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(54) **IMMUNOSTIMULATORY NUCLEIC ACIDS FOR THE TREATMENT OF ASTHMA AND ALLERGY**

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(57) **ABSTRACT**

The invention involves administration of an immunostimulatory nucleic acid alone or in combination with an asthma/allergy medicament for the treatment or prevention of asthma and allergy in subjects. The combination of drugs are administered in synergistic amounts or in various dosages or at various time schedules. The invention also relates to kits and compositions concerning the combination of drugs.

IMMUNOSTIMULATORY NUCLEIC ACIDS FOR THE TREATMENT OF ASTHMA AND ALLERGY

PRIORITY OF THE INVENTION

[0001] This application claims priority under Title 35 §119(e), of U.S. Provisional Application No. 60/179,991, filed Feb. 3, 2000, entitled IMMUNOSTIMULATORY NUCLEIC ACIDS FOR THE TREATMENT OF ASTHMA AND ALLERGY, the entire contents of which are incorporated herein by reference.

BACKGROUND OF THE INVENTION

[0002] Asthma is a chronic inflammatory disease effecting 14-15 million persons in the U.S. alone. Symptoms of asthma include recurrent episodes of wheezing, breathlessness, and chest tightness, and coughing, resulting from airflow obstruction. Airway inflammation associated with asthma can be detected through observation of a number of physiological changes, such as, denudation of airway epithelium, collagen deposition beneath basement membrane, edema, mast cell activation, inflammatory cell infiltration, including neutrophils, eosinophils, and lymphocytes. As a result of the airway inflammation, asthma patients often experience airway hyper-responsiveness, airflow limitation, respiratory symptoms, and disease chronicity. Airflow limitations include acute bronchoconstriction, airway edema, mucous plug formation, and airway remodeling, features which often lead to bronchial obstruction. In some cases of asthma, subbasement membrane fibrosis may occur, leading to persistent abnormalities in lung function.

[0003] Research over the past several years has revealed that asthma likely results from complex interactions among inflammatory cells, mediators, and other cells and tissues resident in the airway. Mast cells, eosinophils, epithelial cells, macrophage, and activated T-cells all play an important role in the inflammatory process associated with asthma (Djukanovic et al., *Am. Rev. Respir. Dis;* 142:434-457; 1990). It is believed that these cells can influence airway function through secretion of preformed and newly synthesized mediators which can act directly or indirectly on the local tissue. It has also been recognized that subpopulations of T-lymphocytes (TH-2) play an important role in regulating allergic inflammation in the airway by releasing selective cytokines and establishing disease chronicity (Robinson, et al. *N. Engl. J. Med.;* 326:298-304; 1992).

[0004] Asthma is a complex disorder which arises at different stages in development and can be classified based on the degree of symptoms of acute, subacute or chronic. An acute inflammatory response is associated with an early recruitment of cells into the airway. The subacute inflammatory response involves the recruitment of cells as well as the activation of resident cells causing a more persistent pattern of inflammation. Chronic inflammatory response is characterized by a persistent level of cell damage and an ongoing repair process, which may result in permanent abnormalities in the airway.

[0005] Medications for the treatment of asthma are generally separated into two categories, quick-relief medications and long-term control medications. Asthma patients take the long-term control medications on a daily basis to achieve and maintain control of persistent asthma. Long-term control medications include anti-inflammatory agents such as corticosteroids, chromolyn sodium and medacromil; long-acting bronchodilators, such as long-acting β_2-agonists and methylxanthines; and leukotriene modifiers. The quick-relief medications include short-acting β_2 agonists, anticholinergics, and systemic corticosteroids. There are many side effects associated with each of these drugs and none of the drugs alone or in combination is capable of preventing or completely treating asthma.

[0006] Allergy is a disease associated with the production of antibodies from a particular class of immunoglobulin, IgE, against allergens. The development of an IgE-mediated response to common aeroallergens is also a factor which indicates predisposition towards the development of asthma. If an allergen encounters a specific IgE which is bound to an Fc IgE receptor on the surface of a basophil (circulating in the blood) or mast cell (dispersed throughout solid tissue), the cell becomes activated, resulting in the production and release of mediators such as histamine, scrotonin, and lipid mediators. Allergic diseases include but are not limited to rhinitis (hay fever) asthma, urticaria and atopic dermatitis.

[0007] Conventional methods for treating or preventing allergy have involved the use of anti-histamines or desensitization therapies. Anti-histamines and other drugs which block the effects of chemical mediators of the allergic reaction help to regulate the severity of the allergic symptoms but do not prevent the allergic reaction and have no effect on subsequent allergic responses. Desensitization therapies are performed by giving small doses of an allergen, usually by injection under the skin, in order to induce an IgG-type response against the allergen. The presence of IgG antibody helps to neutralize the production of mediators resulting from the induction of IgE antibodies, it is believed. Initially, the subject is treated with a very low dose of the allergen to avoid inducing a severe reaction and the dose is slowly increased. This type of therapy is dangerous because the subject is actually administered the compounds which cause the allergic response and severe allergic reactions can result.

SUMMARY OF THE INVENTION

[0008] Improved methods and products for the prevention and/or treatment of asthma and allergy are provided according to the invention. The invention is based, in some aspects, on the finding that when immunostimulatory nucleic acid molecules are used in conjunction with medicaments for the treatment of asthma and allergy, some unexpected and improved results are observed. For instance, the efficacy of the combination of immunostimulatory nucleic acids and asthma and allergy medicaments is profoundly improved over the use of each of the medicaments alone. The results are surprising in part because the drugs act through different mechanisms and would not necessarily be expected to improve the efficacy of one another in a synergistic manner.

[0009] In some aspects, the invention is a method for preventing or treating asthma or allergy by administering a synergistic combination of an immunostimulatory nucleic acid and an asthma/allergy medicament, wherein the combination is administered in an effective amount for synergistically reducing the immune or inflammatory response caused by a mediator of asthma or allergy. It was surprisingly discovered according to the invention that the combination of the immunostimulatory nucleic acid and the

asthma/allergy medicament worked synergistically to reduce the immune or inflammatory response initiated when a mediator of asthma or allergy is encountered.

[0010] In other aspects, the invention is a method for altering the dosage of the asthma/allergy medicament that is required to treat a subject suffering from asthma or allergy. The invention in one aspect is a method for increasing the dose of an asthma/allergy medicament without inducing the level of side effects ordinarily observed with that dose of an asthma/allergy medicament. The method is accomplished by administering to a subject suffering from asthma or allergy or at risk of developing asthma or allergy, an asthma/allergy medicament in a dose which would ordinarily induce side effects, administering an immunostimulatory nucleic acid to the subject, wherein administration of the immunostimulatory nucleic acid prevents the side effects associated with the high dose of the asthma/allergy medicament. The method provides a basis for administering higher therapeutic doses of an asthma/allergy medicament to a subject in order to prevent or reduce the symptoms associated with an asthmatic or an allergic response more sufficiently than a lower dose. It is not desirable to administer such high doses alone, in the absence of the immunostimulatory nucleic acid, because of the side effects resulting from the high dose.

[0011] In another aspect, the invention includes a method for decreasing the dose of an asthma/allergy medicament by administering to a subject having asthma or allergy or at risk of developing asthma or allergy an asthma/allergy medicament in a sub-therapeutic dosage and an immunostimulatory nucleic acid, wherein the combination of the sub-therapeutic dose of the asthma/allergy medicament and the immunostimulatory nucleic acid produce a therapeutic result in the prevention or treatment of asthma or allergy in the subject. The method allows a lower dose of the asthma/allergy medicament to be used. This provides several advantages, including lower costs associated with using less drugs and less chances of inducing side effects resulting from the medications by using lower doses.

[0012] According to other aspects, the invention involves methods for treating or preventing asthma and/or allergy by administering an immunostimulatory nucleic acid and an asthma/allergy medicament in different dosing schedules. In one aspect, the invention is a method for preventing or treating asthma or allergy by administering to a subject an effective amount of an immunostimulatory nucleic acid in an effective amount for producing the immune response and subsequently administering to the subject an asthma/allergy medicament. In other aspects, the invention is a method for preventing or treating asthma or allergy by administering to a subject an allergy/asthma medicament in an effective amount for providing some symptomatic relief and subsequently administering an immunostimulatory nucleic acid to the subject. In some embodiments, the immunostimulatory nucleic acid is administered in an effective amount for redirecting the immune response from a Th2 to a Th1 immune response. In some embodiments, the immunostimulatory nucleic acid is administered consistently over a period of time, such as, for instance, in a sustained release vehicle.

[0013] In another aspect of the invention is a method for treating asthma or allergy by administering to a subject having asthma or allergy or at risk of developing asthma or allergy an immunostimulatory nucleic acid and an asthma/allergy medicament, wherein the immunostimulatory nucleic acid is administered systemically and the asthma/allergy medicament is administered locally. In yet another aspect, the immunostimulatory nucleic acid is administered locally and the asthma/allergy medicament is administered systemically.

[0014] According to yet another aspect of the invention, a method for treating or preventing asthma/allergy is provided. The method is accomplished by administering to a subject having asthma or allergy or at risk of developing asthma or allergy, an immunostimulatory nucleic acid and an asthma/allergy medicament on a routine schedule. In some embodiments, the routine schedule is a daily, weekly, monthly, or quarterly administration of the medicaments. In other embodiments, the immunostimulatory nucleic acid and/or the asthma/allergy medicament is administered in two or more doses.

[0015] The immunostimulatory nucleic acid can be administered on a recurring basis, such as daily, weekly, or monthly in one or more doses. Alternatively, it can be administered on a non-regular basis e.g. whenever symptoms being. In yet other embodiments, the asthma/allergy medicament is a quick relief asthma/allergy medicament and in other embodiments it is a long-lasting asthma/allergy medicament.

[0016] According to yet another aspect of the invention, methods for treating or preventing asthma or allergy using specific immunostimulatory nucleic acid molecules are provided. The method in one aspect involves a method for preventing or treating asthma or allergy by administering to a subject suffering from asthma or allergy or at risk of developing asthma or allergy, an immunostimulatory nucleic acid having a sequence selected from the group consisting of SEQ ID NO:1 through to SEQ ID NO:1093 and administering to the subject an asthma/allergy medicament.

[0017] In yet another aspect of the invention, a method for preventing or treating asthma or allergy utilizing different routes of administration is provided. In one aspect, the method involves the step of administering to a subject having asthma or allergy or at risk of developing asthma or allergy, an immunostimulatory nucleic acid, wherein the immunostimulatory is administered systemically and wherein the asthma/allergy medicament is administered locally. In a related embodiment, the immunostimulatory nucleic acid molecule may be administered locally and the asthma/allergy medicament is administered systemically. In still other embodiments, the immunostimulatory nucleic acid and the asthma/allergy medicament are administered by the same route (i.e., both delivered locally or both delivered systemically), and optionally at the same time.

[0018] The invention according to another aspect is a method of preventing or treating asthma or allergy by administering a poly-G nucleic acid, in an effective amount for treating or preventing asthma or allergy. In some embodiments the poly-G nucleic acid is administered alone and in other embodiments the poly-G nucleic acid is administered in conjunction with an asthma/allergy medicament. The poly-G nucleic acid in preferred embodiments comprises one of the following formulas: 5'$X_1X_2GGGX_3X_4$ 3', wherein X_1, X_2, X_3, and X_4 are nucleotides, 5' GGGNGGG 3' or 5' GGGNGGGNGGG 3', wherein N represents between 0 and 20 nucleotides. In some embodiments at least one of

X_3 and X_4 are a G and in other embodiments both of X_3 and X_4 are a G. Accordingly, in some embodiments, the poly-G nucleic acid may comprise a sequence of 5' $X_1X_2GGGGX_4$ 3'. In still other embodiments, the poly-G nucleic acid is one which is rich in G (e.g., six out of seven bases are G, or six out of eight bases are G).

