser therapy, cryotherapy, hyperthermia and immunotherapy. The choice of treatment depends on the type of cancer and degree of dissemination. Unless the malignant growth is confined to a discrete area in the body, it is difficult to remove only malignant tissue without affecting normal cells.

Malignant disorders commonly diagnosed in dogs and cats include but are not limited to lymphosarcoma, osteosarcoma, mammary tumors, mastocytoma, brain tumor, melanoma, adenocarcinoma, carcinoid lung tumor, bronchial gland tumor, bronchiolar adenocarcinoma, fibroma, myxochondroma, pulmonary sarcoma, neurosarcoma, osteoma, papilloma, retinoblastoma, Ewing’s sarcoma, Wilms’ tumor, Burkitt’s lymphoma, microglioma, neuroblastoma, osteoclastoma, oral neoplasia, fibrosarcoma, osteosarcoma and rhabdomyosarcoma. Other neoplasias in dogs include genital squamous cell carcinoma, transmissible venereal tumor, testi- tular tumor, seminoma, Sertoli cell tumor, hemangiosper- cytoma, histiocytoma, choroma (granulocytoma sarcoma), corn- eal papilloma, corneal squamous cell carcinoma, hemangiosarcoma, pleural mesothelioma, basal cell tumor, thymoma, stomach tumor, adrenal gland carcinoma, oral papillomatosis, hemangioendothelioma and cystadenoma. Additional malignancies diagnosed in cats include follicular lympho- phoma, intestinal lymphosarcoma, fibrosarcoma and pulmonary squamous cell carcinoma. The ferret, an ever- more popular house pet, is known to develop insulinoma, lymphoma, sarcoma, neurofibroma, pancreatic islet cell tumor, gastric MALT lymphoma and gastric adenocarcinoma.

Neoplasias affecting agricultural livestock include leuko- mia, hemangiospercytoma and bovine ocular neoplasmia (in cattle); preputial fibrosarcoma, ulcerative squamous cell carci- noma, preputial carcinoma, connective tissue neoplasia and masto- psmia (in horses); hepatocellular carcinoma (in swine); lymphoma and pulmonary adenomatosis (in sheep); pulmonary sarcoma, lymphoma, Ros sarcoma, reticuloen- dotheliosis, fibrosarcoma, nephroblastoma. B-cell lympho- phoma and lymphoid leukosis (in avian species); retinoblasto- ma, hepatic neoplasia, lymphosarcoma (lymphoblastic lymphoma), pneumocytoid leukemia and swinbladder sarco- ma (in fish), caseous lymphadenitis (CLA): chronic, infec- tious, contagious disease of sheep and goats caused by the bacterium Corynebacterium pseudotuberculosis, and conta- gious lung tumor of sheep caused by jagshekte.

In one aspect, a method for treating cancer is provided which involves administering the compositions of the inven- tion to a subject having cancer. A “subject having cancer” is a subject that has been diagnosed with a cancer. In some embodiments, the subject has a cancer type characterized by a solid mass tumor. The solid tumor mass, if present, may be a primary tumor mass. A primary tumor mass refers to a growth of cancer cells in a tissue resulting from the transformation of a normal cell of that tissue. In most cases, the primary tumor mass is identified by the presence of a cyst, which can be found through visual inspection or palpation methods, or by irregularity in shape, texture or weight of the tissue.

However, some primary tumors are not palpable and can be detected only through medical imaging techniques such as X-rays (e.g., mammography), or by needle aspirations. The use of these latter techniques is more common in early detection. Molecular and phenotypic analysis of cancer cells within a tissue will usually confirm if the cancer is endogenous to the tissue or if the lesion is due to metastasis from another site.

With respect to the prophylactic treatment methods, the invention is aimed at administering the compositions of the invention to a subject at risk of developing cancer. A subject at risk of developing a cancer is one who has a high probability of developing cancer. These subjects include, for instance, subjects having a genetic abnormality, the presence of which has been demonstrated, to have a correlational relation to a higher likelihood of developing a cancer. Subjects exposed to cancer-causing agents such as tobacco, asbestos, or other chemical toxins are also subjects at risk of developing cancers used herein. When a subject at risk of developing a cancer is treated with an immunostimulatory nucleic acid, an antibody and optionally a cancer therapy, on a regular basis, such as monthly, the cancer growth will be prevented from initiating. This aspect of the invention is particularly advantageous when the subjects employed in certain trades which are exposed to cancer-causing agents on an ongoing basis. For example, many airborne, or inhaled, carcinogens such as tobacco smoke and asbestos have been associated with lung cancer.

A carcinogen is an agent capable of initiating development of malignant cancers. Exposure to carcinogens generally increases the risk of neoplasms in subjects, usually by affecting DNA directly. Carcinogens may take one of several forms such as chemical, electromagnetic radiation, or may be an inert solid body.

Substances for which there is sufficient evidence to establish a causal relationship in cancer in humans are referred to as confirmed human carcinogens. Included in this category are the following substances: Aflatoxins, Alcoholic beverages, Aluminium production, 4-aminobiphenyl, Arsenic and arsenic compounds, Asbestos, Manufacture of aunamine, Azathioprine, Benzene, Benzidine, Beryllium and beryllium compounds, Benet quid with tobacco, Bis(chloromethyl)ether and chloromethyl methyl ether (technical grade), Boot and shoe manufacture and repair (occupational exposure), 1,4 Butanediol dimethanesulphonate (Myleran), Cadmium and cadmium compounds, Chlorambucil, Chlorphenazone, 1-(2- Chlorethyl)-3-(4-methylcyclohexyl)-1 nitrosoarene, Chloromethyl methyl ether (technical), Chromium compounds (hexavalent), Coal gasification, Coal tar pitches, Coal tars, Coke production, Cyclophosphamide, Cyclosporin, Eriochrome, Ethylene oxide, Furniture and cabinet making, Underground haematite mining with exposure to radon, Iron and steel founding, Isopropyl alcohol manufacture (strong acid pro- cess), Manufacture of mephtal, 8-Methoxypсорal en (Methoxsalen) plus ultraviolet radiation, Mineral oils-unobstructed and mildly-treated oils, MOPP and other combined chemotherapy for cancer, Mustard gas (sulphur mustard), 2-Naphthylamine, Nickel and nickel compounds (essentially sulphate and sulphide), Nonsteroidal estrogens (not necessarily all in group) includes diethylstilbesterol, Estrogen replacement therapy, and Combined oral contraceptives and sequen-
tial oral contraceptives, Steroidal estrogens (not all in group), Painter (occupational exposure as a painter), Phenacetin (analgesic mixtures containing), Rubber industry, Salted fish (Chinese style), Solar radiation, Stale oils, Soots, Sulphuric acid (occupational exposures to strong-inorganic-acid mixtures of sulphuric acid), Tale containing asbestos fibres, Thiotepa, Tobacco products (smokeless), Tobacco smoke, Treosulphan, and Vinyl chloride.

Substances for which there is a lesser degree of evidence in humans but sufficient evidence in animal studies, or degrees of evidence considered unequivocal of mutagenicity in mammalian cells, are referred to as probable human carcinogens. This category of substances includes: Acrylamide, Acrylonitrile, Adriamycin, Anabolic steroids, Azacitidine, Benzantracene, Benzidine-based dyes (technical grade), Direct Black 58, Direct Blue 6, Direct Brown 95, Benzopyrene, 3-Butadiene, Captafol, Bischloroethyl nitrosourea (BCNU), 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), Chloramphenicol-para-Chloro-ortho-toluidine and its strong acid salts, Chlorozotocin, Cisplatin, Cremosole, Dibenzenoacridine, Diesel engine exhaust, Diethyl sulphate, Dimethylcarbamoyl chloride, Dimethyl sulphone, Epichlorohydrin, Ethylene dibromide, N-Ethyl-N-nitrosourea, Formaldehyde, Glass manufacturing industry (occupational exposure), Art glass (glass containers and pressed ware), Hairdresser or barber (occupational exposure, probably dyes), Insecticide use (occupational exposure), IQ (2-Amino-3-methylimidazo[4,5-f]quinoline), Mate drinking (hot), 5-Methoxyxypyrrole, 4,4'-Methylenebis(2-chloroaniline) (MOCA), N-Methyl N-Nitro-N-nitrosoguanidine (MINNG), N-Methyl-N-Nitrosourea, Nitrogen mustard, N-Nitrosodimethylamine, N-Nitrosodimethylamine, Petroleum refining (occupational refining exposures), Phenacetin, Polychlorinated biphenyls, Procarbazine hydrochloride, Silica (crystalline), Styrene-7,8-oxide, Tris-[{aziridinyl}phosphine sulphide (Thiotepa), Tris(2,3-dibromopropyl) phosphate, Ultraviolet radiation: A, B and C including sunlamps and sunbeds, and Vinyl bromide.

Substances for which there is sufficient evidence in animal tests are referred to as possible human carcinogens. This category of substances includes: A-C (2-Amino-9H-pyrido[2,3-b]indole), Acetaldehyde, Acetamide, AF-2[2-(2-Furyl)-3-(5-nitro-2-furyl)]acrylamide, para-Aminooazobenzene, ortho-Aminooazobenzene, 2-Amino-5-(5-nitro-2-furyl)-1,3,4-thiadiazole, Amirole, ortho-Anisidine, Antimony trioxide, Aramine, Atrazine, Attapulgite, Azaserine, Benzol[ghi]fluoranthene, Benzol[ghi]fluoranthene, Benzol[ghi]fluoranthene, Benzol[ghi]fluoranthene, Benzo[ghi]fluoranthene, Biphenyl, Bitumens (extracts of steam-refined and air-refined bitumens), Bleomycins, Bracken ferns, Bromochloromethane, Butylated hydroxyanisole (BHA), Butylresorcinol, Caffeine acid, Carbon black extract, Carbon tetrachloride, Carrageenan (degraded), Ceramic fibres, Chloramphenicol, Chlorane, Chloroethylene, Chloropicrin, Chlorinated paraffins of a average carbon-chain length C12 and average degree of chlorination approx 60%, alpha-Chlorinated toluenes (not necessarily all in group), Benzo(a)chloroaniline, Chloroform, Chlorophenols, Pentachlorophenol, 2,4,6-Trichlorophenol, Chlorophenoxycarboxylic acids (not necessarily all in group), 4-Chloro-ortho-phenoxylenediamine, CI Acid Red 114, CI Basic Red 9, CI Direct Blue 15, CI Red 9 No. 2, Cobalt and cobalt compounds, Coffee (bladder), Cora-Cresidine, Cycasin, Daecarbazane, Dantron (1,8-dihydroxyanthraquinone), Daunomycin, DDT, NN-Dicyetylbenzene, 4,4'-Diaminodiphenyl ether, 2,4-Diaminothluene, Dibenzo[a,h]carbazine, Dibenzo[a,i]carbazine, 7H-Dibenzo[c,g]carbazole, Dibenzo[a,e]pyrene, Dibenz[a, h]pyrene, Dibenz[a]anthracene, 1,2-Dibromo-3-chloropropane, para-Dichlorobenzene, 3,3'-Dichlorobenzene, DBP, 3,3'-Dichloro-4,4'-diaminodiphenyl ether, 1,2-Dichloroethane, Dichloromethane, 1,3-Dichloropropene (technical grade), Dichlorvos, Dioxybutane, Diesel fuel (marine), Di(2-ethylhexyl)phthalate, 1,2-Diethylhydrazine, Diglycidylresorcinolet ether, Diisopropylfluore, Diisopropyl sulphate, 3,3'-Dimethoxybenzidine, para-Dimethyleniminoazobenzene, trans-2-[(Dimethylenimino)methyl]iminio]-5-[2-(5-nitro-2-furylvinyl]-1,3,4-oxidiazole, 2,6-Dimethylaniline (2,6-Xyldiene), 3,3'-Dimethylbenzidine (ortho-tolidine), Dimethylformamide, 1,1-Dimethylhydrazine, 1,2-Dimethylhydrazine, 1,6-Dinitropyrene, 1,8-Dinitropyrene, 1,4-Dioxane, Disperse Blue, Ethyl acrylate, Ethylene thiourea, Ethyl methanesulphonate, 2-(2-Formylhydrazino)-4-(5-nitro-2-furyl)thiazole, Fuel oils (residual, heavy), Fusarium moniliforme (toxins derived from), Fumonisin B1; Fumonisin B2; Fusarin C, Gasoline, Gasoline engine exhausts, Glasswool, Glu-P-1 (2-Amino-6-methyl-2-pyridinyl)-2H[3a,3'-3H]-diamidazole, Glu-P-2(Amino-pyrindiazol-1,2-a:3'-3':2'-diamidazol), Glycidaldehyde, Griseofulvin, HC Blue No 1, Heptachlor, Hexachlorobenzene, Hexachlorocyclohexanes Technical grades alpha isomer gamma isomer (lindane), Hexamethylphosphoramide, Hydrazine, Indeno[1,2,3-cd]pyrene, Iron-dextran complex, Isoprene, Lasicaproic, Lead and lead compounds (inorganic), Magneta (containing CI Basic Red 9), Man-made mineral fibres (see glasswool, rockwool, slagwool, and ceramic fibres), Me4-A-C (2-Amino-3-methyl-9H-pyrid[2,3-b]indole), MeIQ (2-Amino-3,4-dimethylimidazo[4,5-f]quinolone), MeIQx (2-Amino-3,8-dimethylimidazo[4,5-f]quinoxaline), Methylmercury compounds (methylmercuric chloride), Melphalan, 2-Methylaziridine, Methylazoxymethanol and its acetate, 5-Methylchrysene, 4,4'-Methylenebis(2-methylaniline), Methylmethanesulphonate, 2-Methyl-1-nitrosothaquinone (uncertain purity), N-Methyl-N-Nitrosourea, Methyliouracil, Metronidazole, Mitoxantrone, N-Nitrosopiperidine, N-Nitrosodipropylene, N-Nitrosodiethylamine, N-Nitrosodiethylamine, N-Nitrosoguanidine, N-Nitrosomethane, N-Nitrosopyrrolidine, N-Nitrososarcosine, Ochratoxin A, Oil Orange, Panfuran S (containing difluoromethylfurans), Phenanthraquinone, Phenobarbital, Phenyldimethylhydrazine, Phenyl glycidyl ether. Phenylmethoxypiper (2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine, Pickled vegetables, traditional Asian, Polynuclear aromatic hydrocarbons, Ponceau MXPonceau 3R, Potassium bromate, 1,3-Propanediol, Propylene oxide, Progestins. Medroxyprogesterone acetate, a-Propiolactone, Propylthiouracil, Rockwool, Saccharin, Saffrole, Slagwool, Sodium ortho-phenylphenate, Sterigmatocystin, Streptozotocin, Styrene, Sulfuric acid, 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD), Tetrachloroethylene, Textile manufacturing (occupational exposures), Thiomercapto carboxamide, 4-Thiodianthiolane, Thiourea, Toluene, trisocyanates-o-toluidine, Toxaphene (polychlorinated camphenes), Trichloromethane (trimethyl hydrochloride), Trp-P-1 (3-Amino-1,4-dimethyl-5H-pyrido[4,5-b]indole), Trp-P-2 (3-Amino-1,4-dimethyl-5H-pyrid[4,5-b]indole), Trypan blue, Uracil mustard, Urethane, 4-Vinylcyclohexene.
clohexene, 4-Vinylclohexene diepoxyde, Welding fumes, Wood industries and Carpentry and joinery.

Subjects at risk of developing cancer also include those who have a genetic predisposition to cancer. In many cases, genetic predisposition to cancer can be identified by studying the occurrence of cancer in family members. Examples of genetic predisposition to common forms of cancer include, but are not limited to, mutation of BRCA1 and BRCA2 in familial breast cancer, mutation of APC in familial colon cancer (familial polyposis coli), mutation of MSH2 and MLH1 in hereditary nonpolyposis colon cancer (HNPCC), mutation of p53 in Li-Fraumeni syndrome, mutation of RB1 in retinoblastoma, mutation of RET in multiple endocrine neoplasia type 2 (MEN2), mutation of VHL in renal cancer and mutation of WT1 in Wilms' tumor. Other cancers for which a familial predisposition has been identified include ovarian, prostate, melanoma and lung cancer.

It has been estimated that almost half of all currently diagnosed cancers will be treated with some form of cancer medication. However, many forms of cancer, including melanoma, colorectal, prostate, endometrial, cervical and bladder cancer, do not respond well to treatment with cancer medicaments. In fact, only about 5-10 percent of cancers can be cured using cancer medicaments alone. These include some forms of leukemias and lymphomas, testicular cancer, choriocarcinoma, Wilms' tumor, Ewing's sarcoma, neuroblastoma, small-cell lung cancer and ovarian cancer. Treatment of other cancers, including breast cancer, requires a combination therapy of surgery or radiotherapy in conjunction with a cancer medicament.

The immunostimulatory nucleic acids are administered in combination with antibodies which specifically bind to cancer cell surface antigens. These antibodies include but are not limited to anti-CD20 antibodies, anti-CD40 antibodies, anti-CD19 antibodies, anti-CD22 antibodies, anti-HLA-DR antibodies, anti-CD80 antibodies, anti-CD86 antibodies, anti-CD54 antibodies, and anti-CD69 antibodies. These antibodies are available from commercial sources or may be synthesized de novo.

Commercially available anti-CD20 antibodies include but are not limited to those presented in Table 1 below.

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<td>AHS2021</td>
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<td>BioSource International</td>
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<td>Mouse Anti-CD20, B-Cell, Human IgG2a Antibody, Kappa, Supernatant, Clone L26, 1 ml</td>
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<tr>
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<td>Lab Vision Corp.</td>
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</table>
| Antibodies are well known to those of ordinary skill in the science of immunology. As used herein, the term “antibody” means not only intact antibody molecules but also fragments of antibody molecules retaining specific binding ability. Such fragments are also well known in the art and are regularly employed both in vitro and in vivo. In particular, as used herein, the term “antibody” means not only intact immunoglobulin molecules but also the well-known active fragments F(ab')2, and Fab F(ab')2, and Fab fragments which lack the Fc region.
fragment of intact antibody, clear more rapidly from the circulation, and may have less non-specific tissue binding of an intact antibody. Wahl R.L. et al., *J Nucl Med* 24:316-25 (1983). Antibody fragments which are particularly useful according to the methods of the invention are those which are bispecific and constructed to enhance FcR binding, e.g., include an Fe portion. These include, but are not limited to Medarex antibodies (MDX-210, 220, 22, 447, and 260). Other non-Fc containing fragments which interact with the antigens induced on the cell surface are also useful. These are particularly useful in combination with immunotoxins and/or radioactivity. The fragments can be delivered separately from the immunotoxins or radioactivity or conjugated thereto (e.g., radiolabeled antibodies or antibody fragments).

Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity-determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the paniote (see, in general, Clark, 1986; Roitt, 1991). In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are four framework regions (FR1 through FR4) separated respectively by three complementarity-determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.

It is now well-established in the art that the non-CDR regions of a mammalian antibody may be replaced with similar regions of conspecific or heterospecific antibodies while retaining the epitope specificity of the original antibody. This is most clearly manifested in the development and use of “humanized” antibodies in which non-human CDRs are covalently joined to human FR and/or Fe/Fc′ regions to produce a functional antibody. Thus, for example, PCT International Publication Number WO 92/04381 teaches the production and use of humanized murine RSV antibodies in which at least a portion of the murine FR regions have been replaced by FR regions of human origin. Such antibodies, including fragments of intact antibodies with antigen-binding ability, are often referred to as “chimeric” antibodies. A “humanized monoclonal antibody” as used herein is a human monoclonal antibody or functionally active fragment thereof having human constant regions and a binding CDR3 region from a mammal of a species other than a human. Humanized monoclonal antibodies may be made by any method known in the art. Humanized monoclonal antibodies, for example, may be constructed by replacing the non-CDR regions of a non-human mammalian antibody with similar regions of human antibodies while retaining the epitope specificity of the original antibody. For example, non-human CDRs and optionally some of the framework regions may be covalently joined to human FR and/or Fe/Fc′ regions to produce a functional antibody. There are entities in the United States which will synthesize humanized antibodies from specific murine antibody regions commercially, such as Protein Design Labs (Mountain View Calif.).