[0019] The poly-G may be free of unmethylated CG dinucleotides, or may include at least one unmethylated CG dinucleotide.

[0020] The poly G nucleic acid in some embodiments is selected from the group consisting of SEQ ID NO: 5, 6, 73, 215, 267-269, 276, 282, 288, 297-299, 355, 359, 386, 387, 444, 476, 531, 557-559, 733, 768, 795, 796, 914-925, 928-931, 933-936, and 938. In other embodiments the poly G nucleic acid includes a sequence selected from the group consisting of SEQ ID NO: 67, 80-82, 141, 147, 148, 173, 178, 183, 185, 214, 224, 264, 265, 315, 329, 434, 435, 475, 519, 521-524, 526, 527, 535, 554, 565, 609, 628, 660, 661, 662, 725, 767, 825, 856, 857, 876, 892, 909, 926, 927, 932, and 937.

[0021] The invention provides, in yet another aspect, a method for treating or preventing asthma or allergy in a hypo-responsive subject. The method involves administering to a hypo-responsive subject having asthma or allergy or at risk of developing asthma or allergy an immunostimulatory nucleic acid. In one embodiment, the method further comprises administering to the hypo-responsive subject an asthma/allergy medicament. If the asthma/allergy medicament is not administered to the hypo-responsive subject, then the immunostimulatory nucleic acid is administered in an amount to treat or prevent the asthma or allergy. If the asthma/allergy medicament is administered to the hypo-responsive subject, then the immunostimulatory nucleic acid and the asthma/allergy medicament are administered in an effective amount to treat or prevent the asthma or allergy. In this latter instance, the amount of the immunostimulatory nucleic acid and the amount of the asthma/allergy medicament may be insufficient (i.e., ineffective) in treating or preventing the asthma or allergy if administered alone. In other words, in some embodiments, the immunostimulatory nucleic acid may be administered to the hypo-responsive subject in a sub-therapeutic amount. Similarly, the asthma/allergy medicament may also be administered in a sub-therapeutic amount. However, the combination of the immunostimulatory nucleic acid and the asthma/allergy medicament allows for lower doses of one or both in order to treat or prevent the asthma or allergy. The immunostimulatory nucleic acid may be administered concurrently with the asthma/allergy medicament, but need not be.

[0022] The hypo-responsive subject may be one who is hypo-responsive to an asthma/allergy medicament. In one embodiment, the hypo-responsive subject is selected from the group consisting of a subject who is refractory to an asthma/allergy medicament, a subject who is a non-responder to an asthma/allergy medicament, an elderly subject and a neonatal subject.

[0023] According to yet another aspect of the invention, a method is provided for preventing asthma or allergy in a subject at risk of developing asthma or allergy which involves administering to a subject at risk of developing asthma or allergy an effective amount of an immunostimulatory nucleic acid substantially prior to an asthmatic or an allergic event.

[0024] In one embodiment, the immunostimulatory nucleic acid is administered at least three months, at least two months, at least one month, or at least 20 days prior to the asthmatic or allergic event. In another embodiment, the immunostimulatory nucleic acid is administered at least two weeks prior to the asthmatic or allergic event. In yet another embodiment, the immunostimulatory nucleic acid is administered at least 10 days, at least 5 days or at least 2 days prior to the asthmatic or allergic event.

[0025] In one embodiment, the asthmatic or allergic event is selected from the group consisting of an asthma attack, seasonal allergic rhinitis, and perennial allergic rhinitis.

[0026] In one embodiment, the immunostimulatory nucleic acid is administered in a routine schedule. In a related embodiment, the routine schedule is selected from the group consisting of a daily routine, a weekly routine, a bi-weekly routine, a monthly routine, and a bimonthly routine.

[0027] In a further aspect, the invention provides another method for decreasing a dose of an asthma/allergy medicament. The method involves administering to a subject at risk of developing asthma or allergy, substantially prior to an asthmatic or allergic event, an immunostimulatory nucleic acid in an amount to decrease an effective amount of an asthma/allergy medicament subsequently administered to the subject in order to treat the asthma or allergy.

[0028] In one embodiment, the immunostimulatory nucleic acid is administered at least three months, at least two months, at least one month or at least 20 days prior to the asthmatic or allergic event. In another embodiment, the immunostimulatory nucleic acid is administered at least two weeks, at least 10 days, at least one week, at least 5 days or at least 2 days prior to the asthmatic or allergic event.

[0029] In one embodiment, the asthmatic or allergic event is selected from the group consisting of an asthma attack, seasonal allergic rhinitis, and perennial allergic rhinitis.

[0030] In one embodiment, the immunostimulatory nucleic acid is administered in a routine schedule. The routine schedule may be selected from the group consisting of a daily routine, a weekly routine, a bi-weekly routine, a monthly routine, and a bi-monthly routine.

[0031] The method may further comprise administering to the subject the asthma/allergy medicament subsequent to the administration of the immunostimulatory nucleic acid. In one embodiment, the asthma/allergy medicament is administered immediately prior to, concurrently with, or following the asthmatic or allergic event. The method may further comprise administering the immunostimulatory nucleic acid concurrently with or following the asthmatic or allergic event. In one embodiment, the immunostimulatory nucleic acid is administered concurrently with the asthma/allergy medicament. In one embodiment, the asthma/allergy medicament is administered in a sub-therapeutic dose.

[0032] In these and other aspects of the invention, the immunostimulatory nucleic acids have a number of attributes. The immunostimulatory nucleic acids may have a modified backbone. In some embodiments, the modified backbone is a phosphate modified backbone, and in related embodiments, the phosphate modified backbone is a phosphorothioate backbone. In certain embodiments, the immu-

nostimulatory nucleic acid is a CpG nucleic acid, in other embodiments, the immunostimulatory nucleic acid is a T-rich nucleic acid, while in still other embodiments, the immunostimulatory nucleic acid is a poly-G nucleic acid. Preferably, the T-rich and poly-G nucleic acids are also CpG nucleic acids. In still other embodiments, the immunostimulatory nucleic acid comprises a poly-G motif (e.g., 5' GGGG 3') and a palindrome. Preferably, the immunostimulatory nucleic acid comprises two poly-G motifs, one 5' and one 3' to a centrally located palindrome sequence. Even more preferably, the backbone of these latter immunostimulatory nucleic acids is chimeric (i.e., it is partially, but not completely, composed of phosphorothioate linkages). In some embodiments, a plurality of immunostimulatory nucleic acids is administered, wherein the plurality comprises CpG nucleic acids and T-rich nucleic acids, or CpG nucleic acids and poly-G nucleic acids, or T-rich nucleic acids and poly-G nucleic acids.

[0033] In these and other aspects of the invention, the asthma/allergy medicaments have a number of attributes. In some embodiments, the asthma/allergy medicament is an asthma medicament, while in still other embodiments, the asthma/allergy medicament is an allergy medicament.

[0034] In some embodiments, the asthma/allergy medicament is selected from the group consisting of a steroid and an immunomodulator. In certain embodiments, the steroid may be selected from the group consisting of beclomethasone, fluticasone, tramcinolone, budesonide, and budesonide. In certain embodiments, the immunomodulator may be selected from the group consisting of an anti-inflammatory agent, a leukotriene antagonist, an IL-4 mutein, a soluble IL-4 receptor, an immunosuppressant, anti-IL-4 antibody, an IL-4 antagonist, an anti-IL-5 antibody, a soluble IL-13 receptor-Fc fusion protein, an anti-IL-9 antibody, a CCR3 antagonist, a CCR5 antagonist, a VLA-4 inhibitor, and a downregulator of IgE. The downregulator of IgE may be an anti-Ig antibody or a fragment thereof, but need not be so limited. The immunosuppressant may be a tolerizing peptide vaccine, but need not be so limited.

[0035] In some embodiments, the asthma/allergy medicament is a medicament selected from the group consisting of a PDE-4 inhibitor, a bronchodilator/beta-2 agonist, a K+ channel opener, a VLA-4 antagonist, a neurokin antagonist, a TXA2 synthesis inhibitor, Xanthanine, an arachidonic acid antagonist, a 5 lipoxygenase inhibitor, a thromboxin A2 receptor antagonist, a thromboxane A2 antagonist, an inhibitor of 5-lipox activation protein, and a protease inhibitor. In certain embodiments, the bronchodilator/beta-2 agonist may be selected from the group consisting of salmeterol, salbutamol, terbutaline, D2522/formoterol, fenoterol and orciprenaline.

[0036] In some embodiments, the asthma/allergy medicament is a medicament selected from the group consisting of an anti-histamine and a prostaglandin inducer. In certain embodiments, the anti-histamine is selected from the group consisting of loratidine, cetirizine, buclizine, ceterizine analogues, fexofenadine, terfenadine, desloratadine, norastemizole, epinastine, ebastine, ebastine, astemizole, levocabastine, azelastine, tranilast, terfenadine, mizolastine, betatastine, CS 560 and HSR 609. The prostaglandin inducer may be S-5751, but is not so limited.

[0037] In still other embodiments, the asthma/allergy medicament is a prostaglandin inhibitor in the form of a cyclooxygenase-2 (COX-2) inhibitor. The COX-2 inhibitor may be selected from the group consisting of celecoxib, rofecoxib, NS-398, 1-745,337, meloxicam, nimesulide, SC236, and C-phycocyanin.

[0038] A composition comprising a poly-G nucleic acid in an aerosol formulation is provided according to other aspects of the invention.

[0039] A kit is provided according to another aspect of the invention. The kit in one aspect includes a sustained-release vehicle containing an immunostimulatory nucleic acid and at least one container housing an asthma/allergy medicament, and instructions for timing of administration of the immunostimulatory nucleic acid and the asthma/allergy medicament. In another aspect, the kit includes containers for multiple administrations of immunostimulatory nucleic acid and/or multiple administrations of immunostimulatory nucleic acid and at least one container housing an asthma/allergy medicament.

[0040] A composition is provided according to another aspect of the invention. The composition includes an immunostimulatory nucleic acid and an asthma/allergy medicament, formulated in a pharmaceutically-acceptable carrier and in an effective amount for preventing or treating an immune response associated with exposure to a mediator of asthma or allergy.

[0041] Formulations of poly-G nucleic acids are also encompassed by the invention. For instance the invention includes a pharmaceutical composition of a poly-G nucleic acid in an aerosol formulation.

[0042] The immunostimulatory nucleic acid may be any of the immunostimulatory nucleic acids described above, and may have any of the attributes of the immunostimulatory nucleic acids described above which are useful in other aspects of the invention.

[0043] The asthma/allergy medicament may be any of the asthma medicaments or allergy medicaments described above which are useful in other aspects of the invention.

[0044] 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.

DETAILED DESCRIPTION OF THE INVENTION

[0045] The invention relates to methods and products for the treatment of asthma/allergy using a combination of immunostimulatory nucleic acids and asthma/allergy medicaments. The compositions can be administered in higher doses without as many side effects as are ordinarily achieved at those dosage levels or in lower doses with higher efficacy than is ordinarily achieved with those doses. The compositions can also be administered on fixed schedules or in different temporal relationships to one another. The various combinations have many advantages over the prior art methods of treating asthma and allergy.

[0046] One method for treating or preventing asthma or allergy includes the step of administering a synergistic combination of an immunostimulatory nucleic acid and an

asthma/allergy medicament in an effective amount to treat or prevent the asthma or allergy.

[0047] An "immunostimulatory nucleic acid" as used herein is any nucleic acid containing an immunostimulatory motif or backbone that induces a Th1 immune response and/or suppresses a Th2 immune response. Immunostimulatory motifs include, but are not limited to, CpG motifs, poly-G motifs, and T-rich motifs. Immunostimulatory backbones include, but are not limited to, phosphate modified backbones, such as phosphorothioate backbones. Immunostimulatory nucleic acids have been described extensively in the prior art and a brief summary of these nucleic acids is presented below.

[0048] The immunostimulatory nucleic acids when combined with the asthma/allergy medicaments have many advantages over each composition alone for the treatment of asthma and allergy. The immunostimulatory nucleic acid functions in some aspects by simultaneously suppressing Th2-type immune responses (IL-4, IgE production, histamine release) that can result in airway inflammation and bronchial spasm, and/or inducing Th1-type immune responses (IFN-γ and IL-12 production) that promote harmless antibody and cellular responses. This creates an environment inside the body that safely and effectively prevents hypersensitive reactions from occurring, thereby eliminating symptoms.

[0049] The immunostimulatory nucleic acids eliminate/reduce bronchial hyperreactivity, bronchoconstriction, bronchial obstruction, airway inflammation and atopy (which improves asthma control, normalizes lung function, prevents irreversible airway injury); and may also inhibit acute response to exercise, cold dry air, and SO_2. The nucleic acids provide long-lasting effects, thus reducing dosing regimes, improving compliance and maintenance therapy, reducing emergency situations; and improving quality of life. These compounds are also useful because they provide early anti-infective activity, which leads to decreasing infectious episodes, which further reduces hyperreactive immune responses. This is especially true in subjects like children or immuno-compromised subjects. Furthermore, use of the immunostimulatory nucleic acids reduces/eliminates use of inhalers, which can exacerbate hypersensitive reactions by providing simpler and safer delivery and by allowing less drugs to be used.

[0050] Immunostimulatory nucleic acids stimulate the immune system to prevent or treat allergy and/or asthma. The strong yet balanced, cellular and humoral immune responses that result from the nucleic acid's stimulation reflect the body's own natural defense system against invading allergens and initiators.

[0051] The terms "nucleic acid" and "oligonucleotide" are used interchangeably to mean 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)). As used herein, the terms refer to oligoribonucleotides as well as oligodeoxyribonucleotides. The terms shall also include polynucleosides (i.e. a polynucleotide minus the phosphate) and any other organic base containing polymer. Nucleic acids include vectors, e.g., plasmids as well as oligonucleotides. Nucleic acid molecules can be obtained from existing nucleic acid sources (e.g. genomic or cDNA), but are preferably synthetic (e.g. produced by oligonucleotide synthesis).

[0052] Exemplary immunostimulatory nucleic acids as those described herein as well as various control nucleic acids include but are not limited to those presented in Table 1.

TABLE 1

SEQ ID NO:	ODN SEQUENCE	BACKBONE
1	tctcccagcgtgcgccat	s
2	ataatccagcttgaaccaag	s
3	ataatcgacgttcaagcaag	s
4	taccgcgtgcgaccctct	s
5	ggggagggt	s
6	ggggagggg	s
7	ggtgaggtg	s
8	tccatgtzgttcctgatgct	o
9	gctaccttagzgtga	o
10	tccatgazgttcctgatgct	o
11	tccatgacgttcztgatgct	o
12	gctagazgttagtgt	o
13	agctccatggtgctcactg	s
14	ccacgtcgaccctcaggcga	s
15	gcacatcgtcccgcagccga	s
16	gtcactcgtggtacctcga	s
17	gttggatacaggccagactttgttg	o
18	gattcaacttgcgctcatcttaggc	o
19	accatggacgaactgtttcccctc	s
20	accatggacgagctgtttcccctc	s
21	accatggacgacctgtttcccctc	s
22	accatggacgtactgtttcccctc	s
23	accatggacggtctgtttcccctc	s
24	accatggacgttctgtttcccctc	s
25	ccactcacatctgctgctccacaag	o

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
26	acttctcatagtccctttggtccag	o
27	tccatgagcttcctgagtct	o
28	gaggaaggigiggaigacgt	o
29	gtgaaticgttcicgggict	o
30	aaaaaa	s
31	cccccc	s
32	ctgtca	s
33	tcgtag	s
34	tcgtgg	s
35	cgtcgt	s
36	tccatgtcggtcctgagtct	sos
37	tccatgccggtcctgagtct	sos
38	tccatgacggtcctgagtct	sos
39	tccatgacggtcctgagtct	sos
40	tccatgtcgatcctgagtct	sos
41	tccatgtcgctcctgagtct	sos
42	tccatgtcgttcctgagtct	sos
43	tccatgacgttcctgagtct	sos
44	tccataacgttcctgagtct	sos
45	tccatgacgtccctgagtct	sos
46	tccatcacgtgcctgagtct	sos
47	tccatgctggtcctgagtct	sos
48	tccatgtzggtcctgagtct	sos
49	ccgcttcctccagatgagctcatgggtttctccaccaag	o
50	cttggtggagaaacccatgagctcatctggaggaagcgg	o
51	ccccaaagggatgagaagtt	o
52	agatagcaaatcggctgacg	o
53	ggttcacgtgctcatggctg	o
54	tctaccagcgtgcgccat	s
55	tctcccagcgtgcgccat	s
56	taccgcgtgcgaccctct	s
57	ataatccagcttgaaccaag	s
58	ataatcgacgttcaagcaag	s
59	tccatgattttcctgatttt	o
60	ttgttttttttgttttttttgttttt	s
61	ttttttttgttttttttgttttt	o
62	tgctgcttttgtgcttttgtgctt	s
63	tgctgcttgtgcttttgtgctt	o
64	gcattcatcaggcgggcaagaat	o
65	taccgagcttcgacgagatttca	o
66	gcatgacgttgagct	s
67	cacgttgaggggcat	s
68	ctgctgagactggag	s
69	tccatgacgttcctgacgtt	s
70	gcatgagcttgagctga	o
71	tcagcgtgcgcc	s
72	atgacgttcctgacgtt	s
73	ttttggggttttggggtttt	s
74	tctaggctttttaggcttcc	s
75	tgcatttttttaggccaccat	s
76	tctcccagcgtgcgtgcgccat	s
77	tctcccagcgggcgcat	s
78	tctcccagcgagcgccat	s
79	tctcccagcgcgcgccat	s
80	ggggtgacgttcaggggggg	sos
81	ggggtccagcgtgcgccatggggg	sos
82	ggggtgtcgttcaggggggg	sos
83	tccatgtcgttcctgtcgtt	s
84	tccatagcgttcctagcgtt	s
85	tcgtcgctgtctccgcttctt	s
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88	tccatgazgttcctgazgtt	s
89	gcatgazgttgagct	o
90	tccagcgtgcgccata	sos
91	tctcccagcgtgcgccat	o
92	tccatgagcttcctgagtct	o
93	gcatgtcgttgagct	sos
94	tcctgacgttcctgacgtt	s
95	gcatgatgttgagct	o
96	gcatttcgaggagct	o
97	gcatgtagctgagct	o

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
98	tccaggacgttcctagttct	o
99	tccaggagcttcctagttct	o
100	tccaggatgttcctagttct	o
101	tccagtctaggcctagttct	o
102	tccagttcgagcctagttct	o
103	gcatggcgttgagct	sos
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105	gcattgcgttgagct	sos
106	gcttgcgttgcgttt	sos
107	tctcccagcgttgcgccatat	sos
108	tctcccagcgtgcgttatat	sos
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114	tcctgacgttccc	o
115	ggaagacgttaga	o
116	tcctgacgttaga	o
117	tcagaccagctggtcgggtgttcctga	o
118	tcaggaacacccgaccagctggtctga	o
119	gctagtcgatagc	o
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123	gcttgacgtcaagc	o
124	gctagacgtttagc	o
125	tccatgacattcctgatgct	o
126	gatagacgtctagc	o
127	ggctatgtcgttcctagcc	o
128	ggctatgtcgatcctagcc	o
129	ctcatgggtttctccaccaag	o
130	cttggtggagaaacccatgag	o
131	tccatgacgttcctagttct	o
132	ccgcttcctccagatgagctcatg	o
133	catgagctcatctggaggaagcgg	o
134	ccagatgagctcatgggtttctcc	o
135	ggagaaacccatgagctcatctgg	o
136	agcatcaggaaagacatgga	o
137	tccatgacgttcctgacgtt	rna
138	gcgcgcgcgcgcgcgcgcg	o
139	ccggccggccggccggccgg	o
140	ttccaatcagccccacccgctctggccccaccctcaccctccc	o
141	tggagggtgagggtggggccagagcgggtggggctgattggac	o
142	tcaaatgtgggattttcccatgagtct	o
143	agactcatgggaaaatcccacatttga	o
144	tgccaagtgctgagtcactaataaaga	o
145	tctttattagtgactcagcacttggca	o
146	tgcaggaagtccgggttttccccaaccccc	o
147	ggggggttggggaaaacccggacttcctgca	o
148	ggggactttccgctggggactttccaggggactttcc	sos
149	tccatgacgttcctctccatgacgttcctctccatgacgttcctc	o
150	gaggaacgtcatggagaggaacgtcatggagaggaacgtcatggc	o
151	ataatagagcttcaagcaag	s
152	tccatgacgttcctgacgtt	s
153	tccatgacgttcctgacgtt	sos
154	tccaggactttcctcaggtt	s
155	tcttgcgatgctaaaggacgtcacattgcacaatcttaataaggt	o
156	accttattaagattgtgcaatgtgacgtcctttagcatcgcacgc	o
157	tcctgacgttcctggcggtcctgtcgct	o
158	tcctgtcgctcctgtcgct	o
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160	tcctgtcgttgaagt	o
161	tcctggcgttgaagt	o
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163	tccttacgttgaagt	o
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165	tcctcacgttgaagt	o
166	tcctgacgatgaagt	o
167	tcctgacgctgaagt	o
168	tcctgacggtgaagt	o
169	tcctgacgtagaagt	o

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
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171	tcctgacgtggaagt	o
172	tcctgagcttgaagt	o
173	gggggacgttgggggg	o
174	tcctgacgttccttc	o
175	tctcccagcgagcgagcgccat	s
176	tcctgacgttccctggcggtcccctgtcgct	o
177	tcctgtcgctcctgtcgctcctgtcgct	o
178	tcctggcggggaagt	o
179	tcctgazgttgaagt	o
180	tcztgacgttgaagt	o
181	tcctagcgttgaagt	o
182	tccagacgttgaagt	o
183	tcctgacggggaagt	o
184	tcctggcggtgaagt	o
185	ggctccggggagggaatttttgtctat	o
186	atagacaaaaattccctccccggagcc	o
187	tccatgagcttccttgagtct	rna
188	tcgtcgctgtctccgcttctt	so
189	tcgtcgctgtctccgcttctt	s2o
190	tcgagacattgcacaatcatctg	o
191	cagattgtgcaatgtctcga	o
192	tccatgtcgttcctgatgcg	o
193	gcgatgtcgttcctgatgct	o
194	gcgatgtcgttcctgatgcg	o
195	tccatgtcgttccgcgcgcg	o
196	tccatgtcgttcctgccgct	o
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199	atcaggaacgtcatgggaagc	o
200	tccatgagcttcctgagtct	p-ethoxy
201	tcaacgtt	p-ethoxy
202	tcaagctt	p-ethoxy
203	tcctgtcgttcctgtcgtt	s
204	tccatgtcgtttttgtcgtt	s
205	tcctgtcgttccttgtcgtt	s
206	tccttgtcgttcctgtcgtt	s
207	btccattccatgacgttcctgatgcttcca	os
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210	tcgtcgctgtctgcccttctt	s
211	tcgtcgctgttgtcgtttctt	s
212	tcctgtcgttcctgtcgttggaacgacagg	o
213	tcctgtcgttcctgtcgtttcaacgtcaggaacgacagga	o
214	ggggtctgtcgttttgggggg	sos
215	ggggtctgtgctttgggggg	sos
216	tccggccgttgaagt	o
217	tccggacggtgaagt	o
218	tcccgccgttgaagt	o
219	tccagacggtgaagt	o
220	tcccgacggtgaagt	o
221	tccagagcttgaagt	o
222	tccatgtzgttcctgtzgtt	s
223	tccatgacgttcctgacgtt	sos
224	ggggttgacgttttgggggg	sos
225	tccaggacttctctcaggtt	s
226	ttttttttttttttttttt	s
227	tccatgccgttcctgccgtt	s
228	tccatggcgggcctggcggg	s
229	tccatgacgttcctgccgtt	s
230	tccatgacgttcctggcggg	s
231	tccatgacgttcctgcgttt	s
232	tccatgacggtcctgacggt	s
233	tccatgcgtgcgtgcgtttt	s
234	tccatgcgttgcgttgcgtt	s
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236	tccatagcgttcctagcgtt	o
237	tccatgtcgttcctgtcgtt	o
238	tccatagcgatcctagcgat	o
239	tccattgcgttccttgcgtt	o
240	tccatagcggtcctagcggt	o
241	tccatgattttcctgcagttcctgatttt	