European Patent Application 0239400, the entire contents of which is hereby incorporated by reference, provides an exemplary teaching of the production and use of humanized monoclonal antibodies in which at least the CDR portion of a murine (or other non-human mammal) antibody is included in the humanized antibody. Briefly, the following methods are useful for constructing a humanized CDR monoclonal antibody including at least a portion of a mouse CDR. A first replicable expression vector including a suitable promoter operably linked to a DNA sequence encoding at least a variable domain of an Ig heavy or light chain and the variable domain comprising framework regions from a human antibody and a CDR region of a murine antibody is prepared. Optionally a second replicable expression vector is prepared which includes a suitable promoter operably linked to a DNA sequence encoding at least the variable domain of a complement­

human Ig light or heavy chain respectively. A cell line is then transformed with the vectors. Preferably the cell line is an immortalized mammalian cell line of lymphoid origin, such as a myeloma, hybridoma, triona, or quadroma cell line, or is a normal lymphoid cell which has been immortal­

ized by transformation with a virus. The transformed cell line is then cultured under conditions known to those of skill in the art to produce the humanized antibody.

As set forth in European Patent Application 0239400 several techniques are well known in the art for creating the particular antibody domains to be inserted into the replicable vector. (Preferred vectors and recombinant techniques are discussed in greater detail below.) For example, the DNA sequence encoding the domain may be prepared by oligonucleotide synthesis. Alternatively a synthetic gene lacking the CDR regions in which four framework regions are fused together with suitable restriction sites at the junctions, such that double-stranded synthetic or restricted subcloned CDR cassettes with sticky ends could be ligated at the junctions of the framework regions. Another method involves the preparation of the DNA sequence encoding the variable CDR containing domain by oligonucleotide site-directed mutagenesis. Each of these methods is well known in the art. Therefore, those skilled in the art will construct humanized antibodies containing a murine CDR region without destroying the specificity of the antibody for its epitope.

Human monoclonal antibodies may be made by any of the methods known in the art, such as those disclosed in U.S. Pat. No. 5,567,610, issued to Borreebaek et al., U.S. Pat. No. 5,565,354, issued to Ostberg, U.S. Pat. No. 5,571,893, issued to Baker et al., Kozbor D et al., *J Immunol* 133:3001-5 (1984), Brodeur et al., Monoclonal Antibody Production Techniques and Applications, pp. 51-63 (Marcel Dekker, Inc, New York, 1987), and Boerner P et al., *J Immunol* 147:86-95 (1991). In addition to the conventional methods for preparing human monoclonal antibodies, such antibodies may be prepared by immunizing transgenic animals that are capable of producing human antibodies (e.g., Jakobovits A et al., *Proc Natl Acad Sci USA* 90:2551-5 (1993); Jakobovits A et al., *Nature* 362:255-8 (1993); Bruggemann et al., *Year in Immunology* 7:33 (1993); and U.S. Pat. No. 5,569,825 issued to Lonberg).

Significantly, as is well-known in the art, only a small portion of an antibody molecule, the paratope, is involved in the binding of the antibody to its epitope (see, in general, Clark, W. R. (1986) *The Experimental Foundations of Modern Immunology*; Wiley & Sons, Inc., New York; Roitt, I. (1991) *Essential Immunology*, 7th Ed., Blackwell Scientific Publications, Oxford). The Fcε and Fc regions, for example, are effectors of the complement cascade but are not involved in antigen binding. An antibody from which the Fεc region has been enzymatically cleaved, or which has been produced without the Fεc region, designated an F(ab')2 fragment, retains both of the antigen binding sites of an intact antibody. Similarly, an antibody from which the Fc region has been enzymatically cleaved, or which has been produced without the Fc region, designated an Fab fragment, retains one of the antigen binding sites of an intact antibody molecule. Proceeding further, Fab fragments consist of a covalently bound antibody light chain and a portion of the antibody heavy chain denoted Fd. The Fd fragments are the major determinant of antibody specificity (a single Fd fragment may be associated with up to ten different light chains without altering antibody specificity) and Fd fragments retain epitope-binding ability in isolation.
Other antibodies useful according to the invention are antibodies of the IgG1 isotype. As mentioned above, anti-IgG1 isotype antibody as used herein refers to a human or humanized anti-IgG1 unless otherwise specified. IgG1 isotype antibodies are well known in the art and include at least the antibodies listed in Table 2 below.

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<tr>
<th>Marketer</th>
<th>Brand Name (Generic Name)</th>
<th>Indication</th>
</tr>
</thead>
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<tr>
<td>CytoGen Corp.</td>
<td>Herceptin, anti-HER2 hMAb</td>
<td>Breast/ovarian</td>
</tr>
<tr>
<td>Centocor/Glaxo/Ajinomoto</td>
<td>Quadramet (CYT-424) radiotherapeutic agent</td>
<td>Bone metastases</td>
</tr>
<tr>
<td>Centocor/Ajinomoto</td>
<td>Panorex® (17-1A) (murine monoclonal antibody)</td>
<td>Adjuvant therapy for colorectal (Dukes-C)</td>
</tr>
<tr>
<td>IDEC</td>
<td>IDEC-Y2B8 (murine, anti-CD20 MAb labeled with Yttrium-90)</td>
<td>Pancreatic, lung, breast, ovary</td>
</tr>
<tr>
<td>IntClone Systems</td>
<td>BEC2 (anti-idiotypic MAb, mimics the GD3 epitope) (with BCG)</td>
<td>non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td>IntClone Systems</td>
<td>C225 (chimeric monoclonic antibody to epidermal growth factor receptor (EGFr))</td>
<td>Small cell lung</td>
</tr>
<tr>
<td>Techniclude International/Alpha Therapeutics</td>
<td>Oncoly (Lyn1-1 monoclonal antibody linked to 131 I isotines)</td>
<td>Renal cell</td>
</tr>
<tr>
<td>Protein Design Labs</td>
<td>SMART M195 Ab, humanized 131I LYM-1 (Oncoly™)</td>
<td>Acute myeloid leukemia</td>
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<tr>
<td>Corporation/Cambridge Antibody Technology</td>
<td>ATRAGEN®</td>
<td>non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td>IntClone Systems</td>
<td>C225 (chimeric anti-EGFr monoclonal antibody) + cisplatin or radiation</td>
<td>Head &amp; neck, non-small cell lung cancer</td>
</tr>
<tr>
<td>Altarex, Canada</td>
<td>Ovares (B43.13, anti-idiotypic CA125, mouse MAb)</td>
<td>Ovarian</td>
</tr>
<tr>
<td>Coulter Pharma (Clinical results have been positive, but the drug has been associated with significant bone marrow toxicity)</td>
<td>Bexxar (anti-CD20 MAb labeled with 131 I)</td>
<td>non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td>Arnelex Pharmaceuticals, Inc.</td>
<td>ATRAGEN® (MAb against CD20) par-B Ab in combo, with chemotherapy</td>
<td>Kaposi’s sarcoma</td>
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<tr>
<td>LeukoSite/lex Oncology</td>
<td>LDP-03, hMAb to the leukocyte antigen CAMPATH</td>
<td>B cell lymphoma</td>
</tr>
<tr>
<td>Center of Molecular Immunology</td>
<td>ir76 (anti CD6, murine MAb) CTCL</td>
<td>Chronic lymphocytic leukemia (CLL)</td>
</tr>
<tr>
<td>Medarex/Novartis</td>
<td>MDX-210 (humanized anti-HER-2 bispecific antibody)</td>
<td>Cancer</td>
</tr>
<tr>
<td>Medarex</td>
<td>MDX-210 (humanized anti-HER-2 bispecific antibody)</td>
<td>Breast, ovarian</td>
</tr>
<tr>
<td>Medarex/Novartis</td>
<td>MDX-11 (complement activating receptor (CAR) monoclonal antibody)</td>
<td>Prostate, non-small cell lung, pancreatic, breast</td>
</tr>
<tr>
<td>Medarex</td>
<td>MDX-11 (complement activating receptor (CAR) monoclonal antibody)</td>
<td>Acute myelogenous leukemia (AML)</td>
</tr>
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<td>Medarex</td>
<td>MDX-22 (humanized bispecific antibody, MAb-conjugates) (complement cascade activators)</td>
<td>Renal and colon</td>
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<td>CytoGen Corp.</td>
<td>OV103 (Ytrium-90 labelled antibody)</td>
<td>Ex vivo bone marrow purging in acute myelogenous leukemia (AML)</td>
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<tr>
<td>CytoGen</td>
<td>OV103 (Ytrium-90 labelled antibody)</td>
<td>Acute myeloid leukaemia</td>
</tr>
<tr>
<td>Arnelex Pharmaceuticals, Inc.</td>
<td>ATRAGEN®</td>
<td>Kaposi’s sarcoma</td>
</tr>
<tr>
<td>Glaxo Wellcome plc</td>
<td>3622W94 MAb that binds to EGFr (17-1A) pancreatic carcinoma antigen on adenocarcinomas</td>
<td>B cell lymphoma</td>
</tr>
<tr>
<td>Genentech</td>
<td>Anti-VEGF, RhuMAb (inhabits angiogenesis)</td>
<td>Chronic lymphocytic leukemia (CLL)</td>
</tr>
<tr>
<td>Protein Design Labs</td>
<td>Zenapax (SMART Anti-Tac (IL-2 receptor) Ab, humanized)</td>
<td>Cancer</td>
</tr>
<tr>
<td>Protein Design Labs</td>
<td>SMART M195 Ab, humanized</td>
<td>Breast, prostate, prostate, colorectal</td>
</tr>
<tr>
<td>ImClone Systems</td>
<td>C225 (chimeric anti-EGFr monoclonal antibody)</td>
<td>Leukemia, lymphoma</td>
</tr>
<tr>
<td>ImClone Systems (licensed from RPR)</td>
<td>C225 (chimeric anti-EGFr monoclonal antibody) + taxol</td>
<td>Acute promyelocytic leukemia</td>
</tr>
<tr>
<td>IntClone Systems</td>
<td>C225 (chimeric anti-EGFr monoclonal antibody)</td>
<td>Breast</td>
</tr>
<tr>
<td>IntClone Systems (licensed from RPR)</td>
<td>C225 (chimeric anti-EGFr monoclonal antibody) + doxorubicin</td>
<td>Prostate</td>
</tr>
<tr>
<td>Marketer</td>
<td>Brand Name (Generic Name)</td>
<td>Indication</td>
</tr>
<tr>
<td>----------</td>
<td>--------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>ImmClone Systems</td>
<td>C225 (chimeric anti-EGFR monoclonal antibody) + adriamycin</td>
<td>prostate</td>
</tr>
<tr>
<td>ImmClone Systems</td>
<td>BEC2 (anti-idiotypic Mab, mimics the GD3 epitope)</td>
<td>Melanoma</td>
</tr>
<tr>
<td>Medarex</td>
<td>MDX-210 (humanized anti-HER-2 bispecific antibody)</td>
<td>Cancer</td>
</tr>
<tr>
<td>Medarex</td>
<td>MDX-220 (bispecific for tumors that express TAG-72)</td>
<td>Lung, colon, prostate, ovarian, endometrial, pancreatic and gastric</td>
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<tr>
<td>Medarex/Novartis</td>
<td>MDX-210 (humanized anti-HER-2 bispecific antibody)</td>
<td>Prostate</td>
</tr>
<tr>
<td>Medarex/Merck KgaA</td>
<td>MDX-447 (humanized anti-EGF receptor bispecific antibody)</td>
<td>EGFR receptor cancers (head &amp; neck, prostate, lung, bladder, cervical, ovarian) Comb. Therapy with G-CSF for various cancers, cap. breast</td>
</tr>
<tr>
<td>Medarex/Novartis</td>
<td>MDX-210 (humanized anti-HER-2 bispecific antibody)</td>
<td></td>
</tr>
<tr>
<td>IDEC</td>
<td>MELIMMUNE-2 (murine monoclonal antibody therapeutic vaccine)</td>
<td>Melanoma</td>
</tr>
<tr>
<td>IDEC</td>
<td>MELIMMUNE-1 (murine monoclonal antibody therapeutic vaccine)</td>
<td>Melanoma</td>
</tr>
<tr>
<td>Immunomedics, Inc.</td>
<td>CEACIDE® (E-131)</td>
<td>Colorectal and other non-Hodgkin's B-cell lymphomas</td>
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<tr>
<td>NeoRx</td>
<td>PreTarget® radioactive antibodies</td>
<td></td>
</tr>
<tr>
<td>Novopharm Biotech, Inc.</td>
<td>NovoMab-G2 (pancreatic specific Ab)</td>
<td>Cancer</td>
</tr>
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<td>Technicline Corporation/Technicline</td>
<td>TNT (chimeric MAb to histone antigens)</td>
<td>Brain</td>
</tr>
<tr>
<td>Cambridge Antibody Technology</td>
<td>TNT (chimeric Mab to histone antigens)</td>
<td>Brain</td>
</tr>
<tr>
<td>International/Cambridge Antibody Technology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novopharm</td>
<td>Gionon-H (Monoclonals - Humanized Abs)</td>
<td>Brain, melanomas, neuroblastomas</td>
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<tr>
<td>Genetics Institute/AHP</td>
<td>GNI-250 Mab</td>
<td>Colorectal</td>
</tr>
<tr>
<td>Merck KgaA</td>
<td>2MD-72000 (chimeric-EGF antagonist)</td>
<td>Cancer</td>
</tr>
<tr>
<td>Immunomedics</td>
<td>LymphiCide (humanized LL2 antibody)</td>
<td>non-Hodgkin’s B-cell lymphoma</td>
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<tr>
<td>Immunex/AHP</td>
<td>CMA 676 (monoclonal antibody conjugate)</td>
<td>Acute myelogenous leukemia</td>
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<tr>
<td>Novopharm Biotech, Inc.</td>
<td>Monopharm-C</td>
<td>Colon, lung, pancreatic</td>
</tr>
<tr>
<td>Novopharm Biotech, Inc.</td>
<td>4B5 anti-idiotypic Ab</td>
<td>Melanoma, small-cell lung</td>
</tr>
<tr>
<td>Center of Molecular Immunology</td>
<td>ior e6/9 (anti EGF-R humanized Ab)</td>
<td>Radioimmunotherapy</td>
</tr>
<tr>
<td>Center of Molecular Immunology</td>
<td>ior e5 (murine MAb colorectal) for radioimmunotherapy</td>
<td>Colorectal</td>
</tr>
<tr>
<td>Creative BioMolecules/Chiron</td>
<td>BAUS (biosynthetic antibody binding site)</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>ImmClone Systems/Clugai</td>
<td>Proteins</td>
<td>Tumor-associated angiogenesis</td>
</tr>
<tr>
<td>ImmunoGen, Inc.</td>
<td>FLK-2 (monoclonal antibody to fetal liver kinase-2 (FLK-2))</td>
<td>Small-cell lung</td>
</tr>
<tr>
<td>Medarex, Inc.</td>
<td>Humanized MAb/small-drug conjugate</td>
<td>Melanoma, glia, neuroblastoma</td>
</tr>
<tr>
<td>Medarex, Inc.</td>
<td>MDX-260 bispecific, targets GD-2</td>
<td></td>
</tr>
<tr>
<td>Precyn Biopharma, Inc.</td>
<td>ANA Ab</td>
<td>Cancer</td>
</tr>
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<td>Protein Design Labs</td>
<td>SMART 1D10 Ab</td>
<td>B-cell lymphoma</td>
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<td>Protein Design Labs/Novartis</td>
<td>SMART ABL 364 Ab</td>
<td>Breast, lung, colon</td>
</tr>
<tr>
<td>Immunomedics, Inc.</td>
<td>ImmuiKAT7-CEA</td>
<td>Colorectal</td>
</tr>
</tbody>
</table>

In some embodiments, the nucleic acid and antibody are administered in combination with a cancer therapy. As used herein, a "cancer therapy" refers to an agent which prevents growth of a cancer cell by decreasing or slowing the rate of growth, by inhibiting growth altogether, or by killing or inducing apoptosis of the cancer cell. Thus, as used herein, "treating cancer" includes preventing the development of a cancer, reducing the symptoms of cancer, and/or inhibiting the growth of an established cancer. In other aspects, the cancer therapy is administered to a subject at risk of developing a cancer for the purpose of reducing the risk of developing the cancer. Various types of medicaments for the treatment of cancer are described herein. For the purpose of this specification, cancer therapies are classified as chemotherapeutic agents, cancer vaccines, hormone therapy, biological response modifiers, surgical procedures, and radiotherapy aimed at treating cancer. Additionally, the methods of the invention are intended to embrace the use of more than one cancer therapy along with the immunostimulatory nucleic acids and antibody. As an example, where appropriate, the immunostimulatory nucleic acids may be administered with both a chemotherapy agent and a radiotherapy.

Cancer therapies function in a variety of ways. Some cancer therapies work by targeting physiological mechanisms that are specific to tumor cells. Examples include the targeting of specific genes and their gene products (i.e., proteins
primarily) which are mutated in cancers. Such genes include but are not limited to oncogenes (e.g., Ras, Her2, bel-2), tumor suppressor genes (e.g., EGF, p53, Rb), and cell cycle targets (e.g., CDK4, p21, telomerase). Cancer therapies can alternately target signal transduction pathways and molecular mechanisms which are altered in cancer cells.

Other cancer therapies target cells other than cancer cells. Foremost, some medications prime the immune system to attack tumor cells (i.e., cancer vaccines). Still other medications, called angiogenesis inhibitors, function by attacking the blood supply of solid tumors. Since the most malignant cancers are able to metastasize (i.e., exit the primary tumor site and seed a distal tissue, thereby forming a secondary tumor), medications that impede this metastasis are also useful in the treatment of cancer. Angiogenic mediators include basic FGF, VEGF, angiopoietins, angiostatin, endostatin, TNF-α, TNF-470, thrombospondin-1, platelet factor 4, CAI, and certain members of the integrin family of proteins. One category of this type of medication is a metalloproteinase inhibitor, which inhibits the enzymes used by the cancer cells to exit the primary tumor site and extravasate into another tissue.

As used herein, chemotherapeutic agents encompass both chemical and biological agents. These agents function to inhibit a cellular activity which the cancer cell is dependent upon for continued survival. Categories of chemotherapeutic agents include alkylating/alkaloid agents, antimetabolites, hormones or hormone analogs, and miscellaneous antineoplastic drugs. Most if not all of these agents are directly toxic to cancer cells and do not require immune stimulation. Chemotherapeutic agents which are currently in development or in use in a clinical setting are shown in Table 3 below.

### Table 3

<table>
<thead>
<tr>
<th>Marketer</th>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott</td>
<td>TNP 470/AGM 1470</td>
<td>Fruglyline</td>
<td>Anti-Angiogenesis in Cancer</td>
</tr>
<tr>
<td>Takeda</td>
<td>TNP 470/AGM 1470</td>
<td>Fruglyline</td>
<td>Anti-Angiogenesis in Cancer</td>
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<td>Scotia</td>
<td>Megalamine GLA</td>
<td>Megalamine GLA</td>
<td>Bladder Cancer</td>
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<td>Medeva</td>
<td>Valstar</td>
<td>Valubicin</td>
<td>Bladder Cancer - Refractory in situ carcinomas</td>
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<tr>
<td>Medeva</td>
<td>Valstar</td>
<td>Valubicin</td>
<td>Bladder Cancer - Papillary Cancer</td>
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<td>Rhone Poulenc</td>
<td>Gliadel Wafer</td>
<td>Camustaine + Polipect-Onan</td>
<td>Brain Tumor</td>
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<td>Warner Lambert</td>
<td>Undisclosed Cancer (b)</td>
<td>Undisclosed Cancer (b)</td>
<td>Cancer</td>
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<td>Bristol-Myers</td>
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<td>RAS Farnesyl Transferase Inhibitor</td>
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<td>Squire</td>
<td>Inhibitor</td>
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<td>Cancer</td>
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<td>Farnesyl Transferase Inhibitor</td>
<td>Farnesyl Transferase Inhibitor</td>
<td>Cancer (Solid tumors - pancreas, colon, lung, breast)</td>
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<td>PFE</td>
<td>Phosphatase</td>
<td>Cancer, angiosisian</td>
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<td>Pyrrolidine Kinase</td>
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<td>Angiogenesis inhibitor</td>
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<td>Malignant Tumor</td>
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<td>Valspoder</td>
<td>Valspoder</td>
<td>Myeloid Leukemia/Ovarian Cancer</td>
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<td>Cancer</td>
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<td>Warner Lambert</td>
<td>Metrate</td>
<td>Metrate</td>
<td>Pain related to hormone refractory prostate cancer</td>
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<td>Anti-VEGF</td>
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<td>Prostate/Breast/Colonrectal/NBCL Cancer</td>
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<td>Batimatstat</td>
<td>Batimatstat (BB94)</td>
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TABLE 3-continued

Cancer Drugs In Development Or On The Market.