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
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243	ggcggcggcggcggcggcgg	o
244	tccacgacgttttcgacgtt	s
245	tcgtcgttgtcgttgtcgtt	s
246	tcgtcgttttgtcgttttgtcgtt	s
247	tcgtcgttgtcgttttgtcgtt	s
248	gcgtgcgttgtcgttgtcgtt	s
249	czggczggczgggczccgg	o
250	gcggcgggcggcgcgcgccc	s
251	agicccgigaacgiattcac	o
252	tgtcgtttgtcgtttgtcgtt	s
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254	tgtcgttgtcgttgtcgttgtcgtt	s
255	tcgtcgtcgtcgtt	s
256	tgtcgttgtcgtt	s
257	cccccccccccccccccccc	s
258	tctagcgtttttagcgttcc	sos
259	tgcatcccccaggccaccat	s
260	tcgtcgtcgtcgtcgtcgtcgtt	sos
261	tcgtcgttgtcgttgtcgtt	sos
262	tcgtcgttttgtcgttttgtcgtt	sos
263	tcgtcgttgtcgttttgtcgtt	sos
264	ggggagggaggaacttcttaaaattcccccagaatgttt	o
265	aaacattctgggggaattttaagaagttcctccctcccc	o
266	atgtttacttcttaaaattcccccagaatgttt	o
267	aaacattctgggggaattttaagaagtaaacat	o
268	atgtttactagacaaaattcccccagaatgttt	o
269	aaacattctgggggaattttgtctagtaaacat	o
270	aaaattgacgttttaaaaaa	sos
271	ccccttgacgttttcccccc	sos
272	ttttcgttgtttttgtcgtt	
273	tcgtcgttttgtcgttttgtcgtt	sos
274	ctgcagcctgggac	o
275	acccgtcgtaattatagtaaaaccc	o
276	ggtacctgtggggacattgtg	o
277	agcaccgaacgtgagagg	o
278	tccatgccgttcctgccgtt	o
279	tccatgacggtcctgacggt	o
280	tccatgccggtcctgccggt	o
281	tccatgcgcgtcctgcgcgt	o
282	ctggtctttctggtttttttctgg	s
283	tcaggggtggggggaacctt	sos
284	tccatgazgttcctagttct	o
285	tccatgatgttcctagttct	o
286	cccgaagtcatttcctcttaacctgg	o
287	ccaggttaagaggaaatgacttcggg	o
288	tcctggzggggaagt	o
289	gzggzgggzggzgzgzgccc	x
290	tccatgtgcttcctgatgat	o
291	tccatgtccttcctgatgct	
292	tccatgtcgttcctagttct	
293	tccaagtagttcctagttct	o
294	tccatgtagttcctagttct	o
295	tcccgcgcgttccgcgcgtt	s
296	tcctggcggtcctggcggtt	s
297	tcctggaggggaagt	o
298	tcctgggggggaagt	o
299	tcctggtggggaagt	o
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301	ctggtctttctggtttttttctgg	o
302	tccatgacgttcctgacgtt	o
303	tccaggacttctctcaggtt	sos
304	tzgtzgttttgtzgttttgtzgtt	o
305	btcgtcgttttgtcgttttgtcgttttttt	os
306	gctatgacgttccaaggg	s
307	tcaacgtt	s
308	tccaggactttcctcaggtt	o
309	ctctctgtaggcccgcttgg	s
310	ctttccgttggacccctggg	s
311	gtccgggccaggccaaagtc	s
312	gtgcgcgcgagcccgaaatc	s
313	tccatgaigttcctgaigtt	s

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
314	aatagtcgccataacaaaac	o
315	aatagtcgccatggcggggc	o
316	bttttttccatgtcgttcctgatgcttttt	os
317	tcctgtcgttgaagtttttt	o
318	gctagctttagagctttagagctt	o
319	tgctgcttcccccccccccc	o
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326	tcctgccgttgaagt	s
327	tcctgacggtgaagt	s
328	tcctgagcttgaagt	s
329	tcctggcggggaagt	s
330	aaaatctgtgcttttaaaaaa	sos
331	gatccagtcacagtgacctggcagaatctggat	o
332	gatccagattctgccaggtcactgtgactggat	o
333	gatccagtcacagtgactcagcagaatctggat	o
334	gatccagattctgctgagtcactgtgactggat	o
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351	tcgtcgttcccccccccccb	o
352	tcgtcgttttgtcgttttgtcgttb	o
353	tccagttccttcctcagtct	o
354	tzgtcgttttgtcgttttgtcgtt	o
355	tcctggaggggaagt	s
356	tcctgaaaaggaagt	s
357	tcgtcgttcccccccc	s
358	tzgtzgttttgtzgttttgtzgtt	s
359	ggggtcaagcttgaggggg	sos
360	tgctgcttcccccccccccc	s
361	tcgtcgtcgtcgtt	s2
362	tcgtcgtcgtcgtt	s20
363	tcgtcgtcgtcgtt	os2
364	tcaacgttga	s
365	tcaacgtt	s
366	atagttttccatttttttac	
367	aatagtcgccatcgcgcgac	o
368	aatagtcgccatcccgggac	o
369	aatagtcgccatcccccccc	o
370	tgctgcttttgtgcttttgtgctt	o
371	ctgtgctttctgtgtttttctgtg	s
372	ctaatctttctaatttttttctaa	s
373	tcgtcgttggtgtcgttggtgtcgtt	s
374	tcgtcgttggttgtcgttttggtt	s
375	accatggacgagctgtttcccctc	
376	tcgtcgttttgcgtgcgttt	s
377	ctgtaagtgagcttggagag	
378	gagaacgctggaccttcc	
379	cgggcgactcagtctatcgg	
380	gttctcagataaagcggaaccagcaacagacacagaa	
381	ttctgtgtatgttgctggttccgctttatctgagaac	
382	cagacacagaagcccgatagacg	
383	agacagacacgaaacgaccg	
384	gtctgtcccatgatctcgaa	
385	gctggccagcttacctcccg	

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
386	ggggcctctatacaacctggg	
387	ggggtccctgagactgcc	
388	gagaacgctggaccttccat	
389	tccatgtcggtcctgatgct	
390	ctcttgcgacctggaaggta	
391	aggtacagccaggactacga	
392	accatggacgacctgtttcccctc	
393	accatggattacctttttcccctt	
394	atggaaggtccagcgttctc	o
395	agcatcaggaccgacatgga	o
396	ctctccaagctcacttacag	
397	tccctgagactgccccacctt	
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399	gtccatggcgtgcgggatga	
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404	ccagtgctgatcaccgatatcctgttcggcagtcg	
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410	ataatcgtcgttcaagcaag	s
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417	ataatcgtgcgttcaagaaag	s
418	ataatcgacgttcccccccc	s
419	tctatcgacgttcaagcaag	s
420	tcc tga cgg gg agt	s
421	tccatgacgttcctgatcc	
422	tccatgacgttcctgatac	
423	tccatgacgttcctgatcc	
424	tcc tgg cgt gga agt	s
425	tccatgacgttcctgatcc	
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427	agcagctttagagctttagagctt	s
428	ccccccccccccccccccccccc	s
429	tcgtcgttttgtcgttttgtcgttttgtcgtt	s
430	tcgtcgtttttttgtcgtttttttgtcgtt	s
431	tcgtcgttttttttttttttt	s
432	tttttcaacgttgatttttt	sos
433	ttttttttttttttttttttttt	s
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436	tcgtcgctgtctccgcttcttcttgcc	s
437	tcgtcgctgtctccg	s
438	ctgtaagtgagcttggagag	
439	gagaacgctggaccttccat	
440	ccaggttgtatagaggc	
441	gctagacgttagcgtga	
442	ggagctcttcgaacgccata	
443	tctccatgatggttttatcg	
444	aaggtggggcagtctcaggga	
445	atcggaggactggcgcgccg	
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447	accacaacgagaggaacgca	
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449	gaaccttccatgctgtt	
450	gctagacgttagcgtga	
451	gcttggagggcctgtaagtg	
452	gtagccttccta	
453	cggtagccttccta	
454	cacggtagccttccta	
455	agcacggtagccttccta	
456	gaacgctggaccttccat	
457	gaccttccat	

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
458	tggaccttccat	
459	gctggaccttccat	
460	acgctggaccttccat	
461	taagctctgtcaacgccagg	
462	gagaacgctggaccttccatgt	
463	tccatgtcggtcctgatgct	
464	ttcatgccttgcaaaatggcg	
465	tgctagctgtgcctgtacct	
466	agcatcaggaccgacatgga	
467	gaccttccatgtcggtcctgat	
468	acaaccacgagaacgggaac	
469	gaaccttccatgctgttccg	
470	caatcaatctgaggagaccc	
471	tcagctctggtacttttca	
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489	cttggagggcctcccggcgg	
490	gctgaaccttccatgctgtt	
491	tagaaacagcattcttcttttagggcagcaca	
492	agatggttctcagataaagcggaa	
493	ttccgctttatctgagaaccatct	
494	gtcccaggttgtatagaggctgc	
495	gcgccagtcctccgatagac	
496	atcggaggactggcgcgccg	
497	ggtctgtcccatattttag	
498	tttttcaacgttgaggggg	sos
499	tttttcaagcgttgatttttt	sos
500	ggggtcaacgttgatttttt	sos
501	ggggttttcaacgttttgaggggg	sos
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504	accatcctgaggccattcgg	
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506	ggccatcccacattgaaagtt	
507	ccaaatatcggtggtcaagcac	
508	gtgcttgaccaccgatatttgg	
509	gtgctgatcaccgatatcctgttcgg	
510	ggccaactttcaatgtgggatggcctc	
511	ttccgccgaatggcctcaggatggtac	
512	tatagtccctgagactgccccaccttctcaacaacc	
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515	tatcggaggactggcgcgccg	
516	gatcggaggactggcgcgccg	
517	ccgaacaggatatcggtgatcagcac	
518	ttttggggtcaacgttgaggggg	
519	ggggtcaacgttgaggggg	sos
520	cgcgcgcgcgcgcgcgcgcg	s
521	ggggcatgacgttcgggggg	ss
522	ggggcatgacgttcaaaaaa	s
523	ggggcatgagcttcgggggg	s
524	ggggcatgacgttcgggggg	sos
525	aaaacatgacgttcaaaaaa	sos
526	aaaacatgacgttcgggggg	sos
527	ggggcatgacgttcaaaaaa	sos
528	accatggacgatctgtttcccctc	s
529	gccatggacgaactgttcccccctc	s

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
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531	gggggggggggggggggggg	sos
532	gctgtaaaatgaatcggccg	sos
533	ttcgggcggactcctccatt	sos
534	tatgccgcgcccggacttat	sos
535	ggggtaatcgatcaggggggg	sos
536	tttgagaacgctggaccttc	sos
537	gatcgctgatctaatgctcg	sos
538	gtcggtcctgatgctgttcc	sos
539	tcgtcgtcagttcgctgtcg	sos
540	ctggaccttccatgtcgg	sos
541	gctcgttcagcgcgtct	sos
542	ctggaccttccatgtc	sos
543	cactgtccttcgtcga	sos
544	cgctggaccttccatgtcgg	sos
545	gctgagctcatgccgtctgc	sos
546	aacgctggaccttccatgtc	sos
547	tgcatgccgtacacagctct	sos
548	ccttccatgtcggtcctgat	sos
549	tactcttcggatcccttgcg	sos
550	ttccatgtcggtcctgat	sos
551	ctgattgctctctcgtga	sos
552	ggcgttattcctgactcgcc	o
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554	ggggtaatcgatgaggggggg	o
555	ttcgggcggactcctccatt	o
556	tttttttttttttttttttt	o
557	gggggttttttttttggggg	o
558	tttttgggggggggggttttt	o
559	gggggggggggggggggggt	o
560	aaaaaaaaaaaaaaaaaaaa	o
561	cccccaaaaaaaaaaccccc	o
562	aaaaaccccccccccaaaaa	o
563	tttgaattcaggactggtgaggttgag	o
564	tttgaatcctcagcggtctccagtggc	o
565	aattctctatcggggcttctgtgtctgttgctggttccgctttct	o
566	ctagataaagcggaaccagcaacagacacagaagccccgatagcg	o
567	ttttctagagaggtgcacaatgctctgg	o
568	tttgaattccgtgtacagaagcgagaagc	o
569	tttgcggccgctagacttaacctgagagata	o
570	tttgggcccacgagagacagagacacttc	o
571	tttgggcccgcttctcgcttctgtacacg	o
572	gagaacgctggaccttccat	s
573	tccatgtcggtcctgatgct	s
574	ctgtcg	s
575	tcgtga	s
576	cgtcga	s
577	agtgct	s
578	ctgtcg	o
579	agtgct	o
580	cgtcga	o
581	tcgtga	o
582	gagaacgctccagcttcgat	o
583	gctagacgtaagcgtga	o
584	gagaacgctcgaccttccat	o
585	gagaacgctggacctatccat	o
586	gctagaggttagcgtga	o
587	gagaacgctggacttccat	o
588	tcacgctaacgtctagc	o
589	bgctagacgttagcgtga	o
590	atggaaggtcgagcgttctc	o
591	gagaacgctggaccttcgat	o
592	gagaacgatggaccttcaat	o
593	gagaacgctggatccat	o
594	gagaacgctccagcactgat	o
595	tccatgtcggtcctgctgat	o
596	atgtcctcggtcctgatgct	o
597	gagaacgctccaccttccat	o
598	gagaacgctggaccttcgta	o
599	batggaaggtccagcgttctc	o
600	tcctga	o
601	tcaacgtt	o

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
602	aacgtt	o
603	aacgttga	o
604	tcacgctaacctctagc	o
605	gagaacgctggaccttgcat	o
606	gctggaccttccat	o
607	gagaacgctggacctcatccat	o
608	gagaacgctggacgctcatccat	o
609	aacgttgaggggcat	o
610	atgcccctcaacgtt	o
611	tcaacgttga	o
612	gctggaccttccat	o
613	caacgtt	o
614	acaacgttga	o
615	tcacgt	o
616	tcaagctt	o
617	tcgtca	o
618	aggatatc	o
619	tagacgtc	o
620	gacgtcat	o
621	ccatcgat	o
622	atcgatgt	o
623	atgcatgt	o
624	ccatgcat	o
625	agcgctga	o
626	tcagcgct	o
627	ccttcgat	o
628	gtgccggggtctccgggc	s
629	gctgtggggcggctcctg	s
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638	agaacgtt	o
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647	gagcaagctggaccttccat	s
648	cgcgta	s
649	cgtacg	s
650	tcaccggt	s
651	caagagatgctaacaatgca	s
652	acccatcaatagctctgtgc	s
653	ccatcgat	o
654	tcgacgtc	o
655	ctagcgct	o
656	taagcgct	o
657	tcgcgaattcgcg	o
658	atggaaggtccagcgttct	o
659	actggacgttagcgtga	o
660	cgcctggggctggtctgg	o
661	gtgtcggggtctccgggc	o
662	gtgccggggtctccgggc	o
663	cgccgtcgcggcggttgg	o
664	gaagttcacgttgaggggcat	o
665	atctggtgagggcaagctatg	s
666	gttgaaacccgagaacatcat	s
667	gcaacgtt	o
668	gtaacgtt	o
669	cgaacgtt	o
670	gaaacgtt	o
671	caaacgtt	o
672	ctaacgtt	o
673	ggaacgtt	o

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
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675	acaacgtt	o
676	ttaacgtt	o
677	aaaacgtt	o
678	ataacgtt	o
679	aacgttct	o
680	tccgatcg	o
681	tccgtacg	o
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684	gagaacgctagaccttctat	o
685	actagacgttagtgtga	o
686	cacaccttggtcaatgtcacgt	o
687	tctccatcctatggttttatcg	o
688	cgctggaccttccat	o
689	caccaccttggtcaatgtcacgt	o
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691	agtgcgattgcagatcg	o
692	ttttcgttttgtggttttgtggtt	
693	ttttcgtttgtcgttttgtcgtt	
694	tttttgttttgtggttttgtggtt	
695	accgcatggattctaggcca	s
696	gctagacgttagcgt	o
697	aacgctggaccttccat	o
698	tcaazgtt	o
699	ccttcgat	o
700	actagacgttagtgtga	s
701	gctagaggttagcgtga	s
702	atggactctccagcgttctc	o
703	atcgactctcgagcgttctc	o
704	gctagacgttagc	o
705	gctagacgt	o
706	agtgcgattcgagatcg	o
707	tcagzgct	o
708	ctgattgctctctcgtga	o
709	tzaacgtt	o
710	gagaazgctggaccttccat	o
711	gctagacgttaggctga	o
712	gctacttagcgtga	o
713	gctaccttagcgtga	o
714	atcgacttcgagcgttctc	o
715	atgcactctgcagcgttctc	o
716	agtgactctccagcgttctc	o
717	gccagatgttagctgga	o
718	atcgactcgagcgttctc	o
719	atcgatcgagcgttctc	o
720	bgagaacgctcgaccttcgat	o
721	gctagacgttagctgga	sos
722	atcgactctcgagcgttctc	sos
723	tagacgttagcgtga	o
724	cgactctcgagcgttctc	o
725	ggggtcgaccttggaggggg	sos
726	gctaacgttagcgtga	o
727	cgtcgtcgt	o
728	gagaacgctggaczttccat	o
729	atcgacctacgtgcgttztc	o
730	atzgacctacgtgcgttctc	o
731	gctagazgttagcgt	o
732	atcgactatcgagzgttctc	o
733	ggggtaatgcatcaggggg	sos
734	ggctgtattcctgactgccc	s
735	ccatgctaacctctagc	o
736	gctagatgttagcgtga	o
737	cgtaccttacggtga	o
738	tccatgctggtcctgatgct	o
739	atcgactctctcgagcgttctc	o
740	gctagagcttagcgtga	o
741	atcgactctcgagtgttctc	o
742	aacgctcgaccttcgat	o
743	ctcaacgctggaccttccat	o
744	atcgacctacgtgcgttctc	o
745	gagaatgctggaccttccat	o

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
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747	bgagaacgctccagcactgat	o
748	bgagcaagctggaccttccat	o
749	cgctagaggttagcgtga	o
750	gctagatgttaacgt	o
751	atggaaggtccacgttctc	o
752	gctagatgttagcgt	o
753	gctagacgttagtgt	o
754	tccatgacggtcctgatgct	o
755	tccatggcggtcctgatgct	o
756	gctagacgatagcgt	o
757	gctagtcgatagcgt	o
758	tccatgacgttcctgatgct	o
759	tccatgtcgttcctgatgct	o
760	gctagacgttagzgt	o
761	gctaggcgttagcgt	o
762	tccatgtzggtcctgatgct	o
763	tccatgtcggtzctgatgct	o
764	atzgactctzgagzgttctc	o
765	atggaaggtccagtgttctc	o
766	gcatgacgttgagct	o
767	ggggtcaacgttgaggggg	s
768	ggggtcaagtctgaggggg	sos
769	cgcgcgcgcgcgcgcgcgcg	o
770	ccccccccccccccccccccccccc	s
771	ccccccccccccccccccccccccccccccccc	s
772	tccatgtcgctcctgatcct	o
773	gctaaacgttagcgt	o
774	tccatgtcgatcctgatgct	o
775	tccatgccggtcctgatgct	o
776	aaaatcaacgttgaaaaaaa	sos
777	tccataacgttcctgatgct	o
778	tggaggtcccaccgagatcggag	o
779	cgtcgtcgtcgtcgtcgtcgt	s
780	ctgctgctgctgctgctgctg	s
781	gagaacgctccgaccttcgat	s
782	gctagatgttagcgt	s
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786	tcaacgttgab	o
787	gcaatattgcb	o
788	gcaatattgcf	o
789	agttgcaact	o
790	tcttcgaa	o
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794	tttttgtttgtcgttttgtcgtt	o
795	ttgggggggtt	s
796	ggggttggggtt	s
797	ggtggtgtaggttttgg	o
798	bgagaazgctcgaccttcgat	o
799	tcaacgttaacgttaacgtt	o
800	bgagcaagztggaccttccat	o
801	bgagaazgctccagcactgat	o
802	tcaazgttgax	o
803	gzaatattgcx	o
804	tgctgcttttgtagttttgtgctt	o
805	ctgcgttagcaatttaactgtg	o
806	tccatgacgttcctgatgct	s
807	tgcatgccgtgcatccgtacacagctct	s
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809	tgcatcagctct	s
810	tgcgctct	s
811	ccccccccccccccccccc	s
812	ccccccccccc	s
813	cccccccc	s
814	tgcatcagctct	sos
815	tgcatgccgtacacagctct	o
816	gagcaagctggaccttccat	s
817	tcaacgttaacgttaacgttaacgttaacgtt	s

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
818	gagaacgctcgaccttcgat	s
819	gtccccatttcccagaggaggaaat	o
820	ctagcggctgacgtcatcaagctag	o
821	ctagcttgatgacgtcagccgctag	o
822	cggctgacgtcatcaa	s
823	ctgacgtg	o
824	ctgacgtcat	o
825	attcgatcggggcggggcgag	o
826	ctcgccccgccccgatcgaat	o
827	gactgacgtcagcgt	o
828	ctagcggctgacgtcataaagctagc	s
829	ctagctttatgacgtcagccgctagc	s
830	ctagcggctgagctcataaagctagc	s
831	ctagtggctgacgtcatcaagctag	s
832	tccaccacgtggtctatgct	s
833	gggaatgaaagattttattataag	o
834	tctaaaaaccatctattcttaaccct	o
835	agctcaacgtcatgc	o
836	ttaacggtggtagcggtattggtc	o
837	ttaagaccaataccgctaccaccg	o
838	gatctagtgatgagtcagccggatc	o
839	gatccggctgactcatcactagatc	o
840	tccaagacgttcctgatgct	o
841	tccatgacgtccctgatgct	o
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843	ccacgtggacctctagc	o
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845	tcaggaacacccgaccacgtggtctga	o
846	catttccacgatttccca	o
847	ttcctctctgcaagagact	o
848	tgtatctctctgaaggact	o
849	ataaagcgaaactagcagcagtttc	o
850	gaaactgctgctagtttcgctttat	o
851	tgcccaaagaggaaaatttgtttcatacag	o
852	ctgtatgaaacaaattttcctctttgggca	o
853	ttagggttagggttagggtt	ss
854	tacatgagcttcctgatgct	ss
855	aaaacatgacgttcaaaaaa	ss
856	aaaacatgacgttcgggggg	ss
857	ggggcatgagcttcgggggg	sos
858	ctaggctgacgtcatcaagctagt	o
859	tctgacgtcatctgacgttggctgacgtct	o
860	ggaattagtaatagatatagaagtt	o
861	tttacctttataaacataactaaaacaaa	o
862	gcgtttttttttgcg	s
863	atatctaatcaaaacattaacaaa	o
864	tctatcccaggtggttcctgttag	o
865	btccatgacgttcctgatgct	o
866	btccatgagcttcctgatgct	o
867	tttttttttttttf	o
868	tttttttttttttf	so
869	ctagcttgatgagctcagccgctag	o
870	ttcagttgtcttgctgcttagctaa	o
871	tccatgagcttcctgagtct	s
872	ctagcggctgacgtcatcaatctag	o
873	tgctagctgtgcctgtacct	s
874	atgctaaaggacgtcacattgca	o
875	tgcaatgtgacgtcctttagcat	o
876	gtaggggactttccgagctcgagatcctatg	o
877	cataggatctcgagctcggaaagtcccctac	o
878	ctgtcaggaactgcaggtaagg	o
879	cataacataggaatatttactcctcgc	o
880	ctccagctccaagaaaggacg	o
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884	tcgtcgtttgtcgttttgtcgtt	s
885	tcctgacgttcggcgcgcgccc	s
886	tgctgcttttgtgcttttgtgctt	
887	tccatgagcttcctgagctt	s
888	tcgtcgtttcgtcgttttgacgtt	s
889	tcgtcgtttgcgtgcgtttcgtcgtt	s