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Another useful anti-cancer therapy is Interferon-α (e.g., INTRON® A, Schering).

The compounds useful according to the invention are nucleic acids. The nucleic acids may be double-stranded or single-stranded. Generally, double-stranded molecules may be more stable in vivo, while single-stranded molecules may have increased activity. The terms “nucleic acid” and “oligonucleotide” refer to multiple nucleotides (i.e., molecules comprising a sugar (e.g., ribose or deoxyribose) linked to a phosphate group and to an exchangeable organic base, which is either a substituted pyrimidine (e.g., cytosine (C), thymine (T) or uracil (U)) or a substituted purine (e.g., adenine (A) or guanine (G)) or a modified base. As used herein, the terms refer to oligoribonucleotides as well as oligodeoxyribonucleotides. The terms shall also include polynucleotides (i.e., a polynucleotide minus the phosphate) and any other organic base-containing polymer. The terms “nucleic acid” and “oligonucleotide” also encompass nucleic acids or oligonucleotides with a covalently modified base and/or sugar. For example, they include nucleic acids having backbone sugars which are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 3‘ position and other than a phosphate group at the 5‘ position. Thus modified nucleic acids may include a 2‘-O-alkylated ribose group. In addition, modified nucleic acids may include sugars such as arabinose instead of ribose. Thus the nucleic acids may be heterogeneous in backbone composition thereby containing any possible combination of polymer units linked together such as peptide-nucleic acids (which have amino acid backbone with nucleic acid bases). In some embodiments the nucleic acids are homogeneous in backbone composition.

Nucleic acids also can include base analogs such as C-5 propyne modified bases. Wagner R W et al., Nature Biotechnol 14:840-4 (1996). Purines and pyrimidines include but are not limited to adenine, cytosine, guanine, thymine, 5-methylcytosine, 2-aminopurine, 2-aminoo-6-chloropurine, 2,6-di-aminopurine, hypoxanthine, and other naturally and non-naturally occurring nucleobases, substituted and unsubstituted aromatic moieties.

The nucleic acid is a linked polymer of bases or nucleotides. As used herein with respect to linked units of a nucleic acid, “linked” or “linkage” means two entities are bound to one another by any physicochemical means. Any linkage known to those of ordinary skill in the art, covalent or non-covalent, is embraced. Such linkages are well known to those of ordinary skill in the art. Natural linkages, which are those ordinarily found in nature connecting the individual units of a nucleic acid, are most common. The individual units of a nucleic acid may be linked, however, by synthetic or modified linkages.

Whenever a nucleic acid is represented by a sequence of letters it will be understood that the nucleotides are in 5‘→3‘ order from left to right and that “A” denotes adenosine, “C” denotes cytosine, “G” denotes guanosine, “T” denotes thymidine, and “U” denotes uracil unless otherwise noted.

Nucleic acid molecules useful according to the invention can be obtained from natural nucleic acid sources (e.g., genomic nuclear or mitochondrial DNA or cDNA), or are synthetic (e.g., produced by oligonucleotide synthesis). Nucleic acids isolated from existing nucleic acid sources are referred to herein as native, natural, or isolated nucleic acids. The nucleic acids useful according to the invention may be isolated from any source, including eukaryotic sources, prokaryotic sources, nuclear DNA, mitochondrial DNA, etc. Thus, the term nucleic acid encompasses both synthetic and isolated nucleic acids. The term “isolated” as used herein refers to a nucleic acid which is substantially free of other nucleic acids, proteins, lipids, carbohydrates or other materials with which it is naturally associated. The nucleic acids can be produced on a large scale in plasmids, (see Sambrook T et al., “Molecular Cloning: A Laboratory Manual”, Cold Spring Harbor Laboratory Press, New York, 1989) and separated into smaller pieces or administered whole. After being administered to a subject the plasmid can be degraded into oligonucleotides. One skilled in the art can purify viral, bacterial,
eukaryotic, etc., nucleic acids using standard techniques, such as those employing restriction enzymes, exonucleases or endonucleases.


In some embodiments, the nucleic acids useful according to the invention are immunostimulatory nucleic acids. An immunostimulatory nucleic acid is any nucleic acid, as described above, which is capable of modulating an immune response. A nucleic acid which modulates an immune response is one which produces any form of immune stimulation, including, but not limited to, induction of cytokines, B-cell activation, T-cell activation, monocyte activation. Immunostimulatory nucleic acids include, but are not limited to, CpG nucleic acids, methylated CpG nucleic acids, T-rich nucleic acids, poly-G nucleic acids, and nucleic acids having phosphate modified backbones, such as phosphorothioate backbones.

A “CpG nucleic acid” or a “CpG immunostimulatory nucleic acid” as used herein is a nucleic acid containing at least one unmethylated CpG dinucleotide (cytosine-guanine dinucleotide sequence, i.e., “CpG DNA” or DNA containing a 5’ cytosine followed by 3’ guanosine and linked by a phosphate bond) and activates a component of the immune system. The entire CpG nucleic acid can be unmethylated or portions may be unmethylated but at least the C of the 5’ CG 3’ must be unmethylated.

In one embodiment the invention provides a CpG nucleic acid represented by at least the formula:

\[ 5’N’_X_1CGX_2_3’ \]

wherein X₁ and X₂ are nucleotides and N is any nucleotide and N₁ and N₂ are nucleic acid sequences composed of from about 0-25 N’s each. In some embodiments X₁ is adenine, guanine, cytosine, thymine, and X₂ is cytosine, adenine, or thymine.

In other embodiments X₁ is cytosine and/or X₂ is guanine.

In other embodiments the CpG nucleic acid is represented by at least the formula:

\[ 5’N’_X_1CGX_2CGX_3_3’ \]

wherein X₁, X₂, and X₃ are nucleotides. In some embodiments, X₁, X₂, X₃ are nucleotides selected from the group consisting of: GpT, GpG, GpA, ApA, ApT, ApG, CpT, CpA, CpG, TpA, TpT, and TpG; and X₁ and X₂ are nucleotides selected from the group consisting of: TpG, TpA, TpT, TpG, ApG, CpG, TpC, ApC, CpC, TpA, ApA, and CpA; N is any nucleotide and N₁ and N₂ are nucleic acid sequences composed of from about 0-25 N’s each. In some embodiments, X₁, X₂, X₃ are GpA or GpT and X₁ and X₂ are TpT. In other embodiments X₁ or X₂ or both are purines and X₂ or X₃ or both are pyrimidines or X₁, X₂ are GpA and X₂ or X₃ or both are pyrimidines.

In some embodiments N₁ and N₂ of the nucleic acid do not contain a CGCG or CCGCG quadrimer or more than one CGG or CGG trimer. The effect of a CCGG or CCGCG quadrimer or more than one CGG or CGG trimer depends in part on the status of the nucleic acid backbone. For instance, if the nucleic acid has a phosphodiester backbone or a chimeric backbone the inclusion of these sequences in the nucleic acid will only have minimal if any affect on the biological activity of the nucleic acid. If the backbone is completely phosphorothioate or significantly phosphorothioate then the inclusion of these sequences may have more influence on the biological activity or the kinetics of the biological activity, but compounds containing these sequences are still useful. In another embodiment the CpG nucleic acid has the sequence 5’ TCN₅TX₁CGX₂X₃₅’ (SEQ ID NO:850).

A “T-rich nucleic acid” or “T-rich immunostimulatory nucleic acid” is a nucleic acid which includes at least one poly-T sequence and/or which has a nucleotide composition of greater than 25% T nucleotide residues and which activates a component of the immune system. A nucleic acid having a poly-T sequence includes at least four Ts in a row, such as 5’ TTTT 3’. Preferably the T-rich nucleic acid includes more than one poly-T sequence. In preferred embodiments the T-rich nucleic acid may have 2, 3, 4, etc., poly-T sequences, such as oligonucleotide #20066 (5’ TCCTCTTTGGTTCCTTTGTCCCTTG 3’, SEQ ID NO: 729). One of the most highly immunostimulatory T-rich oligonucleotides discovered according to the invention is a nucleic acid composed entirely of T nucleotide residues, e.g., oligonucleotide #2183 (5’TTTTTTTTTTTTTTTTTTTTTTT 3’, SEQ ID NO: 841). Other T-rich nucleic acids have a nucleotide composition of greater than 25% T nucleotide residues, but do not necessarily include a poly-T sequence. In these T-rich nucleic acids the T nucleotide resides may be separated from one another by other types of nucleotide residues, i.e., G, C, and A. In some embodiments the T-rich nucleic acids have a nucleotide composition of greater than 30%, 40%, 50%, 60%, 70%, 80%, 90%, and 99%, T nucleotide residues and every integer % in between. Preferably the T-rich nucleic acids have at least one poly-T sequence and a nucleotide composition of greater than 25% T nucleotide residues.

In one embodiment the T-rich nucleic acid is represented by at least the formula:

\[ 5’N’X_1TTTX_2X_3 3’ \]

wherein X₁, X₂, and X₃ are nucleotides. In one embodiment X₁ is TT and/or X₃ is TT. In another embodiment X₁, X₃ are any one of the following nucleotides TA, TG, GC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC, and X₂ is any one of the following nucleotides TA, TG, GC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.

In some embodiments it is preferred that the T-rich nucleic acid does not contain poly-C (CCCC), poly-A (AAAA), poly-G (GGGG), CpG motifs, or multiple Gs. In other embodiments the T-rich nucleic acid includes these motifs. Thus in some embodiments of the invention the T-rich nucleic acids include CpG dinucleotides and in other embodiments the T-rich nucleic acids are free of CpG dinucleotides. The CpG dinucleotides may be methylated or unmethylated.


Poly G nucleic acids preferably are nucleic acids having the following formulas:

\[ 5’N’X_1GGGGX_2X_3 3’ \]
wherein $X_1$, $X_2$, $X_3$, and $X_4$ are nucleotides. In preferred embodiments at least one of $X_1$ and $X_4$ are a G. In other embodiments both of $X_1$ and $X_4$ are a G. In yet other embodiments the preferred formula is 5'-GGGGG'G, or 5'-GGGNGGGGGG'G (SEQ ID NO:849) wherein $N$ represents between 0 and 20 nucleotides. In other embodiments the poly-G nucleic acid is free of unmethylated CG dinucleotides, such as, for example, the nucleic acids listed in Table 4 below as SEQ ID Nos: 12-14, 56, 100, 155, 163, 182, 227, 237, 246, 400, 407, 429, 430, 432, 435, 438, 439, 446, 450, 451, 480, 487, 493, 522, 661, 662, 671-673, 807, 808, 821, 823, and 834. In other embodiments the poly-G nucleic acid includes at least one unmethylated CG dinucleotide, such as, for example, the nucleic acids listed in Table 4 below as SEQ ID Nos: 6, 7, 22, 26, 28-30, 87, 115, 141, 177, 191, 209, 254, 258, 267, 303, 317, 329, 335, 344, 345, 395, 414, 417, 418, 423-426, 428, 431, 433, 434, 436, 437, 440, 442-445, 447-449, 458, 460, 463, 467-469, 474, 515, 516, 594, 638-640, 663, 664, 727, 752, 776, 795, 799, 817, 818, 831, and 832.

Nucleic acids having modified backbones, such as phosphorothioate backbones, also fall within the class of immunostimulatory nucleic acids. U.S. Pat. Nos. 5,723,335 and 5,663,153 issued to Hutcherson, et al. and related PCT publication WO95/26204 describe immune stimulation using phosphorothioate oligonucleotide analogues. These patents describe the ability of the phosphorothioate backbone to stimulate an immune response in a non-sequence specific manner.

The immunostimulatory nucleic acids may be any size but in some embodiments are in the range of between 6 and 100 or in some embodiments between 8 and 35 nucleotides in size. Immunostimulatory nucleic acids can be produced on a large scale in plasmids. These may be administered in plasmid form or alternatively they can be degraded into oligonucleotides.

"Palindromic sequence" shall mean an inverted repeat (i.e., a sequence such as ABCDEDCBA in which A and A' are bases capable of forming the usual Watson-Crick base pairs and which includes at least 6 nucleotides in the palindrome. In vivo, such sequences may form double-stranded structures. In one embodiment the nucleic acid contains a palindromic sequence. In some embodiments when the nucleic acid is a CpG nucleic acid, a palindromic sequence used in this context refers to a palindrome in which the CpG is part of the palindrome, and optionally is the center of the palindrome. In another embodiment the nucleic acid is free of a palindrome.

A nucleic acid that is free of a palindromic does not have any regions of 6 nucleotides or greater in length which are palindromic. A nucleic acid that is free of a palindrome can include a region of less than 6 nucleotides which are palindromic.

A "stabilized nucleic acid molecule" shall mean a nucleic acid molecule that is relatively resistant to in vivo degradation (e.g., via an exonuclease or endonuclease). Stabilization can be a function of length or secondary structure. Nucleic acids that are tens to hundreds of kbs long are relatively resistant to in vivo degradation. For shorter nucleic acids, secondary structure can stabilize and increase their effect. For example, if the 3' end of an oligonucleotide has self-complementarity to an upstream region, so that it can fold back and form a sort of stem loop structure, then the oligonucleotide becomes stabilized and therefore exhibits more activity.

Some stabilized oligonucleotides of the instant invention have a modified backbone. It has been demonstrated that modification of the oligonucleotide backbone provides enhanced activity of the nucleic acids when administered in vivo. Nucleic acids, including at least two phosphorothioate linkages at the 5' end of the oligonucleotide and multiple phosphorothioate linkages at the 3' end, preferably 5, may provide maximal activity and protect the oligonucleotide from degradation by intracellular exo- and endo-nucleases. Other modified oligonucleotides include phosphodiester modified oligonucleotide, combinations of phosphodiester and phosphorothioate oligonucleotide, methylphosphonate, methylphosphorothioate, phosphorothioate, and combinations thereof. Each of these combinations and their particular effects on immune cells is discussed in more detail in PCT Published Patent Application WO98/18810 claiming priority to U.S. Ser. No. 08/738,652 (now issued as U.S. Pat. No. 6,207,646 B1) and Ser. No. 08/960,774 (now issued as U.S. Pat. No. 6,239,116 B1), filed on Oct. 30, 1996 and Oct. 30, 1997 respectively, the entire contents of which is hereby incorporated by reference. It is believed that these modified oligonucleotides may show more stimulatory activity due to enhanced nuclear resistance, increased cellular uptake, increased protein binding, and/or altered intracellular localization. Both phosphorothioate and phosphodiester nucleic acids are active in immune cells.

Other stabilized oligonucleotides include nonionic DNA analogs, such as alkyl- and aryl-phosphates (in which the charged phosphate oxygen is replaced by an alkyl or aryI group), phosphodiester and alkylphosphodiesters, in which the charged oxygen moiety is alkylated. Oligonucleotides which contain diol, such as tetraethyleneglycol or hexamethyl-ene-glycol, at either or both termini have also been shown to be substantially resistant to nuclease degradation.

For use in vivo, nucleic acids are preferably relatively resistant to degradation (e.g., via endonucleases and exonucleases). Secondary structures, such as stem loops, can stabilize nucleic acids against degradation. Alternatively, nucleic acid stabilization can be accomplished via phosphate backbone modifications. One type of stabilized nucleic acid has at least a partial phosphorothioate modified backbone. Phosphorothioates may be synthesized using automated techniques employing either phosphoramidite or H-phosphonate chemistries. Aryl- and alkyl-phosphonates can be made, e.g., as described in U.S. Pat. No. 4,469,863; and alkylphosphodiesters (in which the charged oxygen moiety is alkylated as described in U.S. Pat. No. 5,023,243 and European Patent No. 092,574) can be prepared by automated solid phase synthesis using commercially available reagents. Methods for making other DNA backbone modifications and substitutions have been described. Uhmann E et al., Chem Rev 90:544-84 (1990); Goodchild J., Bioconjugate Chem 1:165-87 (1990).

The immunostimulatory nucleic acids having backbone modifications useful according to the invention in some embodiments are S- or R-chiral immunostimulatory nucleic acids. An "S chiral immunostimulatory nucleic acid" as used herein is an immunostimulatory nucleic acid wherein at least two nucleotides have a backbone modification forming a chiral center and wherein a plurality of the chiral centers have S chirality. An "R chiral immunostimulatory nucleic acid" as used herein is an immunostimulatory nucleic acid wherein at least two nucleotides have a backbone modification forming a chiral center and wherein a plurality of the chiral centers have R chirality. The backbone modification may be any type of modification that forms a chiral center. The modifications include but are not limited to phosphorothioate, methylphosphonate, methylphosphorothioate, phosphorothioate, 2'-OMe and combinations thereof. In other embodiments they are non-chiral. A non-chiral nucleic acid is any nucleic acid which does not have at least two chiral centers.

The chiral immunostimulatory nucleic acids must have at least two nucleotides within the nucleic acid that have a
backbone modification. All or less than all of the nucleotides in the nucleic acid, however, may have a modified backbone. Of the nucleotides having a modified backbone (referred to as chiral centers), a plurality have a single chirality, S or R. A “plurality” as used herein refers to an amount greater than or equal to 75%. Thus, less than all of the chiral centers may have S or R chirality as long as a plurality of the chiral centers have S or R chirality. In some embodiments at least 75%, 80%, 85%, 90%, 95%, or 100% of the chiral centers have S or R chirality. In other embodiments at least 75%, 80%, 85%, 90%, 95%, or 100% of the nucleic acids have backbone modifications.


Other sources of nucleic acids useful according to the invention include standard viral and bacterial vectors, many of which are commercially available. In its broadest sense, a “vector” is any nucleic acid material which is ordinarily used to deliver and facilitate the transfer of nucleic acids to cells. The vector as used herein may be an empty vector or a vector carrying a gene which can be expressed. In the case when the vector is carrying a gene the vector generally transports the gene to the target cells with reduced degradation relative to the extent of degradation that would result in the absence of the vector. In this case the vector optionally includes gene expression sequences to enhance expression of the gene in target cells such as immune cells, but it is not required that the gene be expressed in the cell.

In general, vectors include, but are not limited to, plasmids, phagemids, viruses, other vehicles derived from viral or bacterial sources. Viral vectors are one type of vector and include, but are not limited to, nucleic acid sequences from the following viruses: retrovirus, such as Moloney murine leukemia virus, Harvey murine sarcoma virus, murine mammary tumor virus, and Rous sarcoma virus; adenovirus, adeno-associated virus; SV40-type viruses; polyoma viruses; Epstein-Barr viruses; papilloma viruses; herpes virus; vaccinia virus; polio virus; and RNA virus such as a retrovirus. One can readily employ other vectors not named but known to the art. Some viral vectors are based on non-cytopathic eukaryotic viruses in which non-essential genes have been replaced with a nucleic acid to be delivered. Non-cytopathic viruses include retroviruses, the life cycle of which involves reverse transcription of genomic viral RNA into DNA.


Other vectors include plasmid vectors. Plasmid vectors have been extensively described in the art and are well-known to those of skill in the art. See e.g., Sambrook et al., “Molecular Cloning: A Laboratory Manual,” Second Edition, Cold Spring Harbor Laboratory Press, 1989. In the last few years, plasmid vectors have been found to be particularly advantageous for delivering genes to cells in vivo because of their inability to replicate within and integrate into a host genome. Some plasmids, however, having a promoter compatible with the host cell, can express a peptide from a gene operatively encoded within the plasmid. Some commonly used plasmids include pBR322, pUC18, pUC19, pcDNA3.1, pSV40, and pBlueScript. Other plasmids are well-known to those of ordinary skill in the art. Additionally, plasmids may be custom designed using restriction enzymes and ligation reactions to remove and add specific fragments of DNA.

It has recently been discovered that plasmids (empty or gene-carrying) can be delivered to the immune system using bacteria. Modified forms of bacteria such as Salmonella can be transfected with the plasmid and used as delivery vehicles. The bacterial delivery vehicles can be administered to a host subject orally or by other administration means. The bacteria deliver the plasmid to immune cells, e.g., dendritic cells, probably by passing through the gut barrier. High levels of immune protection have been established using this methodology. Such methods of delivery are useful for the aspects of the invention utilizing systemic delivery of nucleic acid.