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
890	tcgcgtgcgttttgtcgttttgacgtt	s
891	ttcgtcgttttgtcgttttgtcgtt	s
892	tcctgacggggaagt	s
893	tcctggcgtggaagt	s
894	tcctggcggtgaagt	s
895	tcctggcgttgaagt	s
896	tcctgacgtggaagt	s
897	gcgacgttcggcgcgcgccc	s
898	gcgacgggcggcgcgcgacc	s
899	gcggcgtgcggcgcgcgccc	s
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901	gcgacggtcggcgcgcgccc	s
902	gcggcgttcggcgcgcgccc	s
903	gcgacgtgcggcgcgcgccc	s
904	tcgtcgctgtctccg	s
905	tgtgggggttttggttttgg	s
906	aggggaggggaggggagggg	s
907	tgtgtgtgtgtgtgtgtgtgt	s
908	ctctctctctctctctctct	chimeric
909	ggggtcgacgtcgaggggg	s
910	atatatatatatatatatatat	s
911	ttttttttttttttttttttttttt	s
912	tttttttttttttttttttt	s
913	ttttttttttttttttt	s
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916	gcatgaggggagct	
917	atggaaggtccaggggctc	
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919	atggaaggtccaaggggctc	
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922	gagaaggggccagcactgat	
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925	tccatgtggggcctgctgat	
926	atggactctccggggttctc	
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929	atggaggctccatggggctc	
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935	tccatggggtgcctgatgct	
936	tccatggggttcctgatgct	
937	tccatcgggggcctgatgct	
938	gctagagggagtgt	
939	tttttttttttttttttt	s
940	gmggtcaacgttgagggmggg	s
941	ggggagttcgttgaggggggg	s
942	tcgtcgtttccccccccccc	s
943	ttgggggggttttttttttttttttt	s
944	tttaaattttaaaatttaaaata	s
945	ttggttttttttggttttttttttgg	s
946	tttccctttttccccttttcccctc	s
947	ggggtcatcgatgagggggg s	sos
948	tccatgacgttcctgacgtt	
949	tccatgacgttcctgacgtt	
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956	tccatgacgttcctgacgtt	
957	tccatgacgttcctgacgtt	
958	tccatgacgttcctgacgtt	
959	gggggacgatcgtcgggggg	sos
960	gggggtcgtacgacgggggg	sos
961	ttttttttttttttttttttttttt	po

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
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963	ccccccccccccccccccccccc	po
964	tcgtcgttttgtcgttttgtcgtt	
965	tcgtcgttttgtcgttttgtcgtt	
966	tcgtcgttttgtcgttttgtcgtt	
967	tcgtcgttttgtcgttttgtcgtt	
968	ggggtcaacgttgaggggggg	
969	ggggtcaacgttgaggggggg	
970	ggggtcaagcttgaggggggg	
971	tgctgcttcccccccccccc	
972	ggggacgtcgacgtgggggg	sos
973	ggggtcgtcgacgaggggggg	sos
974	ggggtcgacgtacgtcgaggggggg	sos
975	ggggaccggtaccggtgggggg	sos
976	gggtcgacgtcgaggggggg	sos
977	ggggtcgacgtcgaggggg	sos
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986	gggggagcatgctgggggggg	sos
987	gggggggggggggggggggg	sos
988	gggggacgatatcgtcgggggg	sos
989	gggggacgacgtcgtcgggggg	sos
990	gggggacgagctcgtcgggggg	sos
991	gggggacgtacgtcgggggg	sos
992	tcaacgtt	
993	tccataccggtcctgatgct	
994	tccataccggtcctaccggt	s
995	gggggacgatcgttgggggg	sos
996	ggggaacgatcgtcgggggg	sos
997	ggg ggg acg atc gtc ggg ggg	sos
998	ggg gga cga tcg tcg ggg ggg	sos
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1000	aaagagcttaaa	po
1001	aaagazgttaaa	po
1002	aaattcggaaaa	po
1003	gggggtcatcgatgaggggggg	sos
1004	gggggtcaacgttgaggggggg	sos
1005	atgtagcttaataacaaagc	po
1006	ggatcccttgagttacttct	po
1007	ccattccacttctgattacc	po
1008	tatgtattatcatgtagata	po
1009	agcctacgtattcaccctcc	po
1010	ttcctgcaactactattgta	po
1011	atagaaggccctacaccagt	po
1012	ttacaccggtctatggaggt	po
1013	ctaaccagatcaagtctagg	po
1014	cctagacttgatctggttag	po
1015	tataagcctcgtccgacatg	po
1016	catgtcggacgaggcttata	po
1017	tggtggtggggagtaagctc	po
1018	gagctactcccccaccacca	po
1019	gccttcgatcttcgttggga	po
1020	tggacttctctttgccgtct	po
1021	atgctgtagcccagcgataa	po
1022	accgaatcagcggaaagtga	po
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1025	accacagaccagcaggcaga	
1026	gagcgtgaactgcgcgaaga	
1027	tcggtacccttgcagcggtt	
1028	ctggagccctagccaaggat	
1029	gcgactccatcaccagcgat	
1030	cctgaagtaagaaccagatgt	
1031	ctgtgttatctgacatacaca	
1032	aattagccttaggtgattggg	
1033	acatctggttcttacttcagg	

TABLE 1-continued

SEQ ID NO:	ODN SEQUENCE	BACKBONE
1034	ataagtcatattttgggaactac	
1035	cccaatcacctaaggctaatt	
1036	ggggtcgtcgacgaggggggg	sos
1037	ggggtcgttcgaacgaggggggg	sos
1038	ggggacgttcgaacgtgggggg	sos
1039	tcctggcggggaagt	s
1040	ggggaacgacgtcgttgggggg	sos
1041	ggggaacgtacgtcgggggg	sos
1042	ggggaacgtacgtacgttgggggg	sos
1043	ggggtcaccggtgaggggggg	sos
1044	ggggtcgacgtacgtcgaggggggg	sos
1045	ggggaccggtaccggtgggggg	sos
1046	gggtcgacgtcgaggggggg	sos
1047	ggggtcgacgtcgagggg	sos
1048	ggggaacgttaacgttgggggg	sos
1049	ggggacgtcgacgtggggg	sos
1050	gcactcttcgaagctacagccggcagcctctgat	
1051	cggctcttccatgaggtctttgctaatcttgg	
1052	cggctcttccatgaaagtctttggacgatgtgagc	
1053	tcctgcaggttaagt	s
1054	gggggtcgttcgttgggggg	sos
1055	gggggatgattgttgggggg	sos
1056	gggggazgatzgttgggggg	sos
1057	gggggagctagcttgggggg	sos
1058	ggttcttttggtccttgtct	s
1059	ggttcttttggtcctcgtct	s
1060	ggttcttttggtccttatct	s
1061	ggttcttggtttccttgtct	s
1062	tggtcttttggtccttgtct	s
1063	ggttcaaatggtccttgtct	s
1064	gggtcttttgggccttgtct	s
1065	tccaggacttctctcaggtttttt	s
1066	tccaaaacttctctcaaatt	s
1067	tactacttttatacttttatactt	s
1068	tgtgtgtgtgtgtgtgtgtgtg	s
1069	ttgttgttgttgtttgttgttgttg	s
1070	ggctccggggagggaatttttgtctat	s
1071	gggacgatcgtcgggggg	sos
1072	gggtcgtcgacgaggggggg	sos
1073	ggtcgtcgacgaggggggg	sos
1074	gggtcgtcgtcgtgggggg	sos
1075	ggggacgatcgtcgggggg	sos
1076	ggggacgtcgtcgtgggggg	sos
1077	ggggtcgacgtcgacgtcgaggggggg	sos
1078	ggggaaccgcggttgggggg	sos
1079	ggggacgacgtcgtgggggg	sos
1080	tcgtcgtcgtcgtcgtgggggg	sos
1081	tcctgccggggaagt	s
1082	tcctgcaggggaagt	s
1083	tcctgaaggggaagt	s
1084	tcctggcgggcaagt	s
1085	tcctggcgggtaagt	s
1086	tcctggcgggaaagt	s
1087	tccgggcggggaagt	s
1088	tcggggcggggaagt	s
1089	tcccggcggggaagt	s
1090	gggggacgttggggg	s
1091	ggggtttttttttgggggg	sos
1092	ggggccccccccccgggggg	sos
1093	ggggttgttgttgttgggggg	sos

[0053] In some embodiments, the immunostimulatory nucleic acid is a CpG nucleic acid. CpG sequences, while relatively rare in human DNA are commonly found in the DNA of infectious organisms such as bacteria. The human immune system has apparently evolved to recognize CpG sequences as an early warning sign of infection and to initiate an immediate and powerful immune response against invading pathogens without causing adverse reactions frequently seen with other immune stimulatory agents. Thus CpG containing nucleic acids, relying on this innate immune defense mechanism can utilize a unique and natural pathway for immune therapy. The effects of CpG nucleic acids on immune modulation have been described extensively in published patent applications, such as PCT US95/01570), PCT/US97/19791, PCT/US98/03678; PCT/US98/10408; PCT/US98/04703; PCT/US99/07335; and PCT/US99/

09863. The entire contents of each of these patent applications is hereby incorporated by reference.

[0054] A CpG nucleic acid is a nucleic acid which includes at least one unmethylated CpG dinucleotide. A nucleic acid containing at least one unmethylated CpG dinucleotide is a nucleic acid molecule which contains an unmethylated cytosine in a 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 the immune system. The CpG nucleic acids can be double-stranded or single-stranded. Generally, double-stranded molecules are more stable in vivo, while single-stranded molecules have increased immune activity. Thus in some aspects of the invention it is preferred that the nucleic acid be single stranded and in other aspects it is preferred that the nucleic acid be double stranded. The terms CpG nucleic acid or CpG oligonucleotide as used herein refer to an immunostimulatory CpG nucleic acid or a nucleic acid unless otherwise indicated. The entire immunostimulatory nucleic acid can be unmethylated or portions may be unmethylated but at least the C of the 5' CG 3' must be unmethylated.

[0055] In one preferred embodiment the invention provides an immunostimulatory nucleic acid which is a CpG nucleic acid represented by at least the formula:

$$5'X_1X_2CGX_3X_43'$$

wherein X_1, X_2,X_3, and X_4 are nucleotides. In one embodiment X_2 is adenine, guanine, cytosine, or thymine. In another embodiment X_3 is cytosine, guanine, adenine, or thymine. In other embodiments X_2 is adenine, guanine, or thymine and X_3 is cytosine, adenine, or thymine.

[0056] In another embodiment the immunostimulatory nucleic acid is an isolated CpG nucleic acid represented by at least the formula:

$$5'N_1X_1X_2CGX_3X_4N_23'$$

wherein X_1, X_2,X_3, and X_4 are nucleotides and N is any nucleotide and N_1 and N_2 are nucleic acid sequences composed of from about 0-25 N's each. In one embodiment X_1X_2 are nucleotides selected from the group consisting of: GpT, GpG, GpA, ApA, ApT, ApG, CpT, CpA, CpG, TpA, TpT, and TpG; and X_3X_4 are nucleotides selected from the group consisting of: TpT, ApT, TpG, ApG, CpG, TpC, ApC, CpC, TpA, ApA, and CpA. Preferably X_1X_2 are GpA or GpT and X_3X_4 are TpT. In other embodiments X_1 or X_2 or both are purines and X_3 or X_4 or both are pyrimidines or X_1X_2 are GpA and X_3 or X_4 or both are pyrimidines. In another preferred embodiment X_1X_2 are nucleotides selected from the group consisting of: TpA, ApA, ApC, ApG, and GpG. In yet another embodiment X_3X_4 are nucleotides selected from the group consisting of: TpT, TpA, TpG, ApA, ApG, ApC, and CpA. X_1X_2 in another embodiment are nucleotides selected from the group consisting of: TpT, TpG, ApT, GpC, CpC, CpT, TpC, GpT and CpG.

[0057] In another preferred embodiment the immunostimulatory nucleic acid has the sequence $5'TCN_1TX_1X_2CGX_3X_43'$. The immunostimulatory nucleic acids of the invention in some embodiments include X_1X_2 selected from the group consisting of GpT, GpG, GpA and ApA and X_3X_4 is selected from the group consisting of TpT, CpT and TpC.

[0058] In other embodiments, the CpG oligonucleotide has a sequence selected from the group consisting of SEQ ID NO: 1, 3, 4, 14-16, 18-24, 28, 29, 33-46, 49, 50, 52-56, 58, 64-67, 69, 71, 72, 76-87, 90, 91, 93, 94, 96, 98, 102-124, 126-128, 131-133, 136-141, 146-150, 152-153, 155-171, 173-178, 180-186, 188-198, 201, 203-214, 216-220, 223, 224, 227-240, 242-256, 258, 260-265, 270-273, 275, 277-281, 286-287, 292, 295-296, 300, 302, 305-307, 309-312, 314-317, 320-327, 329, 335, 337-341, 343-352, 354, 357, 361-365, 367-369, 373-376, 378-385, 388-392, 394, 395, 399, 401-404, 406-426, 429-433, 434-437, 439, 441-443, 445, 447, 448, 450, 453-456, 460-464, 466-469, 472-475, 477, 478, 480, 483-485, 488, 489, 492, 493, 495-502, 504-505, 507-509, 511, 513-529, 532-541, 543-555, 564-566, 568-576, 578, 580, 599, 601-605, 607-611, 613-615, 617, 619-622, 625-646, 648-650, 653-664, 666-697,699-706, 708, 709,711-716,718-732, 736, 737,739-744, 746, 747,749-761, 763,766-767, 769, 772-779, 781-783, 785-786, 7900792, 798-799, 804-808, 810, 815, 817, 818, 820-832, 835-846, 849-850, 855-859, 862, 865, 872, 874-877, 879-881, 883-885, 888-904, and 909-913.

[0059] For facilitating uptake into cells, the immunostimulatory nucleic acids are preferably in the range of 6 to 100 bases in length. However, nucleic acids of any size greater than 6 nucleotides (even many kb long) are capable of inducing an immune response according to the invention if sufficient immunostimulatory motifs are present. Preferably the immunostimulatory nucleic acid is in the range of between 8 and 100 and in some embodiments between 8 and 50 or 8 and 30 nucleotides in size.

[0060] "Palindromic sequence" shall mean an inverted repeat (i.e. a sequence such as ABCDEE'D'C'B'A' in which A and A' are bases capable of forming the usual Watson-Crick base pairs. In vivo, such sequences may form double-stranded structures. In one embodiment the CpG nucleic acid contains a palindromic sequence. A palindromic sequence used in this context refers to a palindrome in which the CpG is part of the palindrome, and preferably is the center of the palindrome. In another embodiment the CpG nucleic acid is free of a palindrome. An immunostimulatory nucleic acid that is free of a palindrome is one in which the CpG dinucleotide is not part of a palindrome. Such an oligonucleotide may include a palindrome in which the CpG is not the center of the palindrome.

[0061] The CpG nucleic acid sequences of the invention are those broadly described above as well as disclosed in PCT Published Patent Applications PCT/US95/01570 and PCT/US97/19791 claiming priority to U.S. Ser. Nos. 08/386,063 and 08/960,774, filed on Feb. 7, 1995 and Oct. 30, 1997 respectively.

[0062] The immunostimulatory nucleic acids of the invention also include nucleic acids having T-rich motifs. It was recently discovered by Dr. Arthur Krieg that T-rich nucleic acids were immunostimulatory. It was presented by Dr. Krieg at the International Workshop on "Immunobiology of Bacterial CpG-DNA" held in Upper Bavaria on Sep. 26-29, 1999 that poly-T nucleic acids of 24 bases in length are immunostimulatory, whereas the same length poly-C oligonucleotide is non-stimulatory. These concepts are also described and claimed in U.S. Provisional Patent Application No. 60/156,113 filed on Sep. 25, 1999, which is hereby incorporated by reference.

[0063] Poly-G containing nucleic acids are also immunostimulatory. PCT published patent application number WO 00/14217, which claims priority to German Patent Application No. 98 11 6652.3, filed on Sep. 3, 1998 describes poly-G-containing oligonucleotides and their uses. A variety of other references, including Pisetsky and Reich, 1993 *Mol. Biol. Reports,* 18:217-221; Krieger and Herz, 1994, *Ann. Rev. Biochem.,* 63:601-637; Macaya et al., 1993, *PNAS,* 90:3745-3749; Wyatt et al., 1994, *PNAS,* 91:1356-1360; Rando and Hogan, 1998, In Applied Antisense Oligonucleotide Technology, ed. Krieg and Stein, p. 335-352; and Kimura et al., 1994, *J. Biochem.* 116, 991-994 also describe the immunostimulatory properties of poly-G nucleic acids. Poly-G-containing nucleotides are useful for treating and preventing bacterial and viral infections.

[0064] In some aspects of the invention the poly-G containing nucleic acids are administered alone for the treatment of asthma and allergy. It was previously suggested in the prior art that poly-G rich oligonucleotides inhibit the production of IFN-δ by compounds such as CpG oligonucleotides, concanavalin A, bacterial DNA, or the combination of PMA and the calcium ionophore A 23187 (Halperin and Pisetsky, 1995, *Immunopharmacol.,* 29:47-52, as well as block the downstream effects of IFN-δ. For instance, Ramanathan et al., 1994, *Transplantation,* 57:612-615, has shown that a poly-G oligonucleotide inhibits the binding of IFN-δ to its receptor, which prevents the normal enhancement of MHC Class 1 and ICAM-1 in response to IFN-δ. Poly-G oligonucleotides were also found to be able to inhibit the secretion of IFN-δ from lymphocytes (Halperin and Pisetsky, 1995, *Immunopharmacol.,* 29:47-52). It was surprisingly, discovered according to the invention that when poly-G nucleic acids are administered in vivo, they are useful for treating or preventing allergy or asthma. Thus, in this aspect of the invention, poly-G nucleic acids are administered alone or optionally with other asthma/allergy medicaments for the treatment of allergy and/or asthma.

[0065] Poly-G nucleic acids preferably are nucleic acids having the following formulas:

$$5'\ X_1X_2GGGX_3X_4\ 3'$$

wherein X_1, X_2, X_3, and X_4 are nucleotides. In preferred embodiments at least one of X_3 and X_4 are a G. In other embodiments both of X_3 and X_4 are a G. In yet other embodiments the preferred formula is 5' GGGNGGG 3', or 5' GGGNGGGNGGG 3' wherein N represents between 0 and 20 nucleotides. In other embodiments the poly-G nucleic acid is free of unmethylated CG dinucleotides, while in other embodiments the poly-G nucleic acid includes at least one unmethylated CG dinucleotide.

[0066] The poly G nucleic acid in some embodiments is selected from the group consisting of SEQ ID NO: 5, 6, 73, 215, 267-269, 276, 282, 288, 297-299, 355, 359, 386, 387, 444, 476, 531, 557-559, 733, 768, 795, 796, 914-925, 928-931, 933-936, and 938. In other embodiments, the poly G nucleic acid includes a sequence selected from the group consisting of SEQ ID NO: 67, 80-82, 141, 147, 148, 173, 178, 183, 185, 214, 224, 264, 265, 315, 329, 434, 435, 475, 519, 521-524, 526, 527, 535, 554, 565, 609, 628, 660, 661, 662, 725, 767, 825, 856, 857, 876, 892, 909, 926, 927, 932, and 937. In some embodiments, the entire backbone of the poly-G nucleic acid is phosphorothioate.

[0067] In related embodiments, the invention also contemplates the use of immunostimulatory nucleic acids that comprise one and preferably two poly-G motifs, even more preferably flanking a palindrome. Such immunostimulatory nucleic acids preferably have a chimeric backbone (i.e., their backbone is comprised of both phosphodiester and phosphorothioate linkages). Even more preferably, the phosphorothioate linkages in these latter immunostimulatory nucleic acids are located at the 5' and 3' ends of the nucleic acid. Examples of suitable palindromes include, but are not limited to AACGTT; AAGCTT; AGCGCT; TCGA; TTCGAA; ACGT; GACGTC; and CACGTG.

[0068] Nucleic acids having modified backbones, such as phosphorothioate backbones, 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.

[0069] The backbone characteristics of the nucleic acids listed in Table 1 are also shown. Some of the designations in the Table are as follows: o or po=phosphodiester, s=phosphorothioate, sos=chimeric.

[0070] In the case when the immunostimulatory nucleic acid is administered in conjunction with a nucleic acid vector, it is preferred that the backbone of the immunostimulatory nucleic acid be a chimeric combination of phosphodiester and phosphorothioate (or other phosphate modification). The cell may have a problem taking up a plasmid vector in the presence of completely phosphorothioate oligonucleotide. Thus when both a vector and an oligonucleotide are delivered to a subject, it is preferred that the oligonucleotide have a chimeric backbone or have a phosphorothioate backbone but that the plasmid is associated with a vehicle that delivers it directly into the cell, thus avoiding the need for cellular uptake. Such vehicles are known in the art and include, for example, liposomes and gene guns.

[0071] For use in the instant invention, the immunostimulatory nucleic acids can be synthesized de novo using any of a number of procedures well known in the art. Such compounds are referred to as "synthetic nucleic acids." For example, the b-cyanoethyl phosphoramidite method (Beaucage, S. L., and Caruthers, M. H., *Tet. Let.* 22:1859, 1981); nucleoside H-phosphonate method (Garegg et al., *Tet. Let.* 27:4051-4054, 1986; Froehler et al., *Nucl. Acid. Res.* 14:5399-5407, 1986,; Garegg et al., *Tet. Let.* 27:4055-4058, 1986, Gaffney et al., *Tet. Let.* 29:2619-2622, 1988). These chemistries can be performed by a variety of automated oligonucleotide synthesizers available in the market. These nucleic acids are referred to as synthetic nucleic acids. Alternatively, immunostimulatory 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. Nucleic acids can be prepared from existing nucleic acid sequences (e.g., genomic or cDNA) using known techniques, such as those employing restriction enzymes, exonucleases or endonucleases. Nucleic acids prepared in this manner are referred to as isolated nucleic acids. The term "immunostimulatory nucleic acid" encompasses both synthetic and isolated immunostimulatory nucleic acids.