As used herein, administration of an immunostimulatory nucleic acid is intended to embrace the administration of one or more immunostimulatory nucleic acids which may or may not differ in terms of their profile, sequence, backbone modifications and biological effect. As an example, CpG nucleic acids and T-rich nucleic acids may be administered to a single subject along with an antibody and optionally a cancer therapy. In another example, a plurality of CpG nucleic acids which differ in nucleotide sequence may also be administered to a subject.

Some of the nucleic acids useful according to the invention and described herein are presented in Table 4 below.

### Table 4: Exemplary Nucleic Acids

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<tr>
<td>ttttttttttttttttttttttt</td>
<td>o 046</td>
</tr>
<tr>
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</tr>
<tr>
<td>ttttttttttttttttttttttt</td>
<td>s 048</td>
</tr>
</tbody>
</table>

In Table 4 with respect to sequences the letter symbols aside from a, c, t, and g are defined as follows: “b” indicates a biotin moiety attached to that end of the oligonucleotide when it is single and is listed on the 5’ or 3’ end of oligonucleotide; “d” represents a, g, or t; “f” represents fluorescein isothiocyanate (FITC) moiety attached to the 5’ or 3’ end of oligonucleotide; “h” represents a, c, or t; “i” represents inosine; “n” represents any nucleotide; “z” represents 5-methylepytosine.

Also in Table 4 with respect to backbones the notations are defined as follows: “o” represents phosphodiester; “os” represents phosphorothioate and phosphodiester chimeric with phosphodiester on 5’ end; “os2” represents phosphorothioate and phosphodiester chimeric with phosphodiester on 5’ end; “p-ethoxy” represents p-ethoxy backbone (see, e.g., U.S. Patent No. 6,015,886); “po” represents phosphodiester, “s” represents phosphorothioate, “s2” represents phosphorothioate; “s2o” represents phosphorothioate and phosphodiester chimeric with phosphodiester on 3’ end, and “sos” represents chimeric phosphorothioate/phosphodiester with phosphorothioate at the 5’ and 3’ ends.

The nucleic acids are delivered in effective amounts. The term “effective amount” of an immunostimulatory nucleic acid refers to the amount necessary or sufficient to achieve a desired biologic effect. For example, an effective amount of an immunostimulatory nucleic acid could be that amount necessary to cause activation of the immune system. According to some aspects of the invention, an effective amount is that amount of an immunostimulatory nucleic acid and that amount of an antibody, which when combined or co-administered, results in the prevention or the treatment of the cancer. In some embodiments a synergistic effect is observed. A synergistic amount is that amount which produces an anti-cancer response that is greater than the sum of the individual effects of either the immunostimulatory nucleic acid and the antibody alone. For example, a synergistic combination of an immunostimulatory nucleic acid and an antibody provides a biological effect which is greater than the combined biological effect which could have been achieved using each of the components (i.e., the nucleic acid and the antibody) separately. The biological effect may be the amelioration and/or absolute elimination of symptoms resulting from the cancer. In another embodiment, the biological effect is the complete abrogation of the cancer, as evidenced for example, by the absence of a tumor or a biopsy or blood smear which is free of cancer cells.

The effective amount of immunostimulatory nucleic acid necessary to treat a cancer or in the reduction of the risk of developing a cancer may vary depending upon the sequence of the immunostimulatory nucleic acid, the backbone constituents of the nucleic acid, and the mode of delivery of the nucleic acid. The effective amount for any particular application can also vary depending on such factors as the cancer being treated, the particular immunostimulatory nucleic acid being administered (e.g., the nature, number or location of immunostimulatory motifs in the nucleic acid), the size of the subject, or the severity of the disease or condition. One of ordinary skill in the art can empirically determine the effective amount of a particular immunostimulatory nucleic acid and antibody combination without necessitating undue experimentation. Combined with the teachings provided herein, by choosing among the various active compounds and weighing factors such as potency, relative bioavailability, patient body weight, severity of adverse side-effects and preferred mode of administration, an effective prophylactic or therapeutic treatment regimen can be planned which does not cause substantial toxicity and yet is entirely effective to treat the particular subject.

Therapeutic doses of cancer therapies are well known in the field of medicine for the treatment of cancer. These dosages have been extensively described in references such as Remington’s Pharmaceutical Sciences, 18th ed., 1990; as well as many other medical references relied upon by the medical profession as guidance for the treatment of cancer. Therapeutic dosages of immunostimulatory nucleic acids have also been described in the art and methods for identifying therapeutic dosages in subjects are described in more detail herein.

Subject doses of the compounds described herein typically range from about 0.1 mg to mg per administration, which depending on the application could be given daily, weekly, or monthly and any other amount of time therebetween. More typically mucosal or local doses range from about 10 μg to 5 mg per administration, and most typically from about 100 μg to 1 mg, with 2-4 administrations being spaced hours, days or weeks apart. More typically, immune stimulant doses range from 1 μg to 10 mg per administration, and most typically 10 μg to 1 mg, with daily or weekly administrations. Subject doses of the compounds described herein for parenteral deliv-
ery, wherein the compounds are delivered without another therapeutic agent are typically 5 to 10,000 times higher than the effective mucosal dose or for immune stimulant applications, and more typically 10 to 1,000 times higher, and most typically 20 to 100 times higher. More typically parenteral doses for these purposes range from about 10 μg to 5 mg per administration, and most typically from about 100 μg to 1 mg, with 2-4 administrations being spaced hours, days or weeks apart. In some embodiments, however, parenteral doses for these purposes may be used in a range of 5 to 10,000 times higher than the typical doses described above.

For any compound described herein the therapeutically effective amount can be initially determined from animal models, e.g., the animal models described herein. A therapeutically effective dose can also be determined from human data for CpG nucleic acids which have been tested in humans (human clinical trials have been initiated and the results publicly disseminated) and for compounds which are known to exhibit similar pharmacological activities. Higher doses may be required for parenteral administration, as described above. The applied dose can be adjusted based on the relative bioavailability and potency of the administered compound. Adjusting the dose to achieve maximal efficacy based on the methods described above and other methods as are well known in the art is well within the capabilities of the ordinarily skilled artisan.

The formulations of the invention are administered in pharmaceutically acceptable solutions, which may routinely contain pharmaceutically acceptable concentrations of salt, buffering agents, preservatives, compatible carriers, adjuvants, and optionally other therapeutic ingredients.

For use in therapy, an effective amount of the nucleic acid can be administered to a subject by any mode that delivers the nucleic acid to a subject. “Administering” the pharmaceutical composition of the present invention may be accomplished by any means known to the skilled artisan. Some routes of administration include but are not limited to oral, intranasal, intratracheal, inhalation, ocular, vaginal, rectal, parenteral (e.g., intramuscular, intradermal, intravenous or subcutaneous injection) and direct injection.

For oral administration, the compounds (i.e., nucleic acids and antibodies) can be delivered alone without any pharmaceutical carriers or formulated readily by combining the active compound(s) with pharmaceutically acceptable carriers well known in the art. The term “pharmaceutically acceptable carrier” means one or more compatible solid or liquid filler, diluents or encapsulating substances which are suitable for administration to a human or other vertebrate animal. The term “carrier” denotes an organic or inorganic ingredient, natural or synthetic, with which the active ingredient is combined to facilitate the application. The components of the pharmaceutical compositions also are capable of being commingled with the compounds of the present invention, and with each other, in a manner such that there is no interaction which would substantially impair the desired pharmaceutical efficiency.

Such carriers enable the compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a subject to be treated. Pharmaceutical preparations for oral use can be obtained as solid excipient, optionally grading or resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Optionally, the oral formulations may also be formulated in saline or buffers for neutralizing intestinal acid conditions.

Dragee cores may be provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. Microspheres formulated for oral administration may also be used. Such microspheres have been well defined in the art. All formulations for oral administration should be in dosages suitable for such administration.

For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention may be conveniently delivered in the form of an aerosol spray, from pressurized packs or a nebulizer, with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of e.g., gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

The compounds, when it is desirable to deliver them systematically, may be formulated for parenteral administration by injection, e.g., by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampoules or in multiple-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulation agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.
Alternatively, the active compounds may be in powder form for constitution with a suitable vehicle, e.g., sterile pyrogen-free water, before use.

The compounds may also be formulated in rectal or vaginal compositions such as suppositories or retention enemas, e.g., containing conventional suppository bases such as cacao butter or other glycerides.

In addition to the formulations described previously, the compounds may also be formulated as a depot preparation. Such long acting formulations may be formulated with suitable polymeric or hydrophilic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols.

Suitable liquid or solid pharmaceutical preparation forms are, for example, aqueous or saline solutions for inhalation, microencapsulated, enclocheled, coated onto microscopic gold particles, contained in liposomes, nebulfized, aerosols, pellets for implantation into the skin, or dried onto a sharp object to be scratched into the skin. The pharmaceutical compositions may also include granules, powders, tablets, coated tablets, (micro)capsules, suppositories, syrups, emulsions, suspensions, creams, drops or preparations with protected release of active compounds, in whose preparation excipients and additives and/or auxiliaries such as disintegrants, binders, coating agents, swelling agents, lubricants, flavorings, sweeteners or solubilizers are customarily used as described above.

The pharmaceutical compositions are suitable for use in a variety of drug delivery systems. For a brief review of present methods for drug delivery, see Langer R., Science 249:1527-33 (1990), which is incorporated herein by reference.

The nucleic acids and/or antibodies may be administered per se (naked) or in the form of a pharmaceutically acceptable salt. When used in medicine the salts should be pharmaceutically acceptable, but non-pharmaceutically acceptable salts may conveniently be used to prepare pharmaceutically acceptable salts thereof. Such salts include, but are not limited to, those prepared from the following acids: hydrochloric, hydrobromic, sulphuric, nitric, phosphoric, maleic, ascorbic, tartaric, citric, methan sulfonic, formic, malonic, succinic, naphthalene-2-sulfonic, and benzene sulfonic. Also, such salts can be prepared as alkaline metal or alkaline earth salts, such as sodium, potassium or calcium salts of the carboxylic acid group.

Suitable buffers include: acetic acid and a salt (1-2% w/v); citric acid and a salt (1-3% w/v); boric acid and a salt (0.5-2.5% w/v); phosphoric acid and a salt (0.8-2% w/v). Suitable preservatives include benzalkonium chloride (0.003-0.03% w/v); chlorobutanol (0.3-0.9% w/v); parabens (0.01-0.25% w/v) and thimerosal (0.004-0.02% w/v).

The nucleic acids or other therapeutics useful in the invention may be delivered in mixtures with additional antibodies. A mixture may consist of several antibodies in addition to the nucleic acid.

A variety of administration routes are available. The particular mode selected will depend, of course, upon the particular nucleic acids or antibodies selected, the particular condition being treated and the dosage required for therapeutic efficacy. The methods of this invention, generally speaking, may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of an immune response without causing clinically unacceptable adverse effects. Preferred modes of administration are discussed above.

The compositions may conveniently be presented in unit dosage form and may be prepared by any of the methods well known in the art of pharmacy. All methods include the step of bringing the compounds into association with a carrier which constitutes one or more accessory ingredients. In general, the compositions are prepared by uniformly and intimately bringing the compounds into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product. Liquid dose units are vials or ampoules. Solid dose units are tablets, capsules and suppositories.

Other delivery systems can include time-release, delayed release or sustained release delivery systems. Such systems can avoid repeated administrations of the compounds, increasing convenience to the subject and the physician. Many types of release delivery systems are available and known to those of ordinary skill in the art. They include polymer base systems such as poly(lactide-glycolide), copolyesters, polyglycolides, polyesteramides, polyorthoesters, polyhydroxybutyric acid, and polyanhydrides. Microcapsules of the foregoing polymers containing drugs are described in, for example, U.S. Pat. Nos. 5,075,109. Delivery systems also include non-polymer systems that are: lipids including sterols such as cholesterol, cholesterol esters and fatty acids or neutral fats such as mono-, di- and tri-glycerides; hydrogel release systems; sylastic systems; peptide based systems; wax coatings; compressed tablets using conventional binders and excipients; partially fused implants; and the like. Specific examples include, but are not limited to:

(a) erosional systems in which an agent of the invention is contained in a form within a matrix — such as those described in U.S. Pat. Nos. 4,452,775, 4,675,189, and 5,736,152, and
(b) diffusion systems in which an active component permeates at a controlled rate from a polymer such as described in U.S. Pat. Nos. 3,854,480, 5,133,974 and 5,407,686. In addition, pump-based hardware delivery systems can be used, some of which are adapted for implantation.

The nucleic acid may be directly administered to the subject or may be administered in conjunction with a pharmaceutically acceptable carrier or a delivery vehicle. The nucleic acid and optionally other therapeutic agents may be administered alone (e.g., in saline or buffer) or using any delivery vehicles known in the art. One type of delivery vehicle is referred to herein as a nucleic acid delivery complex. A “nucleic acid delivery complex” shall mean a nucleic acid molecule associated with (e.g., ionically or covalently bound to; or encapsulated within) a targeting means (e.g., a molecule that results in higher affinity binding to target cell (e.g., dendritic cell surfaces and/or increased cellular uptake by target cells). Examples of nucleic acid delivery complexes include nucleic acids associated with: a sterol (e.g., cholesterol), a lipid (e.g., a cationic lipid, virome or liposome), or a target cell specific binding agent (e.g., a ligand recognized by target cell specific receptor). Preferred complexes may be sufficiently stable in vivo to reduce significant uncoupling prior to internalization by the target cell. However, the complex may be cleavable under appropriate conditions within the cell so that the nucleic acid may be released in a functional form.

The nucleic acids may be delivered by non-invasive methods as described above. Non-invasive delivery of compounds is desirable for treatment of children, elderly, animals, and even adults and also to avoid the risk of needle-stick injury. Delivery vehicles for delivering compounds to mucosal surfaces have been described and include but are not limited to: Coelenterates (Gould-Fogerite et al., 1994, 1996); Emulsomes
(Vancott et al., 1998, Lowell et al., 1997); ISCOMs (Mowat et al., 1993, Carlsson et al., 1991, Hu et al., 1998, Morein et al., 1999); Liposomes (Childers et al., 1999, Michalek et al., 1899, 1992, de Haan 1995a, 1995b); Live bacterial vectors (e.g., Salmonella, Escherichia coli; Bacillus Calmette-Guérin, Shigella Lactobacillus) (Hone et al., 1996, Paulwells et al., 1998, Chatfield et al., 1993, Stover et al., 1991, Nugent et al., 1998); Live viral vectors (e.g., Vaccinia, adenovirus, Herpes Simplex) (Gallahan et al., 1993, 1995, Moss et al., 1996, Nugent et al., 1998, Flexner et al., 1988, Morrow et al., 1999); Microspheres (Gupta et al., 1998, Jones et al., 1996, Maloy et al., 1994, Moore et al., 1995, O’Hagan et al., 1994, Eldridge et al., 1989); nucleic acid vaccines (Fynan et al., 1993, Kuklin et al., 1997, Sasaki et al., 1998, Okada et al., 1997, Ishii et al., 1997); Polymers (e.g., carboxymethylcellulose, chitosan) (Hamajima et al., 1998, Jabal-Gill et al., 1998); Polymer rings (Wyatt et al., 1998); Proteosomes (Vancott et al., 1998, Lowell et al., 1988, 1996, 1997); Sodium Fluoride (Hashi et al., 1998); Transgenic plants (Tackett et al., 1998, Mason et al., 1998, Haq et al., 1995); Viruses (Gluck et al., 1992, Mengardi et al., 1995, Czyz et al., 1998); Virus-like particles (Jiang et al., 1999, Leibl et al., 1998).

The invention also includes kits. The kits generally include a package with a plurality of containers housing active ingredients and instructions for carrying out the methods of the invention. The active ingredients include but are not limited to immunostimulatory nucleic acids, antibodies such as antibodies specific for a cell surface antigen, and anti-cancer therapies.

The following examples are provided to illustrate specific instances of the practice of the present invention and are not to be construed as limiting the present invention to these examples. As will be apparent to one of ordinary skill in the art, the present invention will find application in a variety of compositions and methods.

**EXAMPLES**

**Introduction:**

Extensive cross-talk exists between healthy B cells and T cells. There is evidence that malignant B cells also communicate with T cells. However, malignant cells appear to differ from their normal counterparts in a number of ways, including a decreased tendency to undergo apoptosis in response to normal signals, altered expression of a variety of surface markers, and altered ability to function as effective antigen presenting cells. Lagneaux L et al., *Blood* 91:2387-96 (1998); Gordon J et al., *Leukemia* 7 Suppl 2: S5-9 (1993); Gordon J et al., *Adv Exp Med Biol* 406:139-44 (1996); Chaperot I et al., *Exp Hematol* 27:479-88 (1999). Immunotherapeutic approaches have recently become part of our therapy of some subtypes of B-cell malignancy. Improved immunotherapy of B-cell malignancy will need to be designed based on the growing understanding of the cellular immunology of this disease. Schultzze J L et al., *J Mol Med* 77:322-32 (1999).


**Materials and Methods:**

Cell culture: Fresh lymph node samples were obtained from the operating suite and were minced with a scalpel under aseptic conditions. The resulting suspension was passed sequentially through a sterilized sieve tissue grinder containing a nylon mesh screen, a 150 μm mesh screen and a 60 μm mesh screen. Alternatively, mononuclear cells were obtained from peripheral blood or pleural fluid as described. Hartmann G et al., *J Pharmacol Exp Ther* 285:920-8 (1998). Red blood cells were removed by resuspending the cells in 5 ml ACK lysis buffer according to standard procedures. Cells were frozen slowly and stored in liquid nitrogen. For analysis, cells were thawed and resuspended in 10% (v/v) heat-inactivated (56° C, 1 h) FCS (HyClone, Logan, UT), 1.5 mM L-glutamine (all from Gibco BRL, Grand Island, N.Y.) and incubated on a 96-well-plate (1x10^6 cells/ml) in the presence of ODN as indicated below. Not all assays were performed for all samples because of the limited number of cells available for some samples.

Oligonucleotides: Nucleoside-resistant phosphorothioate-modified oligodeoxynucleotide (ODN) were purchased from Operon Technologies (Alameda, Calif.) and Hybridot Specialty Products (Milford, Mass.). Sequences were as follows: CpG ODN 2006: 5’-TCGTCCGTTTGTCGTTGTTGTTG-3’ (SEQ ID NO: 729), and control ODN 2017: 5’-CCCCCCCCCCCCCCCCCCCCC-3’ (SEQ ID NO: 168). ODN was diluted in TE (10 mM Tris-HCl, 1 mM EDTA, pH 8) using pyrogen-free reagents. ODN was added at a final concentration of 5 μg/ml.

Flow cytometry: Cells were washed and resuspended in ice-cold PBS or Annexin V binding buffer (10 mM HEPES/ NaOH, 140 mM NaCl, 2.5 mM CaCl₂, pH 7.4). Murine or human serum was added (final concentration 1%) to block non-specific binding of antibodies. Surface antigen staining was performed as described. Hartmann G et al., *J Pharmacol Exp Ther* 285:920-8 (1998). In brief, 1x10^5 cells per sample were stained with CyChrome-labeled anti-CD19 and FITC- or PE-labeled antibodies as indicated for 20 min on ice. They were then washed and analyzed by flow cytometry. Monoclonal antibodies to CD40 (5C3), CD69 (FN50), CD80 (L307.4), CD86 (IT2.2), CD54 (HA58), MHC I (G46-2.6) and MHC II (TU39) as well as isotype controls (IgG1, MOPC-21 and IgG2a, G155-178) were purchased from Pharmingen, San Diego, Calif. FITC-labeled polyclonal anti-human Ig was purchased from Southern Biotech, Birmingham, Ala. 1D10, a monoclonal humanized antibody directed against a variant of HLA-DR was produced in our laboratory as described earlier. Link B K et al., *Blood* 81:3343-9 (1993). C2B8, a monoclonal humanized anti-CD20 antibody, was purchased from IDEC Pharmaceuticals, San Diego, Calif. 1D10 and C2B8 were labeled with FITC according to standard protocols. The analysis gate was set on viable cells identified according to FSC/SSC characteristics and Annexin V staining (>97% viable cells within analysis gate). Spectral
overlap was corrected by appropriate compensation. Flow cytometric data from 1×10^6 cells per sample were acquired on a FACSScan (Beckton Dickinson Immunocytometry Systems, San Jose, Calif.). Data were analyzed using the computer program Flowjo (version 2.5.1, Tree Star, Inc., Stanford, Calif.).

CFSE staining: CFSE 5- (and 6-) carboxyfluorescein diacetate succinimidyl ester, Molecular Probes, USA, is a fluorescein-derived intracellular fluorescent label which is divided equally between daughter cells upon cell division. Staining of cells with CFSE allows both quantification and immunophenotyping of proliferating cells in a mixed cell suspension. Interference between oligonucleotide degradation products and thymidine uptake (standard proliferation assay) is avoided by using this method. The technique has described in detail previously. Lyons A B et al., J Immunol Methods 171:131-7 (1994). Briefly, cells were washed twice in PBS, resuspended in PBS (1×10^6 cells/ml) containing CFSE at a final concentration of 1 μM, and incubated at 37°C for 10 minutes. Cells were washed three times with PBS.

TUNEL assay: A two-color DNA strand break labeling assay, based on a modification of the assay described by Li et al. (Li X et al., Exp Cell Res 222:28-37 (1996)) was used to assess B-cell proliferation in response to CpG ODN. This assay involved terminal transferase-mediated dUTP nick end labeling (TUNEL) before and after induction of DNA strand breaks in BrdU-labeled cells. Briefly, cells were cultured for 3 days with and without CpG ODN. They were then incubated for 16 hours in 10 μM BrdU and placed onto slides by cytospin. Cells were then in 1% paraformaldehyde in PBS for 15 minutes followed by 20 minutes in 70% ethanol. DNA cleavage indicative of apoptosis was detected by labeling the 3'-DNA end of nicked strands with FITC-dUTP (Boehringer-Mannheim). The use of 5'-dUTP prevented further elongation of the 3'-ends in subsequent steps. Slides were then placed face-down on a 2 mm support at both ends on a UV transilluminator and exposed for 5 minutes. The new DNA strand breaks induced by photolysis at sites of BrdU incorporation (i.e., proliferating cells) were detected by a second TUNEL labeling using tetramethylrhodamine-dUTP (TMR-dUTP, Boehringer-Mannheim). Both TUNEL staining steps included incubating slides in 50 μl of TdT mix (34 μl distilled water, 10 μl of 5x TdT buffer, 5 μl of 25 mM cobalt chloride, 12.5 units terminal transferase and 0.5 nmol fluorochrome-conjugated-dUTP) (Boehringer-Mannheim) under a coverslip for one hour at 37°C in a humidified chamber. The slides were then washed in 5 quick changes of distilled water followed by 3 changes of 2x SSC containing 30% formamide for 5 minutes each at room temperature. After the second TUNEL labeling step, cells were counterstained for CD19, and also stained with Wright solution for blood cell differentiation and mounted in Vectashield media containing DAPI-counterstain (Vector Laboratories, Burlingame, Calif.). The morphology and staining of cells were assessed using both visible light and fluorescence microscopy. Apoptotic cells were identified by green fluorescence (FITC label), and proliferating cells by red fluorescence (TMR label). The percentage of apoptotic and proliferating cells was determined by counting at least 200 cells per sample by three observers blinded to whether cells were treated or control. Mean and standard error were determined for each sample based on these three readings.

Our prior studies demonstrated that activation of naïve human B cells by CpG ODN results in increased cell size (FSC) and granularity (SSC). Hartmann G et al., J Immunol 164:944-53 (2000). We therefore first determined whether such changes also occur in malignant B cells. Primary malignant B cells were obtained from lymph node biopsies, peripheral blood, or pleural fluid of patients with various types of B-cell malignancy. In addition, cells from the lymph node of a patient with benign reactive follicular hyperplasia were studied. Nine samples in total were evaluated (see Table 5). Cells were incubated for 72 hours in media containing CpG ODN 2006 (5 μg/ml) or control ODN 2017. FSC and SSC were examined with gating on CD19+ viable cells (FIG. 1).

Varying degrees of change in FSC and SSC were noted in response to CpG ODN 2006 when compared to control ODN 2017 or medium alone. Comparable changes were not found in the cells from the patient with benign reactive follicular hyperplasia.

FIG. 1 depicts the morphologic changes of marginal zone lymphoma cells upon CpG ODN stimulation. Malignant B cells from a patient with marginal zone lymphoma were stimulated with 5 μg/ml of CpG ODN (A and D), control ODN (B and E) or CpG ODN (C and F) for 72 hours and analyzed by flow cytometry. A, B, and C illustrate FSC (x-axis) vs. SSC (y-axis). D, E, and F illustrate CD19 expression (x-axis) against FSC (y-axis), allowing for separation of B cells from other leukocyte subpopulations. Upon stimulation with CpG ODN, B cells shifted up and to the right, indicating an increase in granularity and size. No changes could be detected without stimulation or on stimulation with the non-CpG ODN.

Expression of CD20, CD40, CD69, CD80, CD86, surface Ig, CD54, MHC I, MHC II, and an HLA-DR variant antigen (mAb 1D10) were examined on viable CD19+ cells after incubation of cells with CpG ODN for 72 hours. Each of these markers was upregulated to varying extents in response to the CpG ODN 2006 compared to control ODN 2017 (FIG. 2, FIG. 3).

FIG. 2 depicts the expression of surface antigens on marginal zone lymphoma cells upon CpG ODN treatment. Flow cytometric analysis of surface antigen expression on malignant B cells from a patient with marginal zone lymphoma was performed 72 hours after stimulation with 5 μg/ml of either CpG ODN or non-CpG ODN. On stimulation with CpG ODN, median fluorescence intensity for all markers tested shifted to the right, indicating an increase in surface expression. Thin curves indicate incubation with medium alone, dotted curves incubation with control ODN, and bold curves incubation with CpG ODN.

FIG. 3 depicts the expression of surface antigens on primary cells representing different B-cell malignancies and cells of a benign follicular hyperplasia upon CpG ODN treatment. Cells from lymph node biopsies, peripheral blood or pleural fluid from patients with different B-cell malignancies were incubated for 72 hours with either media alone, control ODN or CpG ODN. Each panel represents one experiment.

CD20 was expressed to varying degrees in all samples tested. As is well known, baseline CD20 expression was lower in the B-CLL samples when compared to the B-cell malignancies of other histologies. CpG-ODN 2006 but not the control ODN 2017 increased CD20 expression in both
B-CLLs and both marginal zone lymphomas. No or only little upregulation was seen in the other lymphoma samples. Nonmalignant CD19+ cells derived from the reactive follicular hyperplasia decreased CD20 expression in response to CpG (Fig. 3). This data demonstrated a reverse correlation between the baseline expression of CD20 and CD40, and expression of these markers after incubation with CpG ODN; thus the lower the baseline level of CD20 and CD40, the higher was the responsiveness to CpG ODN (r = -0.6; -0.4) (Fig. 4). This correlation was less clear for the other markers. CD19+ cells derived from the reactive follicular hyperplasia showed high baseline expression of activation markers which was not further upregulated by CpG.

Fig. 4 shows the CpG ODN effect on CD20 and CD40 is dependent on the baseline level of expression. Cells from lymph node biopsies, peripheral blood or pleural fluid from patients with different B-cell malignancies (see Table 5) were incubated with or without CpG ODN for 72 hours. Expression of CD20 and CD40 was measured by flow cytometry. Baseline expression of CD20 and CD40 with medium alone was compared to the expression of CD20 and CD40 in the presence of CpG ODN. The coefficients of correlation are indicated.

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<th>Sample Number</th>
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<td>1</td>
<td>Chronic Lymphocytic Leukemia 1</td>
<td>25.9</td>
<td>21.5</td>
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<tr>
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<td>32.6</td>
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<td>5</td>
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<td>7</td>
<td>Marginal Zone Lymphoma</td>
<td>32.9</td>
<td>32.8</td>
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A TUNEL assay was utilized to assess the effect of CpG ODN on both proliferation and apoptosis. The results are shown in Table 7.

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Example 2

Immunostimulatory Nucleic Acids Induce Proliferation and Apoptosis of Malignant B Cells

CpG induces a strong proliferative response of primary human B cells. Hartmann G et al., J Immunol 164:94-53 (2000). Two techniques were used to assess whether CpG ODN is capable of inducing proliferation of B-CLL cells. For select samples, cells were stained with CFSE and incubated for four days. Proliferation of cells is indicated by a loss of CFSE stain with every cell division. In B-CLL, CD5 can be used to identify malignant B cells which are CD19+ cells. Proliferation of malignant B cells (CD5+ and CD4+cells) was also evaluated at baseline normal B cells (CD5+ and CD4+) (Fig. 5). For the marginal zone lymphoma, CpG ODN 2006 induced proliferation of the CD19+ cell population (Fig. 5). Fig. 5 shows a comparison of CpG ODN induced proliferation of malignant and normal B cells. Peripheral blood mononuclear cells from two patients, one with B-CLL and one with marginal zone lymphoma with circulating malignant cells, were incubated for 72 hours with CpG ODN or medium alone and evaluated by two-color flow cytometry.
vival that was similar to those treated with murine IgG1 antibody alone (MST 28 days and 27 days, respectively). In contrast, mice treated with murine IgG2a plus CPG ODN had survival that was significantly improved when compared to mice treated with murine IgG2a alone (MST 45 days and 37 days, respectively).

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the examples provided, since the examples are intended as a single illustration of one aspect of the invention and other functionally equivalent embodiments are within the scope of the invention. Various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims. The advantages and objects of the invention are not necessarily encompassed by each embodiment of the invention.

All references, patents and patent publications that are recited in this application are incorporated in their entirety herein by reference.
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NAME/KEY: misc_feature
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OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 23

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OTHER INFORMATION: phosphodiester backbone

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NAME/KEY: misc_feature
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OTHER INFORMATION: phosphodiester backbone
SEQUENCE: 27

aatagtcgcc atcgctggac

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NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone
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NAME/KEY: misc_feature
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<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 76

ataaagcgsa actgcgacca gtttc

<210> SEQ ID NO 77
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 77

ataagcgtt

<210> SEQ ID NO 78
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 78

ataagcgc ttcagcgaag

<210> SEQ ID NO 79
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
ataatccagttgaaccaag

ataatgacgttcccgccccc

ataatctgctttcaagcaag

ataatcagaaattttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttt
<210> SEQ ID NO 85
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 85
atatatatatatatatatatatat 18

<210> SEQ ID NO 86
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 86
atatcatactc aasacatcasa a 24

dacagaaaag cttatggtgaag c

<210> SEQ ID NO 87
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 87
atcagaaaag cttatggtgaag c 21

<210> SEQ ID NO 88
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 88
atcagacgtc gtttttc 20

<210> SEQ ID NO 89
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (18)...(18)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 89
atcagacgtc gtttttc 20
<210> SEQ ID NO 90
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 90

atcgactcga ggttgttcg

<210> SEQ ID NO 91
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 91

atcgactcgc ggcgttgttcg

<210> SEQ ID NO 92
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 92

atcgactcgc ggcgttgttcg

<210> SEQ ID NO 93
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 93

atcgactcgc ggcgttgttcg

<210> SEQ ID NO 94
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (14) ...(14)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 94

atcgactcgc ggcgttgttcg
<210> SEQ ID NO 95
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 95

atcgactctctc tgcagcttctc tc

<210> SEQ ID NO 96
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 96

atcgactttg agctttctc

<210> SEQ ID NO 97
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 97

atcgatcag ctctctc

<210> SEQ ID NO 98
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 98

atcgtatgt

<210> SEQ ID NO 99
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 99

atcgagagc tgcgagcgcg

<210> SEQ ID NO 100
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorochoate backbone

SEQUENCE: 100
atcgttgag gcagacgtat g 21

SEQ ID NO: 101
LENGTH: 17
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorochoate backbone

SEQUENCE: 101
atgacgcttc tgacgttt 17

SEQ ID NO: 102
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 102
atgcactctg cagctttgtc 20

SEQ ID NO: 103
LENGTH: 8
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 103
atgcagtt 8

SEQ ID NO: 104
LENGTH: 15
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 104
atgccctca aagtt 15

SEQ ID NO: 105
LENGTH: 23
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 105
atgtaagg agtcacatt gca

<210> SEQ ID NO 106
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 106

atggaagtc cagcgttctc

<210> SEQ ID NO 107
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 107

atggaagtc cagcgttctc

<210> SEQ ID NO 108
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 108

atggaagtc cagcgttctc

<210> SEQ ID NO 109
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 109

atggaagtc cagcgttctc

<210> SEQ ID NO 110
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 110

atggaagtc cagcgttctc

<210> SEQ ID NO 111
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 111

atggaagtc cagcgttctc

<210> SEQ ID NO 112
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 112

atggaagtc cagcgttctc
atgacctcga caggtttcctc

atgacctcgg tctgtgctct

atgttacta gacaaatcc cccgagaagt ttt

atgttacttt cttaaatc ccacgagatg ttt

atgtcgcgg gcggggcga g
-continued

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (3) ... (3)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 116

atgacctac gtcggttctc

<210> SEQ ID NO 117
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (3) ... (3)
<223> OTHER INFORMATION: m5c
<221> NAME/KEY: modified_base
<222> LOCATION: (14) ... (14)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 117

atgacctctn gagnnttctc

<210> SEQ ID NO 118
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (1) ... (1)
<223> OTHER INFORMATION: biotinylated at 5’ end

<400> SEQUENCE: 119

atggaaggtc cagcgttctc

<210> SEQ ID NO 119
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (1) ... (1)
<223> OTHER INFORMATION: biotinylated 5’ end

<400> SEQUENCE: 119

gagaacggtc cagcactgat

<210> SEQ ID NO 120
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated 5' end

SEQUENCE: 120

```gagaagcgcg gaccttcgat```

SEQ ID NO 121
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated 5' end
NAME/KEY: modified_base
LOCATION: (6)...(6)
OTHER INFORMATION: m5c

SEQUENCE: 121

```gagaangctc cagcactgat```

SEQ ID NO 122
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated 5' end
NAME/KEY: modified_base
LOCATION: (6)...(6)
OTHER INFORMATION: m5c

SEQUENCE: 122

```gagaangctc gagcttcgat```

SEQ ID NO 123
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

SEQUENCE: 123

```gagaagctg gagcttcgat```

SEQ ID NO 124
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
gacaagntg gaccttccat

SEQ ID NO 125
LENGTH: 17
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: misc_feature
LOCATION: (1) ... (1)
OTHER INFORMATION: biotinylated at 5' end

gctagacgtt acgtga

SEQ ID NO 126
LENGTH: 8
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: misc_feature
LOCATION: (1) ... (1)
OTHER INFORMATION: biotinylated at 5' end

tcacgtt

SEQ ID NO 127
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: misc_feature
LOCATION: (1) ... (1)
OTHER INFORMATION: biotinylated at 5' end

tcatgacgt tcgtgatgtc

SEQ ID NO 128
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

SEQUENCE: 128

tcagtagcgt tcagtagcgt

SEQ ID NO: 129
LENGTH: 29
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 5' end
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

SEQUENCE: 129

tcagtagcgt gcagtagcgt agctttcca

SEQ ID NO: 130
LENGTH: 30
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 5' end
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

SEQUENCE: 130

tcagtagcgt tcagtagcgt agctttcca

SEQ ID NO: 131
LENGTH: 29
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 5' end
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

SEQUENCE: 131

tcagtagcgt gcagtagcgt gcgtttttt
cgtttttt

SEQ ID NO: 132
LENGTH: 29
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 5' end
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

SEQ ID NO: 133
LENGTH: 30
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 5' end
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

SEQ ID NO: 134
LENGTH: 29
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 5' end
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

SEQ ID NO: 135
LENGTH: 30
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 5' end
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

SEQ ID NO: 136
LENGTH: 29
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 5' end
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end
tttttcaatg tcgttctgta tgcctttt

SEQ ID NO 133
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 5' end
NAME/KEY: misc_feature
LOCATION: (1)...(1)
OTHER INFORMATION: biotinylated at 5' end

ttttttcgtcg ttttccccccc ccccc

SEQ ID NO 134
LENGTH: 8
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

caacggtt

SEQ ID NO 135
LENGTH: 7
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

caacggtt

SEQ ID NO 136
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

caagagatgc taacagtga

SEQ ID NO 137
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

caatcaatct gaggagacc
<210> SEQ ID NO 138
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 139

cacaccttg tcaatgtcac gt

<210> SEQ ID NO 139
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 139

cacacaccttg tcaatgtcaca cgt

<210> SEQ ID NO 140
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 140

cacggtagcc ttctca

<210> SEQ ID NO 141
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 141

cacggttagg ggcat

<210> SEQ ID NO 142
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 142

cactgtcctt cgctgca

<210> SEQ ID NO 143
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 143

cagacaacaga agcgcgatag acg

SEQ ID NO 144
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc.feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 144

cagattgtgc aatgtctcga

SEQ ID NO 145
LENGTH: 27
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc.feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 145

cataacatag gaatattac tcctgc

SEQ ID NO 146
LENGTH: 31
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc.feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 146

cataggactt cgagctgga aagtcoccta c

SEQ ID NO 147
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc.feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 147

catsagctca tctgagggaa gcgg

SEQ ID NO 148
LENGTH: 16
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc.feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 148
catttccag atttccta

<210> SEQ ID NO 149
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 149

<210> SEQ ID NO 150
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 150

ccasatacg gtgtcaagc ac

<210> SEQ ID NO 151
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 151

ccasagt

<210> SEQ ID NO 152
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 152

ccasagtgcac cctcagcggcga

<210> SEQ ID NO 153
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 153

ccasagtgcac cctcagc

<210> SEQ ID NO 154
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 154
ccacctcacat c tgtgctcc acag

SEQ ID NO 155
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 155
ccagatgagct c tgtggttct cc

SEQ ID NO 156
LENGTH: 26
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 156
ccaggttaaag aggaatgcct tcgg

SEQ ID NO 157
LENGTH: 17
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 157
ccaggttgtga taaggcc

SEQ ID NO 158
LENGTH: 35
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 158
ccagtgcgtga taccgatat c tgtgcggc agtcg

SEQ ID NO 159
LENGTH: 35
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 159
ccatgcagt

SEQ ID NO 160
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 160
ccatgcct 8
cctactagc
<211> SEQ ID NO 161
<212> LENGTH: 17
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 161
cctgctaaccctctagc 17
cctctgctgctctgctgctg
<211> SEQ ID NO 163
<212> LENGTH: 19
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 163
cctctgctgcctgctgctgctg 19
cctgctgctgctgctgctgctg
<211> SEQ ID NO 164
<212> LENGTH: 20
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 164
ccccaaagggatgsgagtt 20
ccccccaaaaaaaaaaaccccc

<211> SEQ ID NO 165
<212> LENGTH: 6
<213> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 165

ccccccc 6

<210> SEQ ID NO 166
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 166

ccccccc 8

<210> SEQ ID NO 167
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 167

ccccccccc cc 12

<210> SEQ ID NO 168
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 168

ccccccccc cccccccc 20

<210> SEQ ID NO 169
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 169

ccccccccc cccccccc 20

<210> SEQ ID NO 170
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 170

cccccccccccccccccc 24

SEQ ID NO 171
LENGTH: 28
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 171

cccccccccccccccccccc 28

SEQ ID NO 172
LENGTH: 35
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 172

cccccccccccccccccccccccccc 35

SEQ ID NO 173
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 173

ccccctgaac ttttcccccc 20

SEQ ID NO 174
LENGTH: 26
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 174

ccccgaagtc ttctcttttt aacctgg 26

SEQ ID NO 175
LENGTH: 26
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 175

cgaacagga tatcggtgat cgcac 26
<210> SEQ ID NO 176
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 176

cgcttcctc casgtgacgt catg

<210> SEQ ID NO 177
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 177

cgcttcctc casgtgacgt catgggtttc tccaccasg

<210> SEQ ID NO 178
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 178

cggccggcc ggccggccg

<210> SEQ ID NO 179
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_difference
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 179

ccgctgttccc ccccccccc

<210> SEQ ID NO 180
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 180

cctacgttgt atgcgcccasg ct

<210> SEQ ID NO 181
<211> LENGTH: 20
<212> TYPE: DNA
ORGANISM: Artificial Sequence

FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 181

cctcagatg aagaacccc 20

SEQ ID NO 182
LENGTH: 19
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 182

cctctataca accgggac 19

SEQ ID NO 183
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 183

cctccacgt cgctctgtg 20

SEQ ID NO 184
LENGTH: 8
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 184

cctttgat 8

SEQ ID NO 185
LENGTH: 8
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 185
cgaaagtt 8

SEQ ID NO 186
LENGTH: 6
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 186
<210> SEQ ID NO 187
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 187

cgacga

<210> SEQ ID NO 188
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 188

cgacgctcga ggtttcgc

<210> SEQ ID NO 189
<211> LENGTH: 35
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 189

cgacgtcgcga acagatcacg gcacgtcg

<210> SEQ ID NO 190
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 190

cgcctcgcgc ggcgttgcc

<210> SEQ ID NO 191
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 191

cgcttggggt ggggttgg

<210> SEQ ID NO 192
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) . . . (0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 192
cgacgacgacgccgacgcg 20

SEQ ID NO 193
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) . . . (0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 193
cgacgacgacgccgacgcg 20

SEQ ID NO 194
LENGTH: 6
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) . . . (0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 194
cgtga 6

SEQ ID NO 195
LENGTH: 10
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) . . . (0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 195
cgtagaggt tagcgtga 18

SEQ ID NO 196
LENGTH: 15
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) . . . (0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 196
cgtgactct tcot 15

SEQ ID NO 197
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) . . . (0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 197
cgtgcagct tcctgctg 20

SEQ ID NO 198
LENGTH: 16
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 198
cgtgcagct catcaaa 16

SEQ ID NO 199
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 199
cgppgcgactc agtcctatg 20

SEQ ID NO 200
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 200
cgppcttacg gggatgtgtg 20

SEQ ID NO 201
LENGTH: 14
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 201
cgtagcttc cct 14

SEQ ID NO 202
LENGTH: 15
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 202
cgtaccttac ggtga 15

SEQ ID NO 203
LENGTH: 6
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 203
cgtaacg 6

SEQ ID NO 204
LENGTH: 6
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 204
cgtcga 6

SEQ ID NO 205
LENGTH: 6
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 205
cgtcga 6

SEQ ID NO 206
LENGTH: 6
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 206
cgtcgt 6

SEQ ID NO 207
LENGTH: 9
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 207
cgtcgtcgt 9

SEQ ID NO 208
LENGTH: 21
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone
<400> SEQUENCE: 208
cgtcgtcg tcgtcgtcg t 21

<210> SEQ ID NO 209
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 209
cgtctatcgg gctctgtgt ctg 23

<210> SEQ ID NO 210
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 210
cgttgcg 6

<210> SEQ ID NO 211
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 211
cgtaacgtt 8

<210> SEQ ID NO 212
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 212
catatctcctaatttttttcattaa 24

<210> SEQ ID NO 213
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 213
ctagataaacggaaccgc aacagacaca gaagocccga tagag 45

<210> SEQ ID NO 214
ctagcccctga
tagctaga

tagcccctga
tagctaga

tagcccctga
tagctaga

tagcccctga
tagctaga
ctagcttgat gacgtcagcc gctag

ctagcttgat gacgtcagcc gctag

ctagctttat gacgtcagcc gctagc

ctaggtgtag gctcatcagc tagt

ctagtggtgt gcgtcatcagc tagt

ctagtggtgt gcgtcatcagc tagt
catcggagg actggccgc c

<210> SEQ ID NO 225
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE: 
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 225

catcggagg actggccgc cg

<210> SEQ ID NO 226
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE: 
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 226

cctcaacgctg gaccttccat

<210> SEQ ID NO 227
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE: 
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 227

cctatgggt ttcggaccaag g

<210> SEQ ID NO 228
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE: 
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 228

cctcgacgctc aagaaagac g

<210> SEQ ID NO 229
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE: 
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 229

cctgcccccgc cccgatggaat t

<210> SEQ ID NO 230
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 230
ccttcaagc tcaacatcaag

SEQ ID NO 231
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 231
cctcctgtag gcgcgttgg

SEQ ID NO 232
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 232
cctttgctag cttgagttga

SEQ ID NO 233
LENGTH: 10
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 233
cgagctcat

SEQ ID NO 234
LENGTH: 8
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 234
cgtacgctg

SEQ ID NO 235
LENGTH: 10
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 235
cgtattgtc ctctcgnga
<210> SEQ ID NO 236
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 236
ctgtggtc ttcgtgta

<210> SEQ ID NO 237
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 237
ctgccagctg ggac

<210> SEQ ID NO 238
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 239
ctgctttacc aatttaacctg tg

<210> SEQ ID NO 239
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 239
ctgctgagac ttgag

<210> SEQ ID NO 240
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 240
cgtgtgtgc tgcgtggtc g

<210> SEQ ID NO 241
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 241

cctgaccttc ctagtgc 16

<210> SEQ ID NO 242
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 242
cctgaccttc ctagtgcg 18

<210> SEQ ID NO 243
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 243
cctgcttttc tgttttttt ctgg 24

<210> SEQ ID NO 244
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 244
cctgcttttc tgttttttt ctgg 24

<210> SEQ ID NO 245
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 245
cctgcagcgt gctttagag 20

<210> SEQ ID NO 246
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<210> SEQ ID NO 247
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 246

cgtatgaa caaattttcc tctttggga

30

<210> SEQ ID NO 247
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 247

cgtgca

6

<210> SEQ ID NO 248
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 248

cgtcagggaa cgtcggttaa gg

22

<210> SEQ ID NO 249
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 249

cgttccata ttttagaca

20

<210> SEQ ID NO 250
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 250

cgtgtcg

6

<210> SEQ ID NO 251
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 251

cgtgtcg

6
<210> SEQ ID NO 252
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 252

ctgtgctttc ccccccccc

<210> SEQ ID NO 253
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphoroxythioate backbone

<400> SEQUENCE: 253

ctgtgctttc tgtgtttttt tgtg

<210> SEQ ID NO 254
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 254

cctggagggc cttccggcgg

<210> SEQ ID NO 255
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 255

cctgggtgag aascccatga g

<210> SEQ ID NO 256
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 256

cctgggtgag aascccatga gctctctgg aggaagcgg

<210> SEQ ID NO 257
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 257

c tt t c g t t g  g a c c c o t g g g

<210> SEQ ID NO 259
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c
<221> NAME/KEY: modified_base
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: m5c
<221> NAME/KEY: modified_base
<222> LOCATION: (10)...(10)
<223> OTHER INFORMATION: m5c
<221> NAME/KEY: modified_base
<222> LOCATION: (15)...(15)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 258

c n g g c n g c n g c n c c g g

<210> SEQ ID NO 259
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(1)
<223> OTHER INFORMATION: FITC labeled

<400> SEQUENCE: 259

a s c g t t g a

<210> SEQ ID NO 260
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(1)
<223> OTHER INFORMATION: FITC labeled

<400> SEQUENCE: 260

c g c a a t t c g c g

<210> SEQ ID NO 261
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(1)
<223> OTHER INFORMATION: FITC labeled

<400> SEQUENCE: 261

tcaacgtt

<210> SEQ ID NO 262
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 262

gaaacgtt

<210> SEQ ID NO 263
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 263

gaaactgtgc ctatgtttgo tttat

<210> SEQ ID NO 264
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 264

gaaccttcca tgcgtggt

<210> SEQ ID NO 265
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 265

gaaccttcca tgcggttcog

<210> SEQ ID NO 266
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 266

gaagctggga cctcccat

<210> SEQ ID NO 267
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<222> NAME/KEY:misc_feature
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 267

gagttccag tgaggggca t

<210> SEQ ID NO 268
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<222> NAME/KEY:misc_feature
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 269

gagtttcttg gtasgtcttc g

<210> SEQ ID NO 269
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<222> NAME/KEY:misc_feature
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 270
gaccttcacat

<210> SEQ ID NO 270
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<222> NAME/KEY:misc_feature
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 271
gaccttcctag tgcgtctctg at

<210> SEQ ID NO 271
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<222> NAME/KEY:misc_feature
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 272
gacgtcat

<210> SEQ ID NO 272
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<222> NAME/KEY:misc_feature
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 273
gacgtcat
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 273

gactgacgtc agcgtt

15

<210> SEQ ID NO: 274
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 274

gagaacgatg gaccttccat

20

<210> SEQ ID NO: 275
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 275

gagaacgccta gaccccttcat

20

<210> SEQ ID NO: 276
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 276

gagaacgcctc gaccccttcat

20

<210> SEQ ID NO: 277
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 277

gagaacgcctc cagccactgat

20

<210> SEQ ID NO: 278
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 279

gagaacgctc cacgttcgat

<210> SEQ ID NO 279
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphoroehoic acid backbone

<400> SEQUENCE: 279

gagaacgctc cacgttcgat
gagaacgctc cgaccttca t

<210> SEQ ID NO 280
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 280

gagaacgctc cgaccttccat

gagaacgctc gcaccttccat

gagaacgctc gcaccttccat

<210> SEQ ID NO 281
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphoroehoic acid backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (20)...(20)
<223> OTHER INFORMATION: biotinylated at 3' end

<400> SEQUENCE: 281

gagaacgctc gcaccttccat

<210> SEQ ID NO 282
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 282

gagaacgctg gaccatatc tca

<210> SEQ ID NO 283
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<210> SEQ ID NO 284
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 284

gagaacgctg gcctctca tccat

<210> SEQ ID NO 285
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 285

gagaacgctg gcctctcc at

<210> SEQ ID NO 286
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 286

gagaacgctg gcctctcc at

<210> SEQ ID NO 287
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 287

gagaacgctg gcctctcc at

<210> SEQ ID NO 288
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 288

gagaacgctg gcctctcc at

<210> SEQ ID NO 289
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 289

gagaagctgtg gaccttcgat

SEQ ID NO 290
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 290

gagaagctgtg gaccttcgta

SEQ ID NO 291
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 291

gagaagctgtg gaccttcgcat

SEQ ID NO 292
LENGTH: 23
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 292

gagaagctgtg gacgctcact cat

SEQ ID NO 293
LENGTH: 19
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 293

gagaagctgtg gacctccat

SEQ ID NO 294
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: modified_base
LOCATION: (14)...(14)
OTHER INFORMATION: m5c

SEQUENCE: 294

gagaacgctg gacnttccat

SEQ ID NO 295
LENGTH: 17
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 295

gagaacgctg gatccat 17

SEQ ID NO 296
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 296

gasatgcgtg gaccttccat 20

SEQ ID NO 297
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: modified_base
LOCATION: (6)...(6)
OTHER INFORMATION: m5c

SEQUENCE: 297

gasangcgcg gaccttccat 20

SEQ ID NO 298
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 298

gasacgcgcg gacctcgcat 20

SEQ ID NO 299
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorochloate backbone
<400> SEQUENCE: 299

gagcaagctg gaccttccat

<210> SEQ ID NO 300
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (20)...(20)
<223> OTHER INFORMATION: biotinylated at 3' end

<400> SEQUENCE: 300

gagcaagctg gaccttccat

<210> SEQ ID NO 301
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 301

gaggaacgtc atggagagga acgtcatgga gaggaagctc atgga

<210> SEQ ID NO 302
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (9)...(9)
<223> OTHER INFORMATION: I
<221> NAME/KEY: modified_base
<222> LOCATION: (11)...(11)
<223> OTHER INFORMATION: I
<221> NAME/KEY: modified_base
<222> LOCATION: (15)...(15)
<223> OTHER INFORMATION: I

<400> SEQUENCE: 302

gaggaagng ngangagct

<210> SEQ ID NO 303
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 303

gaggggacca tttacgggc

<210> SEQ ID NO 304
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 304

gatccagatt cttgcaagtc actgtgactg gat

<210> SEQ ID NO 305
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 305

gatccagatt cttgcaagtc actgtgactg gat

<210> SEQ ID NO 306
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 306

gatccagta cagtgacctg gcgaaatctg gat

<210> SEQ ID NO 307
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 307

gatccagta cagtgacctg gcgaaatctg gat

<210> SEQ ID NO 308
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 308

gatcggctg acctataact agatc

<210> SEQ ID NO 309
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 309

gatgcgtgat ctaatgctog

SEQ ID NO: 310
LENGTH: 21
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 310

gatcggagga ctgcgcgcgc g

SEQ ID NO: 311
LENGTH: 25
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 311

gatctatgta tgagtcgcgc ggtc

SEQ ID NO: 312
LENGTH: 25
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 312

gatctactg gcgccgtctct taggc

SEQ ID NO: 313
LENGTH: 8
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 313

gcaacgct

SEQ ID NO: 314
LENGTH: 10
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone
NAME/KEY: misc_feature
LOCATION: (10)...(10)
OTHER INFORMATION: biotinylated at 3' end

SEQUENCE: 314
gcaattgct
<210> SEQ ID NO 315
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (10) ...(10)
<223> OTHER INFORMATION: FITC labeled
<400> SEQUENCE: 315

gcaattgct

<210> SEQ ID NO 316
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<400> SEQUENCE: 316

gcacatgctc cgcagcogga

<210> SEQ ID NO 317
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<400> SEQUENCE: 317

gcgcctccta tscasctcgg gcgggga

<210> SEQ ID NO 318
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: chimeric phosphothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends
<400> SEQUENCE: 319

gcatagcgtt gagctt

<210> SEQ ID NO 319
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<400> SEQUENCE: 319

gcatagcgtt gagctt

<210> SEQ ID NO 320
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 320

gcatgacgtt gagct
15

<210> SEQ ID NO 321
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 321

gcatgacgtt gagct
15

<210> SEQ ID NO 322
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 322

gcatgacgtt gagct
15

<210> SEQ ID NO 323
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 323

gcatgagcttgagctga
17

<210> SEQ ID NO 324
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 324

gcatgatgtt gagct
15

<210> SEQ ID NO 325
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (7) . . . (7)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 325

gcatgangtt gagct

<210> SEQ ID NO 326
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 326

gcatggcgtt gagct

<210> SEQ ID NO 327
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 327

gcatgtagct gagct

<210> SEQ ID NO 328
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 328

gcattgtcgtt gagct

<210> SEQ ID NO 329
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) . . . (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 329

gccctcatta gggggaag aat

<210> SEQ ID NO 330
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 330

gcattggttgagct
15

SEQ ID NO 331
LENGTH: 15
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 331

gcatttggagct
15

SEQ ID NO 332
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 332

gccacccaatctgtctcag
20

SEQ ID NO 333
LENGTH: 17
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 333

gccagatgtagctgga
17

SEQ ID NO 334
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 334

gcataagctgtagctcctccctc
24

SEQ ID NO 335
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone
<400> SEQUENCE: 335

gcgaggggc gcggcgccc

<210> SEQ ID NO: 336
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 336

gcgacgtgc gcgcgcgcc

<210> SEQ ID NO: 337
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 337

gcgacgtgc gcgcgcgcc

<210> SEQ ID NO: 338
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 339

gcgatgtgc gcgcgcgcc

<210> SEQ ID NO: 339
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 339

gcgatgtgc gcgcgcgcc

<210> SEQ ID NO: 340
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 340

gcgatgtgc gcgcgcgcc
<400> SEQUENCE: 346

gcgccgctcg gcgcgcgcc
  20

<210> SEQ ID NO 347
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<233> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 347

gcgccgctcg gcgcgcgcc
  20

<210> SEQ ID NO 348
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<233> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 348

gcgccgctcg gcgcgcgcc
  20

<210> SEQ ID NO 349
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<233> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 349

gctgctcttcccaccccc
  20

<210> SEQ ID NO 350
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<233> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 350

gctgctctt cgttgtgctg t
  21

<210> SEQ ID NO 351
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<222> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<233> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 351

gctttttttttttgctg
  15
This page continues the description of sequences.

**SEQ ID NO 352**
- **LENGTH**: 15
- **TYPE**: DNA
- **ORGANISM**: Artificial Sequence
- **FEATURE**:
  - **OTHER INFORMATION**: Synthetic oligonucleotide
  - **NAME/KEY**: misc_feature
  - **LOCATION**: (0) ...(0)
- **OTHER INFORMATION**: phosphodiester backbone

SEQUENCE: 352
```
gctaaacgtt agcgt
```

**SEQ ID NO 353**
- **LENGTH**: 16
- **TYPE**: DNA
- **ORGANISM**: Artificial Sequence
- **FEATURE**:
  - **OTHER INFORMATION**: Synthetic oligonucleotide
  - **NAME/KEY**: misc_feature
  - **LOCATION**: (0) ...(0)
- **OTHER INFORMATION**: phosphodiester backbone

SEQUENCE: 353
```
gctaaacgtta ggtga
```

**SEQ ID NO 354**
- **LENGTH**: 15
- **TYPE**: DNA
- **ORGANISM**: Artificial Sequence
- **FEATURE**:
  - **OTHER INFORMATION**: Synthetic oligonucleotide
  - **NAME/KEY**: misc_feature
  - **LOCATION**: (0) ...(0)
- **OTHER INFORMATION**: phosphodiester backbone

SEQUENCE: 354
```
gctacctag cgtga
```

**SEQ ID NO 355**
- **LENGTH**: 15
- **TYPE**: DNA
- **ORGANISM**: Artificial Sequence
- **FEATURE**:
  - **OTHER INFORMATION**: Synthetic oligonucleotide
  - **NAME/KEY**: misc_feature
  - **LOCATION**: (0) ...(0)
- **OTHER INFORMATION**: phosphodiester backbone
  - **NAME/KEY**: modified_base
  - **LOCATION**: (11) ...(11)
- **OTHER INFORMATION**: m5c

SEQUENCE: 355
```
gctaccttag ngtga
```

**SEQ ID NO 356**
- **LENGTH**: 14
- **TYPE**: DNA
- **ORGANISM**: Artificial Sequence
- **FEATURE**:
  - **OTHER INFORMATION**: Synthetic oligonucleotide
  - **NAME/KEY**: misc_feature
  - **LOCATION**: (0) ...(0)
- **OTHER INFORMATION**: phosphodiester backbone

SEQUENCE: 356
```
gctacttagc gtga
```

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<210> SEQ ID NO 357
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 357

gctagacgt aagctg 15

<210> SEQ ID NO 358
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 358

gctagacgt aagctgta 17

<210> SEQ ID NO 359
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 359

gctagacgt 9

<210> SEQ ID NO 360
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 360

gctagacgt aagctgta 17

<210> SEQ ID NO 361
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 361

gctagacgtc tagc 14

<210> SEQ ID NO 362
<211> LENGTH: 13
<212> TYPE: DNA
ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0)...(0)

OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 362

gctagacgtt agc

SEQ ID NO 363

LENGTH: 15

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0)...(0)

OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 363

gctagacgtt agcgt

SEQ ID NO 364

LENGTH: 17

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0)...(0)

OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 364

gctagacgtt agcgtga

SEQ ID NO 365

LENGTH: 17

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0)...(0)

OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 365

gctagacgtt agctgga

SEQ ID NO 366

LENGTH: 17

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0)...(0)

OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 366

gctagacgtt agctgga

SEQ ID NO 367

LENGTH: 17

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0)...(0)

OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 367

gctagacgtt aggctga

<210> SEQ ID NO 368
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 368

gctagacgtt agcgt

<210> SEQ ID NO 369
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (13)...(13)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 369

gctagacgtt agngt

<210> SEQ ID NO 370
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 370

gctagacgtt tgcg

<210> SEQ ID NO 371
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 371

gctagacgtt agcgtga

<210> SEQ ID NO 372
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
gctagagtt agcsgta 17

-gctagagtt agcsgta-

<400> SEQUENCE: 372

<210> SEQ ID NO 373
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 373

gctagagtt agcsgta 17

<210> SEQ ID NO 374
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 374

gctagatgtt aacgt 15

<210> SEQ ID NO 375
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 375

gctagagtt agcsgt 15

<210> SEQ ID NO 376
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 376

gctagatgtt aacgt 15

<210> SEQ ID NO 377
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 377

gctagagtt agcsgta 17
<210> SEQ ID NO 378
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (7) ... (7)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 378

gctagagtt agcgt

15

<210> SEQ ID NO 379
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (7) ... (7)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 379

gctagagtt agcgt

15

<210> SEQ ID NO 380
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 380

gctagctttta gagcatttaga gctt

24

<210> SEQ ID NO 381
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 381

gctagccggtt agcgt

15

<210> SEQ ID NO 382
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 382

gctagtgcgt agc

13
<210> SEQ ID NO 383
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 383

gctagtcag tacgt 15

<210> SEQ ID NO 384
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 384

gctagtcgct agc 13

<210> SEQ ID NO 385
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 385

gctandogh agc 13

<210> SEQ ID NO 386
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 386

gctatgacgct tccasagg 18

<210> SEQ ID NO 387
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_difference
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 387

gctcga 6

<210> SEQ ID NO 388
<211> LENGTH: 17

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)  ... (0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester back bone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 389

gctcgattcag ccggtctt

17

<210> SEQ ID NO 389
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 389

gctgaacctt ccattgtgtt

20

<210> SEQ ID NO 390
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)  ... (0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester back bone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 390

gctgagctca tgccgtctgc

20

<210> SEQ ID NO 391
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 391

gctgacacctt ccat

14

<210> SEQ ID NO 392
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)  ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 392

gctgacacctt ccat

14

<210> SEQ ID NO 393
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 393

gctggcagc ttacctcccg

20
<210> SEQ ID NO 394
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 394

gctgtaaat gatcgggccg 20

<210> SEQ ID NO 395
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 395

gctgtgggcc ggtctctg 18

<210> SEQ ID NO 396
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 396

gttgaagtc asgc 14

<210> SEQ ID NO 397
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 397

gttgaagt tagc 14

<210> SEQ ID NO 398
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 398

gttgaagtt tagc 14

<210> SEQ ID NO 399
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 399

gcggcgttg cggtt

<210> SEQ ID NO 400
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 400

gcgtgsggg cctgtaagtg

<210> SEQ ID NO 401
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 401

ggagcgtt

<210> SEQ ID NO 402
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 402

ggaagacggtt aga

<210> SEQ ID NO 403
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 403

ggaatagta atagatatag aagtt

<210> SEQ ID NO 404
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature

SEQUENCE: 404

ggaatagagtt
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 404

ggagaaccc atgagtcat ctg

<210> SEQ ID NO 405
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 405

ggagctottc gaacgccata

<210> SEQ ID NO 406
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 406

ggcagtgtcg gttccagggg

<210> SEQ ID NO 407
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 407

ggocacacat caatgtggga tgctctc

<210> SEQ ID NO 408
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 408

ggcatocca catgaaagt t

<210> SEQ ID NO 409
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 409

ggctttttc cccccccccc

<210> SEQ ID NO 410
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 410

gggaggcccc gggaggcccc 20

SEQ ID NO 411
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 411
ggggtatttc tgcctgcgcc 20

SEQ ID NO 412
LENGTH: 19
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 412
ggctatgtg cttccagtgc 19

SEQ ID NO 413
LENGTH: 19
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 413
ggctatgtg cttccagtgc 19

SEQ ID NO 414
LENGTH: 27
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 414
ggctcggggg agggaatttt tgtctat 27

SEQ ID NO 415
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 415
ggtgtattc tgaactgc

<210> SEQ ID NO 416
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 416

ggsatgaa gttttattaa taag

<210> SEQ ID NO 417
<211> LENGTH: 38
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 417

gggcactttc cgctggggac tttecagggg gacctttccc

<210> SEQ ID NO 418
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 418

gggsagggag gaacctotta aattecoccc agaagttt

<210> SEQ ID NO 419
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 419

9ggsagggg

<210> SEQ ID NO 420
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 420

9ggsagggg
<210> SEQ ID NO 421
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 421

ggggcatgac gttaaaaaaa

<210> SEQ ID NO 422
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 422

ggggcatgac gttaaaaaaa

<210> SEQ ID NO 423
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorodithioate backbone

<400> SEQUENCE: 423

ggggcatgac gtgcggggggg

<210> SEQ ID NO 424
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 424

ggggcatgac gtgcggggggg

<210> SEQ ID NO 425
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 425

ggggcatgag gtgcggggggg

<210> SEQ ID NO 426
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 426

gggcatggg ctccggggggg

20

<210> SEQ ID NO 427
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 427

gggccctctacacacctg g
g

21

<210> SEQ ID NO 428
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 428

9gggggacg ttgggg

15

<210> SEQ ID NO 429
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 429

9999999999 9999999999

20

<210> SEQ ID NO 430
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 430

9999999999 9999999999

20

<210> SEQ ID NO 431
<211> LENGTH: 31
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature

<400> SEQUENCE: 431
LOCATION: (0)...

OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 431

gggggttgg ggaacaagcg gacctctgc a

SEQ ID NO 432
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 432

gggggttttt ttttgtggggg

SEQ ID NO 433
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 433

gggttaactg atcggggtggg

SEQ ID NO 434
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 434

gggttaactg atcggggtggg

SEQ ID NO 435
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 435

gggttaactgc atcggggtggg

SEQ ID NO 436
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester
backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 436

ggggtcaacg tgaggggggg

<210> SEQ ID NO 437
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 437

ggggtcaacg tgaggggggg

<210> SEQ ID NO 438
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 438

ggggtcaacg tgaggggggg

<210> SEQ ID NO 439
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 439

ggggtcaggt cgaggggggg

<210> SEQ ID NO 440
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 440

ggggtcagcg tgtgcgcattg gggg

<210> SEQ ID NO 441
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 441
<210> SEQ ID NO 442
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 442

ggggtccgct agactgcc

<210> SEQ ID NO 443
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 443

ggggtcagcg tcgagggggg

<210> SEQ ID NO 444
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 444

ggggtctcgcc ttttgaggggg

<210> SEQ ID NO 445
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 445

ggggtctgct gcctttsggggg

<210> SEQ ID NO 446
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 446

ggggtctgct gcctttsggggg

<210> SEQ ID NO 447
<210> SEQ ID NO 449
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 449

gggtgtacgt tcaagggggg

<210> SEQ ID NO 449
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LOCATION: (2)...(2)
OTHER INFORMATION: m5c

SEQUENCE: 479

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SEQ ID NO 480
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: modified_base
LOCATION: (2)...(2)
OTHER INFORMATION: m5c
NAME/KEY: modified_base
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OTHER INFORMATION: m5c

SEQUENCE: 480

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FEATURE:
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NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 481
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NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 482
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LENGTH: 36
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FEATURE:
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SEQUENCE: 490
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LENGTH: 31
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ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 491
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SEQ ID NO 492
LENGTH: 20
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ORGANISM: Artificial Sequence
FEATURE:
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NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 492
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SEQ ID NO 493
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NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 493
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<225> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 515

tgacaccagtgctcggtgtttctcgtga

<210> SEQ ID NO 516
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<225> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 516

tgacaccagtgctcggtgtttctcgtga

<210> SEQ ID NO 517
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<225> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 517

tcagctcgt

<210> SEQ ID NO 518
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<225> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 518

tcagctcgccgc

<210> SEQ ID NO 519
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<225> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 519

tcagctctggactttttcga
<210> SEQ ID NO 520
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<200> SEQUENCE: 520
tcaggacac cogaccagct ggtctga

<210> SEQ ID NO 521
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<200> SEQUENCE: 521
tcaggacac cogaccagct ggtctga

<210> SEQ ID NO 522
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<200> SEQUENCE: 522
tcagggtgtg gggtcscttt

<210> SEQ ID NO 523
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c

<200> SEQUENCE: 523
tcagngct

<210> SEQ ID NO 524
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<200> SEQUENCE: 524
tcactcgcgat
<210> SEQ ID NO 525
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 525

tccagacgt tctgatgcgt

20

<210> SEQ ID NO 526
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 526

tcaccgtc agttcgtc

20

<210> SEQ ID NO 527
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 527

tcaccacgt ggctgatcgt

20

<210> SEQ ID NO 528
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 528

tcaccacgt ggtctgatcgt

20

<210> SEQ ID NO 529
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 529

tcacagcgt ttgacacgtt

20

<210> SEQ ID NO 530
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> OTHER INFORMATION: Synthetic oligonucleotide
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 530

tccagcgt gaagt  15

<210> SEQ ID NO 531
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> OTHER INFORMATION: Synthetic oligonucleotide
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 531
tccagcgtt gaagt  15

<210> SEQ ID NO 532
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> OTHER INFORMATION: Synthetic oligonucleotide
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 532

tccagcgttgc gcata  16

<210> SEQ ID NO 533
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> OTHER INFORMATION: Synthetic oligonucleotide
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 534
tccagcgtgt ctcagttct  20

<210> SEQ ID NO 535
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> OTHER INFORMATION: Synthetic oligonucleotide
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 535
tccagcgtc tctagttct  20
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 535

tccaggct tctcaggtt

SEQ ID NO 536
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 536

tccaggct tctcaggtt

SEQ ID NO 537
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 537

tccaggct tctcaggtt

SEQ ID NO 538
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 538

tccaggct tctcaggtt

SEQ ID NO 539
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 539

tccaggct tctcaggtt

SEQ ID NO 540
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 540
tcagagctg tctagtctc 20

<210> SEQ ID NO 541
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc.feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 541
tcagtcagc gccagctcc 20

<210> SEQ ID NO 542
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc.feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 542
tcagttcct tcagcagctc 20

<210> SEQ ID NO 543
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc.feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 543
tcagttcag gcacagctcc 20

<210> SEQ ID NO 544
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc.feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 544
tcataagct ttctgtacgct 20

<210> SEQ ID NO 545
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc.feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 545
tcataagct ttctgtacgct 20
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<210> SEQ ID NO 546
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 546

tccataggct tcctagcgat
20

<210> SEQ ID NO 547
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 547

tccataggcg ttcctagcggt
20

<210> SEQ ID NO 548
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 549

tccataggct ttcctagcggt
20

<210> SEQ ID NO 549
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 549

tccataggct ttcctagcggt
20

<210> SEQ ID NO 550
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 550

tccatcagct gccgagct
20

<210> SEQ ID NO 551
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 551

tccatgacct tcctgacgct

<210> SEQ ID NO: 552
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 552

tccatgacgg tcctgacgct

<210> SEQ ID NO: 553
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 553

tccatgacgg tcctgacgct

<210> SEQ ID NO: 554
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 554

tccatgacgg tcctgagctct

<210> SEQ ID NO: 555
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 555

tccatgacgg tcctgagtct

<210> SEQ ID NO: 556
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 556
tcatgacgt cctgatgct 20

SEQ ID NO 557
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 557
tcatgacgt cctgatgct 20

SEQ ID NO 559
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 559
tcatgacgt tcctagttct tcatgacgt tcctc 45

SEQ ID NO 560
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 560
tcatgacgt tcctaggtct 20

SEQ ID NO 561
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
<400> SEQUENCE: 561

tccatgacgt tcctgacggt 20

<210> SEQ ID NO 562
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 562

tccatgacgt tcctgacggt 20

<210> SEQ ID NO 563
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 563

tccatgacgt tcctgacggt 20

<210> SEQ ID NO 564
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 564

tccatgacgt tcctgagct 20

<210> SEQ ID NO 565
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 565

tccatgacgt tccgtgatcc 19

<210> SEQ ID NO 566
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 566

tccatgacgt tcctgagct 20
<210> SEQ ID NO 567
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<400> SEQUENCE: 567
tccatgacgt toctgagct

<210> SEQ ID NO 568
<211> LENGTH: 29
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<400> SEQUENCE: 568
tccatgacgt toctgagctt cctgagctt

<210> SEQ ID NO 569
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<400> SEQUENCE: 569
tccatgacgt toctgacgtt

<210> SEQ ID NO 570
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<400> SEQUENCE: 570
tccatgacgt toctgcgctt

<210> SEQ ID NO 571
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<400> SEQUENCE: 571
tccatgacgt toctgacggg

<210> SEQ ID NO 572
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (13)...(13)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 572

tccatgagct tcctgagcgt 20

<210> SEQ ID NO 573
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 573

tccatgagct tcctgagcgt 20

<210> SEQ ID NO 574
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 574

tccatgagct tcctgagcgt 20

<210> SEQ ID NO 575
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: p-ethoxy backbone

<400> SEQUENCE: 575

tccatgagct tcctgagcgt 20

<210> SEQ ID NO 576
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 576

tccatgagct tcctgagcgt 20

<210> SEQ ID NO 577
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 577

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tccatgagt tcttgagct
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20

<210> SEQ ID NO 578
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 578

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tccatgagt tcttgagct t
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21

<210> SEQ ID NO 579
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: I

<400> SEQUENCE: 579

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tccatgagt tcttgagtt
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20

<210> SEQ ID NO 580
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 580

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tccatgagt tctagtct
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20

<210> SEQ ID NO 581
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 581

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tccatgagt tctagtct
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20

<210> SEQ ID NO 582
<211> LENGTH: 20
<212> TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
- OTHER INFORMATION: Synthetic oligonucleotide
- NAME/KEY: misc_feature
- LOCATION: (0)...(0)
- OTHER INFORMATION: phosphodiester backbone
- NAME/KEY: modified_base
- LOCATION: (8)...(8)
- OTHER INFORMATION: m5c

SEQUENCE: 582

tccatgangt tctgtagctg

SEQ ID NO 583
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
- OTHER INFORMATION: Synthetic oligonucleotide
- NAME/KEY: misc_feature
- LOCATION: (0)...(0)
- OTHER INFORMATION: phosphorothioate backbone
- NAME/KEY: modified_base
- LOCATION: (8)...(8)
- OTHER INFORMATION: m5c
- NAME/KEY: modified_base
- LOCATION: (17)...(17)
- OTHER INFORMATION: m5c

SEQUENCE: 583

tccatgangt tctgangtt

SEQ ID NO 584
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
- OTHER INFORMATION: Synthetic oligonucleotide
- NAME/KEY: misc_feature
- LOCATION: (0)...(0)
- OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 584

tccatgcgg tctgtagctg

SEQ ID NO 585
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
- OTHER INFORMATION: Synthetic oligonucleotide
- NAME/KEY: misc_feature
- LOCATION: (0)...(0)
- OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 585

tccatgcgg tctgtagctg

SEQ ID NO 586
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
- OTHER INFORMATION: Synthetic oligonucleotide
- NAME/KEY: misc_feature
- LOCATION: (0)...(0)
- OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 586
tcctgccccg tcctgccccgt

<210> SEQ ID NO 587
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 587

tcctgccccg tcctgccccgt

<210> SEQ ID NO 588
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 588

tcctgccccg tcctgccccgt

<210> SEQ ID NO 589
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 589

tcctgccccg tcctgccccgt

<210> SEQ ID NO 590
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 590

tcctgccccg gtgcgtttttt

<210> SEQ ID NO 591
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 591

tcctgccccg ggtgccccgt

<210> SEQ ID NO 592
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 592
tccatgcgtggtctgtgagtc

<210> SEQ ID NO 593
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 593
tccatgcgtggtctgtgagtc

<210> SEQ ID NO 594
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 594
tccatggcgggtcctgtgagtc

<210> SEQ ID NO 595
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 595
tccatggcgggtcctgtgagtc

<210> SEQ ID NO 596
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 596
tccatgtagtctgtgagtc

<210> SEQ ID NO 597
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 597

tccatgctc tccagtacct

SEQ ID NO 598
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 598

tccatgcta tccgagtacct

SEQ ID NO 599
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 599

tccatgctg tccagtacct

SEQ ID NO 600
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 600

tccatgtgctc tccagttacct

SEQ ID NO 601
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 601

tccatgtgcg tccgatgctc

SEQ ID NO 602
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ... (0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester
backbone with phosphoroxybate at 5' and 3' ends

<400> SEQUENCE: 602
tccatgctgg tctgagagct

<210> SEQ ID NO 603
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 603
tccatgctgg tctgagagct

<210> SEQ ID NO 604
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphoroxybate backbone

<400> SEQUENCE: 604
tccatgctgg tctgagagct

<210> SEQ ID NO 605
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 605
tccatgctgg tctgagagct

<210> SEQ ID NO 606
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (12) ... (12)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 606
tccatgctgg tctgagagct

<210> SEQ ID NO 607
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 607
tccatgctgg tctgagagct
tccatgtcgt tcgccgcccgt
<210> SEQ ID NO 608
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<400> SEQUENCE: 608

tccatgtcgt tcctagtcct
<210> SEQ ID NO 609
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends
<400> SEQUENCE: 609

tccatgtcgt tcctgatgcg
<210> SEQ ID NO 610
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 610

tccatgtcgt tcctgatgcg
<210> SEQ ID NO 611
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 611

tccatgtcgt tcctgatgcct
<210> SEQ ID NO 612
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 612

tccatgtcgt tcctgccgct
<210> SEQ ID NO 613
<211> LENGTH: 20
<212> TYPE: DNA
US 7,534,772 B2

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ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 613

tcctgctgt tcctgtagct

SEQ ID NO 614
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 614

tcctgctgt tcctgtcggt

SEQ ID NO 615
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 615

tcctgctgt tcctgtcggt

SEQ ID NO 616
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 616

tcctgctgt ttttgtcggt

SEQ ID NO 617
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 617

tcctgctgt tcctgtatgcgt

SEQ ID NO 618
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
<220> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5’ and 3’ ends
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 618

tccatgtnng tctgtgatct

<210> SEQ ID NO 619
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 619

tccatgtnng tctgtgatct

<210> SEQ ID NO 620
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 620

tccatgtnng tctgtgatct

<210> SEQ ID NO 621
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: m5c
<221> NAME/KEY: modified_base
<222> LOCATION: (17)...(17)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 621

tccatgtnng tctgtgnttt

<210> SEQ ID NO 622
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 622
tcattggt tcctggtt
  20

<210> SEQ ID NO 623
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 623
tccccgctgt gaagt
  15

<210> SEQ ID NO 624
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 624
tccccgctgt gaagt
  15

<210> SEQ ID NO 625
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 625
tccccgctgt tcctgctgtt
  20

<210> SEQ ID NO 626
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 626
tccccagac tgccccacct t
  21

<210> SEQ ID NO 627
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 627
tccgatcg
  8

<210> SEQ ID NO 628
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 628
tccggacggt gaagt

15

<210> SEQ ID NO 629
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 629
tccggccggtt gaagt

15

<210> SEQ ID NO 630
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 630
tccgtacg

8

<210> SEQ ID NO 631
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 631
tcctaacgtt gaagt

15

<210> SEQ ID NO 632
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 632
tcctagcggtt gaagt

15

<210> SEQ ID NO 633
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<211> NAME/KEY: misc_feature
<221> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 633

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tctacggt gaag  
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<211> SEQ ID NO: 634
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 634

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tctcga  
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<211> SEQ ID NO: 635
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 635

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tctgaaag gaag  
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<211> SEQ ID NO: 636
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 636

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tctgagct gaag  
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<211> SEQ ID NO: 637
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 637

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tctgagcgt gaag  
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<211> SEQ ID NO: 638
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 639

tctgacgagga

<210> SEQ ID NO 639
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 640

tctgacgagga

<210> SEQ ID NO 640
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 641

tctgacgagtga

<210> SEQ ID NO 641
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 642

tctgacgagtga

<210> SEQ ID NO 642
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 643

tctgacgagtga

<210> SEQ ID NO 643
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 644

tctgacgagtga
<210> SEQ ID NO 644
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 644

tcctgacgtc gaagt

<210> SEQ ID NO 645
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 645

tcctgacgtg gaagt

<210> SEQ ID NO 646
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 646

tcctgacgtg gaagt

<210> SEQ ID NO 647
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 647

tcctgacgtt aga

<210> SEQ ID NO 648
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 648

tcctgacgtt ccc

<210> SEQ ID NO 649
<211> LENGTH: 32
<212> TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 649

32

tctgacgtt ccctgaggg tccctgtcg ct

32

SEQ ID NO 650
LENGTH: 19
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 650

19

tctgacgtt
tctgacgtt

19

SEQ ID NO 651
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 651

20

tctgacggtt ctgaggg tcgcttgct

tctgaggtt ctgaggg tcgcttgct

20

SEQ ID NO 652
LENGTH: 15
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 652

15

tctgacggtt ctgtc

tctgacggtt ctgtc

15

SEQ ID NO 653
LENGTH: 22
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0) ...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 653

22

tctgacggtt cgccgcgcgc cc

tctgacggtt cgccgcgcgc cc

22

SEQ ID NO 654
LENGTH: 15
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
toctgaagtt gaagtt

<210> SEQ ID NO 655
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 655

toctgaagtt gaagtt

<210> SEQ ID NO 656
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 656

toctgaagtt gaagtt

<210> SEQ ID NO 657
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 657

toctgaagtt gaagtt

<210> SEQ ID NO 658
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (?)...(?)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 658

toctgaagtt gaagtt

<210> SEQ ID NO 659
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 659

tctgcggtt gaag 15

<210> SEQ ID NO 660
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 660

tctgcggtt gaag 15

<210> SEQ ID NO 661
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 661

tctggaggg gaag 15

<210> SEQ ID NO 662
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 662

tctggaggg gaag 15

<210> SEQ ID NO 663
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 663

tctggoggg gaag 15

<210> SEQ ID NO 664
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 664
tctggcggg 15

tctggcgtt 20

tctggcggg 15

tctggcgtt 15

tctggcgttg 15

tctggcgtt 15

tctggcgttg 15

tctggcgtt 15

<210> SEQ ID NO: 665
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 665

<210> SEQ ID NO: 666
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 666

<210> SEQ ID NO: 667
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 667

<210> SEQ ID NO: 668
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 668

<210> SEQ ID NO: 669
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 669
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 670

tctggcgtt gaagt 15

<210> SEQ ID NO 671
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 671

tcttggggg gaagt 15

<210> SEQ ID NO 672
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 672

tctgtgtgg gaagt 15

<210> SEQ ID NO 673
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 673

tctggnugg gaagt 15

<210> SEQ ID NO 674
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 674

tcctgtcgct cctgtcgct 19

<210> SEQ ID NO 675
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 675

tcctgtgctc cctgtgctc 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 675

tctgtcgct cctgctgctc ctgctgct

28

<210> SEQ ID NO 676
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 676

tctgtcgctt cctgctgct

19

<210> SEQ ID NO 677
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 677

tctgtcgctt cctgctgctg ascgscagg

30

<210> SEQ ID NO 678
<211> LENGTH: 40
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 678

tctgtcgctt cctgctgcttt ascgscagg ascgscagg

40

<210> SEQ ID NO 679
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 679

tctgtcgctt cctgctgctt

20

<210> SEQ ID NO 680
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<400> SEQUENCE: 685
tgacgctc 8

<210> SEQ ID NO 686
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 686
tgacgctc cccccccccccc 20

<210> SEQ ID NO 687
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 687
tgagaacatt gcacaatcat ctg 23

<210> SEQ ID NO 688
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 689
tgacgcttc cccccccccccc 20

<210> SEQ ID NO 689
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 689
tgacgctgcg tttgtgcttt tgcgctt 27

<210> SEQ ID NO 690
<211> LENGTH: 5
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 690
tgcs

tgsga 5
<210> SEQ ID NO 691
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 691

tcggcgttcc ccccccoccc

<210> SEQ ID NO 692
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_difference
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 692

tcgtag

<210> SEQ ID NO 693
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 693

tcgctca

<210> SEQ ID NO 694
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 694

tcgtcatctcc ccccccocccccc

<210> SEQ ID NO 695
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 695

tcgtgatcc ccccccocccccc

<210> SEQ ID NO 696
<211> LENGTH: 20
<212> TYPE: DNA

ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 696

tgctgtgct cccc cccc

SEQ ID NO 697
LENGTH: 15
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 697
tgctgtgct ctcgg

SEQ ID NO 698
LENGTH: 21
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: phosphorothioate backbone with phosphodiester on 3' end

SEQUENCE: 698
tgctgtgct ctcgctctc t

SEQ ID NO 699
LENGTH: 21
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 3' end

SEQUENCE: 699
tgctgtgct ctcgctctc t

SEQ ID NO 700
LENGTH: 21
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 3' end

SEQUENCE: 700
tgctgtgct ctcgctctc t

SEQ ID NO 701
LENGTH: 27
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 701
tgctgcgtgc tctgcttctcttgcct  27

SEQ ID NO 702
LENGTH: 21
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 702
tgctgcgtgc tgcctctctc t  21

SEQ ID NO 703
LENGTH: 21
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 703
tgctgcgtgc tgtgctttctct  21

SEQ ID NO 704
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 704
tgctgcgtgc ccccccccc  20

SEQ ID NO 705
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 705
tgctgcgtgc tgtgcttctgc  20

SEQ ID NO 706
LENGTH: 23
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQ: 706

tgctgcgt gctgcgtgc gtt

SEQ: 707

tgctgcgt gcttt

SEQ: 708

tgctgcgt gcttt

SEQ: 709

tgctgcgt gcttt

SEQ: 710

tgctgcgt gcttt

SEQ: 711

tgctgcgt gcttt
<400> SEQUENCE: 711

tgcgtctcc cccccc

17

<210> SEQ ID NO 712
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 712

tgcgtctcc cccccc

20

<210> SEQ ID NO 713
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (20)...(20)
<223> OTHER INFORMATION: biotinylated at 3' end

<400> SEQUENCE: 713

tgcgtctcc cccccc

20

<210> SEQ ID NO 714
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (16)...(16)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 714

tgcgtctcc cccccc

20

<210> SEQ ID NO 715
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 715

tgcgtctgg tgtcgttgtgt tgtcgt

26

<210> SEQ ID NO 716
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 716

tg tgt gttg tgtg tgtttt gtt

SEQ ID NO 717
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 717

tg tgtg tgtg tgtg tgtg tgtg tgtg tgtg

SEQ ID NO 718
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 718

tg tgtg tgtg tgtg tgtg tgtg tgtg tgtg

SEQ ID NO 719
LENGTH: 22
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 719

tg tgtg tgtg cgtg tgtg tgtg tgtg tt

SEQ ID NO 720
LENGTH: 22
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 720

tg tgtg tgtg cgtg tgtg tgtg tgtg tt

SEQ ID NO 721
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone
SEQUENCE: 721

tg.tcgtt
tcg.tgttga cg tt

SEQUENCE: 722

tcg.tcgtt
tcg.tgttga cg tt

SEQUENCE: 723

tcg.tcgtt
tg.ttttcgt tt

SEQUENCE: 724

tcg.tcgttt
gtcg.tgttga cg tt

SEQUENCE: 725

tcg.tcgttt
gtcg.tgttga cg tt

SEQUENCE: 726

tcg.tcgttt
gtcg.togttt
SEQ ID NO 727
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
SEQUENCE: 727
tgctgtttttgtcgttttgg gggg

SEQ ID NO 728
LENGTH: 23
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)....(0)
OTHER INFORMATION: phosphorodithioate backbone
SEQUENCE: 729
tgctgtttttgtcgttttctg

SEQ ID NO 729
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)....(0)
OTHER INFORMATION: phosphorothioate backbone
SEQUENCE: 729
tgctgtttttgtcgttttctg

SEQ ID NO 730
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)....(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends
SEQUENCE: 730
tgctgtttttgtcgttttctg

SEQ ID NO 731
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)....(0)
OTHER INFORMATION: phosphodiester backbone
SEQUENCE: 731
tgctgtttttgtcgttttctg

SEQ ID NO 732
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 732

tgctgctttt gcgttttttg ccgt 24

<210> SEQ ID NO 733
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: misc_feature
<222> LOCATION: (24)...(24)
<223> OTHER INFORMATION: biotinylated at 3' end

<400> SEQUENCE: 733

tgctgctttt gcgttttttg ccgt 24

<210> SEQ ID NO 734
<211> LENGTH: 32
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 734

tgctgctttt gcgttttttg ccgtttttttc gtt 32

<210> SEQ ID NO 735
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 735

tgctgctttt gcgttttttg ccgt 24

<210> SEQ ID NO 736
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 736

tgctgctttt tgctgtttttg ccgt 28

<210> SEQ ID NO 737
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 737

tcgtgtttttttttttttttttttttttttt

<210> SEQ ID NO 738
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 738

tcgtga

<210> SEQ ID NO 739
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 739

tcgtga

<210> SEQ ID NO 740
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 740

tcgtgg

<210> SEQ ID NO 741
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 741

tcngntcccccccccc

<210> SEQ ID NO 742
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 742

tctgcttt tctgntntnt cgtm 24

<210> SEQ ID NO 743
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 743

tcttaaaacc atctatttc aacctt 26

<210> SEQ ID NO 744
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester
backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 744

tctacgcct ttagcttccc 20

<210> SEQ ID NO 745
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 745

tcatccccag gtgttctctg ttac 24

<210> SEQ ID NO 746
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 746

tctatgacg ttcasagcaag 20

<210> SEQ ID NO 747
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 747

tctccatct atggttttat cg
  22

<210> SEQ ID NO 748
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 749

tctccatgat ggttttatcg
  20

<210> SEQ ID NO 749
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 749

<210> SEQ ID NO 750
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 750

<210> SEQ ID NO 750
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 751

<210> SEQ ID NO 751
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 752

tctccagcg agcgcgc
  18

<210> SEQ ID NO 752
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 752

<210> SEQ ID NO 753
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<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 753

``tcctccacoctagccat 18``

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<210> SEQ ID NO 754
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 754

``tcctccacoctcgcct 17``

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<210> SEQ ID NO 755
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 755

``tcctccacoctgcccatt 18``

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<210> SEQ ID NO 756
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 756

``tcctccacoctgcccatt 18``

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<210> SEQ ID NO 757
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 757

``tcctccacoctgcccatt 20``

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<210> SEQ ID NO 758
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0) ...(0)

OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 758

tccgccagc tgccgctttt

20

SEQ ID NO 759

LENGTH: 22

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0) ...(0)

OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 759

tccgccagc tgccgctttt at

22

SEQ ID NO 760

LENGTH: 20

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0) ...(0)

OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 760

tccgccagc tgccgtat at

20

SEQ ID NO 761

LENGTH: 18

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0) ...(0)

OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 761

tccgccagc tgccgtttt

18

SEQ ID NO 762

LENGTH: 21

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:

OTHER INFORMATION: Synthetic oligonucleotide

NAME/KEY: misc_feature

LOCATION: (0) ...(0)

OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 762

tccgccagc tgccgctttt at

21

SEQ ID NO 763

LENGTH: 17

TYPE: DNA

ORGANISM: Artificial Sequence

FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 763
tctccccatg tgcccat

SEQ ID NO: 764
LENGTH: 18
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 764
tctcccgacg tgccgcat

SEQ ID NO: 765
LENGTH: 18
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 765
tctcccgctg tgccgcat

SEQ ID NO: 766
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 766
tctcctgctg tgccgcatat

SEQ ID NO: 767
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

SEQUENCE: 767
tctctctcg gtcgcccatat

SEQ ID NO: 769
LENGTH: 30
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
tctgagctga tctgagcttg gctgaagctt
  30
<210> SEQ ID NO 769
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends
<400> SEQUENCE: 769

30

<210> SEQ ID NO 770
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 770

tcttcgaa

<210> SEQ ID NO 771
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 771

tctggcgatg ctaaagggcgc tcaacttgca caatttaaat aaggt

<210> SEQ ID NO 772
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<400> SEQUENCE: 772

tctttatatag tgaacctgcac cttggca

<210> SEQ ID NO 773
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified.base
LOCATION: (3)...(3)
OTHER INFORMATION: m5c

SEQUENCE: 773

tontgaagtt gaagtt 15

SEQ ID NO 774
LENGTH: 8
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 774
tgaaagtt 8

SEQ ID NO 775
LENGTH: 23
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 775
tgcaatgta ogtcttttag cat 23

SEQ ID NO 776
LENGTH: 31
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 776
tgcaggaagt cogggttttc cccaaccccc c 31

SEQ ID NO 777
LENGTH: 12
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 777
tgcatacgct ct 12

SEQ ID NO 778
LENGTH: 12
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends
<400> SEQUENCE: 779

tgcatacagtcct 12

<210> SEQ ID NO 779
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 779

tgcataccccc agccaccat 20

<210> SEQ ID NO 780
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 780

tgcatgcccc gtacagtcctct 20

<210> SEQ ID NO 781
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 781

tgcatgcccc gtacagtcctct 20

<210> SEQ ID NO 782
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 782

tgcatgcccc gtacagtcctct 20

<210> SEQ ID NO 783
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 783

tgcatgcgggg gcacggtac acagtcctct 28
<210> SEQ ID NO 784
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<240> SEQUENCE: 784
tgccaagtc gcagtcacta ataaaga 27

<210> SEQ ID NO 785
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<240> SEQUENCE: 785
tgccaagaag gaaaaatttg ttccatacag 30

<210> SEQ ID NO 786
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<240> SEQUENCE: 786
tgcgccctc 8

<210> SEQ ID NO 787
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<240> SEQUENCE: 787
tgtgactgt gctgtactc 20

<210> SEQ ID NO 788
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<240> SEQUENCE: 788
tgtgactgt gctgtactc 20

<210> SEQ ID NO 789
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 789
tgtgcttcc ccccccoccc

SEQ ID NO 790
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 790
tgtgcttcc ccccccoccc

SEQ ID NO 791
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 791
tgtgcttttt tgtccttttt tgtt

SEQ ID NO 792
LENGTH: 24
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 792
tgtgcttttt tgtccttttt tgtt

SEQ ID NO 793
LENGTH: 12
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 793
tggaccttcc at

SEQ ID NO 794
LENGTH: 20
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 794
tggaccttct atgtgcttcc
<210> SEQ ID NO 795
<211> LENGTH: 43
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 795
tgagggtga gggtgagggcc agagccgggtg gggtgattg gas

<210> SEQ ID NO 796
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 796
tgagggtccc accgagatcg gag

<210> SEQ ID NO 797
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 797
tggtaaggt ctgtcccctgt

<210> SEQ ID NO 798
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 798
tgatatctctc tgaaggaact

<210> SEQ ID NO 799
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 799
tgctcagccg aggggaccat

<210> SEQ ID NO 800
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 800
tgctccatgt ttttagaagc
<210> SEQ ID NO 801
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 801

tgcggtggtc gtt

13

<210> SEQ ID NO 802
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 802

tgcggtggtc gttgctgtg tgcgt

25

<210> SEQ ID NO 803
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 803

tgcggtggtg cgttgtgcgt t

21

<210> SEQ ID NO 804
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 804

ttaacggttg taccgcgtatt gtc

24

<210> SEQ ID NO 805
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 805

ttaacggtt

8

<210> SEQ ID NO 806
<211> LENGTH: 24
SEQUENCE: 806

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ttasgacaa attcgcataacc accg
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SEQUENCE: 807

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ttaggacag gcctaggggtg
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SEQUENCE: 808

```
ttagggttag ggttaggggt
```

SEQUENCE: 809

```
ttcagttgtc tgtggtgtaa gctaa
```

SEQUENCE: 810

```
ttcatgtcct gcacagttgcc g
```

SEQUENCE: 811

```
ttcagttgtc tgtggtgtaa gctaa
```

SEQUENCE: 811
ttccatcag cccccaccgc tctggcgcce a cctctaccct ccs

<210> SEQ ID NO 812
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 812

tttcatgtcg ttcggtctgg

<210> SEQ ID NO 813
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphothioate/phosphodiester backbone at 5' and 3' ends

<400> SEQUENCE: 813

tttcatgtcg gttcctgtg

<210> SEQ ID NO 814
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 814

tttcgccgaa tggcctcaggtggtac

<210> SEQ ID NO 815
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 815

tttcgcttta tctgagace ctct

<210> SEQ ID NO 816
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 816

tttcctctctg cagagact

<210> SEQ ID NO 817
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphothioate/phosphodiester
backbone with phosphorothonlate at 5’ and 3’ ends

<400> SEQUENCE: 817

ttcggccgga ctcttcccatt

<210> SEQ ID NO 818
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 818

ttcggccgga ctcttcccatt

<210> SEQ ID NO 819
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothonlate backbone

<400> SEQUENCE: 819

ttcgtcgttt tgtcgttttg tcgtt

<210> SEQ ID NO 820
<211> LENGTH: 37
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 820

ttcgttgtct gtgtgcgttgt cctgcttattc tgagaac

<210> SEQ ID NO 821
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 821

ttgaacgtga ggtgggac

<210> SEQ ID NO 822
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 822

ttgccccata tttagaaaac

<210> SEQ ID NO 823
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphorothioate backbone

SEQUENCE: 823

ttgccccccc 

SEQ ID NO: 924
LENGTH: 12
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide

SEQUENCE: 924

ttgactctc cagatggttt

SEQ ID NO: 825
LENGTH: 30
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 825

tttacctttt ataacaataa ctaaaacaa

SEQ ID NO: 826
LENGTH: 27
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 826

tttgaatcct cagcggactc cagtggc

SEQ ID NO: 827
LENGTH: 27
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 827

tttgaatcra ggactggcta ggttgag

SEQ ID NO: 828
LENGTH: 29
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Synthetic oligonucleotide
NAME/KEY: misc_feature
LOCATION: (0)...(0)
OTHER INFORMATION: phosphodiester backbone

SEQUENCE: 828

tttgaatcct ggtacagaa gcgagaagc
<210> SEQ ID NO 829
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphorothioate at 5' and 3' ends

<400> SEQUENCE: 829

tttgagaacg ctgacacccc

<210> SEQ ID NO 830
<211> LENGTH: 31
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 830

tttgogccccg ttaggacttas ccctgagagat a

<210> SEQ ID NO 831
<211> LENGTH: 29
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 831

tttgogccca ccgagacag agacactcc

<210> SEQ ID NO 832
<211> LENGTH: 29
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 832

tttgogcccg cttctcggtt ctgtacacg

<210> SEQ ID NO 833
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 833

ttttctagag aagtcgcaaa taagcttgg

<210> SEQ ID NO 834
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 934

tttttgaggg ggggtttttt

<210> SEQ ID NO 935
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 935

ttttttttttttt

<210> SEQ ID NO 936
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: chimeric phosphorothioate/phosphodiester backbone with phosphodiester on 3' end
<221> NAME/KEY: misc_difference
<222> LOCATION: (13) ... (13)
<223> OTHER INFORMATION: FITC labeled

<400> SEQUENCE: 936

ttttttttttttt

<210> SEQ ID NO 937
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 937

ttttttttttttttttt

<210> SEQ ID NO 938
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0) ... (0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 938

tttttttttttttttttttttttttttt
<210> SEQ ID NO 839
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone

<400> SEQUENCE: 839

tttttttttt ttttttttttt ttttttttttt ttttttttttt ttttttttttt ttttttttttt

20

<210> SEQ ID NO 840
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 840

tttttttttt ttttttttttt t ttttttttttt

21

<210> SEQ ID NO 841
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 841

tttttttttt ttttttttttt ttttttttttt

24

<210> SEQ ID NO 842
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphorothioate backbone

<400> SEQUENCE: 842

tttttttttt ttttttttttt ttttttttttt ttttttttttt ttttttttttt ttttttttttt

27

<210> SEQ ID NO 843
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 843

tnaacgtt

8
<210> SEQ ID NO 844
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 844

cgtctgctcc cccccccccc

<210> SEQ ID NO 845
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 845

gcgtctgcttt gcgtctgctt gcgt
cgtt

<210> SEQ ID NO 846
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 846

<210> SEQ ID NO 847
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: phosphodiester backbone
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c
<221> NAME/KEY: modified_base
<222> LOCATION: (13)...(13)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 847
We claim:
1. A method for treating a subject having a B-cell malignancy resistant to therapy with an antibody specific for a surface antigen selected from CD19, CD20, and CD22, wherein cells of the malignancy have low or no baseline expression of the surface antigen, the method comprising:
   administering to the subject the immunostimulatory CpG oligonucleotide ODN 2006 (SEQ ID NO:729) comprising a backbone modification and an unmethylated C, in an effective amount to upregulate expression of the antigen by the cells of the lymphoma or leukemia; and
   administering to the subject an antibody specific for the upregulated antigen, in an effective amount to treat the subject.

2. A method for treating a subject having a B-cell malignancy, wherein cells of the B-cell malignancy have low or no baseline expression of CD20, the method comprising:
   administering to the subject the immunostimulatory CpG oligonucleotide ODN 2006 (SEQ ID NO:729) comprising a backbone modification and an unmethylated C, in an effective amount to upregulate expression of CD20 by the cells; and
   administering to the subject an antibody specific for CD20, in an effective amount to treat the subject.

3. A method for treating a subject having a marginal zone lymphoma or B-cell chronic lymphocytic leukemia, wherein cells of the lymphoma or leukemia have low or no baseline expression of an antigen selected from CD19 and CD22, the method comprising:
   administering to the subject the immunostimulatory CpG oligonucleotide ODN 2006 (SEQ ID NO:729) comprising a backbone modification and an unmethylated C, in an effective amount to upregulate expression of the surface antigen by the cells; and
   administering to the subject an antibody specific for the upregulated surface antigen, in an amount effective to treat the subject.

   * * * * *