[0072] For use in vivo, nucleic acids are preferably relatively resistant to degradation (e.g., are stabilized). A "stabilized nucleic acid molecule" shall mean a nucleic acid molecule that is relatively resistant to in vivo degradation (e.g. via an exo- or endo-nuclease). Stabilization can be a function of length or secondary structure. Immunostimulatory nucleic acids that are tens to hundreds of kbs long are relatively resistant to in vivo degradation. For shorter immunostimulatory nucleic acids, secondary structure can stabilize and increase their effect. For example, if the 3' end of a nucleic acid has self-complementarity to an upstream region, so that it can fold back and form a sort of stem loop structure, then the o nucleic acid becomes stabilized and therefore exhibits more activity.

[0073] Alternatively, nucleic acid stabilization can be accomplished via backbone modifications. Preferred stabilized nucleic acids of the instant invention have a modified backbone. It has been demonstrated that modification of the nucleic acid backbone provides enhanced activity of the immunostimulatory nucleic acids when administered in vivo. One type of modified backbone is a phosphate backbone modification. Immunostimulatory 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, can in some circumstances provide maximal activity and protect the nucleic acid from degradation by intracellular exo- and endo-nucleases. Other phosphate modified nucleic acids include phosphodiester modified nucleic acids, combinations of phosphodiester and phosphorothioate nucleic acids, methylphosphonate, methylphosphorothioate, phosphorodithioate, and combinations thereof. Each of these combinations in CpG nucleic acids and their particular effects on immune cells is discussed in more detail in PCT Published Patent Applications PCT/US95/01570 and PCT/US97/19791, the entire contents of which are hereby incorporated by reference. Although Applicants are not bound by the theory, it is believed that these phosphate modified nucleic acids may show more stimulatory activity due to enhanced nuclease resistance, increased cellular uptake, increased protein binding, and/or altered intracellular localization.

[0074] Modified backbones such as phosphorothioates may be synthesized using automated techniques employing either phosphoramidate or H-phosphonate chemistries. Aryl-and alkyl-phosphonates can be made, e.g., as described in U.S. Pat. No. 4,469,863; and alkylphosphotriesters (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 (Uhlmann, E. and Peyman, A., *Chem. Rev.* 90:544, 1990; Goodchild, J., *Bioconjugate Chem.* 1:165, 1990).

[0075] Both phosphorothioate and phosphodiester nucleic acids containing immunostimulatory motifs are active in immune cells. However, based on the concentration needed to induce immunostimulatory nucleic acid specific effects, the nuclease resistant phosphorothioate backbone immunostimulatory nucleic acids are more potent (2 μg/ml for the phosphorothioate vs. a total of 90 μg/ml for phosphodiester).

[0076] Another type of modified backbone, useful according to the invention, is a peptide nucleic acid. The backbone is composed of aminoethylglycine and supports bases which provide the DNA-character. The backbone does not include any phosphate and thus may optionally have no net charge. The lack of charge allows for stronger DNA-DNA binding because the charge repulsion between the two strands does not exist. Additionally, because the backbone has an extra methylene group, the oligonucleotides are enzyme/protease resistant. Peptide nucleic acids can be purchased from various commercial sources, e.g., Perkin Elmer, C. A. or synthesized de novo.

[0077] Another class of backbone modifications include 2'-O-methylribonucleosides (2'-Ome). These types of substitutions are described extensively in the prior art and in particular with respect to their immunostimulating properties in Zhao et al., *Bioorganic and Medicinal Chemistry Letters,* 1999, 9:24:3453. Zhao et al. describes methods of preparing 2'-Ome modifications to nucleic acids.

[0078] The nucleic acid molecules of the invention may include naturally-occurring or synthetic purine or pyrimidine heterocyclic bases as well as modified backbones. Purine or pyrimidine heterocyclic bases include, but are not limited to, adenine, guanine, cytosine, thymidine, uracil, and inosine. Other representative heterocyclic bases are disclosed in U.S. Pat. No. 3,687,808, issued to Merigan, et al. The term purine or pyrimidine or bases are used herein to refer to both naturally-occurring or synthetic purines, pyrimidines or bases.

[0079] Other stabilized nucleic acids include: nonionic DNA analogs, such as alkyl- and aryl-phosphates (in which the charged phosphonate oxygen is replaced by an alkyl or aryl group), phosphodiester and alkylphosphotriesters, in which the charged oxygen moiety is alkylated. Nucleic acids which contain diol, such as tetraethyleneglycol or hexaethyleneglycol, at either or both termini have also been shown to be substantially resistant to nuclease degradation.

[0080] 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, phosphorodithioate, 2'-Ome and combinations thereof.

[0081] 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 within the context of modified backbones refers to an amount greater than 50%. 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 55%, 60%, 65%, 70%, 75%, 80,%, 85%, 90%, 95%, or 100% of the chiral centers have S or R chirality. In other embodiments at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% of the nucleotides have backbone modifications.

[0082] The S- and R-chiral immunostimulatory nucleic acids may be prepared by any method known in the art for producing chirally pure oligonucleotides. The Stec et al reference teaches methods for producing stereopure phosphorothioate oligodeoxynucleotides using an oxathiaphospholane. (Stec, W. J., et al., 1995, *J. Am. Chem. Soc.,* 117:12019). Other methods for making chirally pure oligonucleotides have been described by companies such as ISIS Pharmaceuticals. US Patents have also described these methods. For instance U.S. Pat. Nos. 5,883,237; 5,837,856; 5,599,797; 5,512,668; 5,856,465; 5,359,052; 5,506,212; 5,521,302; and 5,212,295, each of which is hereby incorporated by reference in its entirety, disclose methods for generating stereopure oligonucleotides.

[0083] The immunostimulatory nucleic acids are useful for treating or preventing allergy or asthma in a subject. A "subject" shall mean a human or vertebrate mammal including but not limited to a dog, cat, horse, cow, pig, sheep, goat, or primate, e.g., monkey.

[0084] The immunostimulatory nucleic acids are useful in some aspects of the invention as a prophylactic for the treatment of a subject at risk of developing an allergy or asthma where the exposure of the subject to an allergen or predisposition to asthma is known or suspected. A "subject at risk" of developing allergy or asthma as used herein is a subject who has any risk of exposure to an allergen or a risk of developing asthma, i.e. someone who has suffered from an asthmatic attack previously or has a predisposition to asthmatic attacks. For instance, a subject at risk may be a subject who is planning to travel to an area where a particular type of allergen or asthmatic initiator is found or it may even be any subject living in an area where an allergen has been identified. If the subject develops allergic responses to a particular antigen and the subject may be exposed to the antigen, i.e., during pollen season, then that subject is at risk of exposure to the antigen. A subject at risk of developing an allergy or asthma includes those subjects that have been identified as having an allergy or asthma but that don't have the active disease during the treatment of the invention as well as subjects that are considered to be at risk of developing these diseases because of genetic or environmental factors.

[0085] In addition to the use of the immunostimulatory nucleic acid and the asthma/allergy medicament for prophylactic treatment, the invention also encompasses the use of the combination of drugs for the treatment of a subject having an allergy or asthma. A "subject having an allergy" is a subject that has an allergic reaction in response to an allergen. An "allergy" refers to acquired hypersensitivity to a substance (allergen).

[0086] The allergic reaction in man and animals has been extensively studied and the basic immune mechanisms involved are well known. Allergic conditions or diseases in humans include but are not limited to eczema, allergic rhinitis or coryza, hay fever, conjunctivitis, bronchial or allergic asthma, urticaria (hives) and food allergies; atopic dermatitis; anaphylaxis; drug allergy; angioedema; and allergic conjunctivitis. Allergic diseases in dogs include but are not limited to seasonal dermatitis; perennial dermatitis; rhinitis: conjunctivitis; allergic asthma; and drug reactions. Allergic diseases in cats include but are not limited to dermatitis and respiratory disorders; and food allergens. Allergic diseases in horses include but are not limited to respiratory disorders such as "heaves" and dermatitis. Allergic diseases in non-human primates include but are not limited to allergic asthma and allergic dermatitis.

[0087] The generic name for molecules that cause an allergic reaction is allergen. There are numerous species of allergens. The allergic reaction occurs when tissue-sensitizing immunoglobulin of the IgE type reacts with foreign allergen. The IgE antibody is bound to mast cells and/or basophils, and these specialized cells release chemical mediators (vasoactive amines) of the allergic reaction when stimulated to do so by allergens bridging the ends of the antibody molecule. Histamine, platelet activating factor, arachidonic acid metabolites, and serotonin are among the best known mediators of allergic reactions in man. Histamine and the other vasoactive amines are normally stored in mast cells and basophil leukocytes. The mast cells are dispersed throughout animal tissue and the basophils circulate within the vascular system. These cells manufacture and store histamine within the cell unless the specialized sequence of events involving IgE binding occurs to trigger its release.

[0088] The symptoms of the allergic reaction vary, depending on the location within the body where the IgE reacts with the antigen. If the reaction occurs along the respiratory epithelium the symptoms are sneezing, coughing and asthmatic reactions. If the interaction occurs in the digestive tract, as in the case of food allergies, abdominal pain and diarrhea are common. Systematic reactions, for example following a bee sting, can be severe and often life threatening.

[0089] Delayed type hypersensitivity, also known as type IV allergy reaction is an allergic reaction characterized by a delay period of at least 12 hours from invasion of the antigen into the allergic subject until appearance of the inflammatory or immune reaction. The T lymphocytes (sensitized T lymphocytes) of individuals in an allergic condition react with the antigen, triggering the T lymphocytes to release lymphokines (macrophage migration inhibitory factor (MIF), macrophage activating factor (MAF), mitogenic factor (MF), skin-reactive factor (SRF), chemotactic factor, neovascularization-accelerating factor, etc.), which function as inflammation mediators, and the biological activity of these lymphokines, together with the direct and indirect effects of locally appearing lymphocytes and other inflammatory immune cells, give rise to the type IV allergy reaction. Delayed allergy reactions include tuberculin type reaction, homograft rejection reaction, cell-dependent type protective reaction, contact dermatitis hypersensitivity reaction, and the like, which are known to be most strongly suppressed by steroidal agents. Consequently, steroidal agents are effective against diseases which are caused by delayed allergy reactions. Long-term use of steroidal agents at concentrations currently being used can, however, lead to the serious side-effect known as steroid dependence. The methods of the invention solve some of these problems, by providing for lower and fewer doses to be administered.

[0090] Immediate hypersensitivity (or anaphylactic response) is a form of allergic reaction which develops very quickly, i.e. within seconds or minutes of exposure of the patient to the causative allergen, and it is mediated by IgE antibodies made by B lymphocytes. In nonallergic patients, there is no IgE antibody of clinical relevance; but, in a person suffering with allergic diseases, IgE antibody mediates immediate hypersensitivity by sensitizing mast cells which are abundant in the skin, lymphoid organs, in the membranes of the eye, nose and mouth, and in the respiratory tract and intestines.

[0091] Mast cells have surface receptors for IgE, and the IgE antibodies in allergy-suffering patients become bound to them. As discussed briefly above, when the bound IgE is subsequently contacted by the appropriate allergen, the mast cell is caused to degranulate and to release various substances called bioactive mediators, such as histamine, into the surrounding tissue. It is the biologic activity of these substances which is responsible for the clinical symptoms typical of immediate hypersensitivity; namely, contraction of smooth muscle in the airways or the intestine, the dilation of small blood vessels and the increase in their permeability to water and plasma proteins, the secretion of thick sticky mucus, and in the skin, redness, swelling and the stimulation of nerve endings that results in itching or pain.

[0092] Many allergies are caused by IgE antibody generation against harmless allergens. The cytokines that are induced by administration of immunostimulatory nucleic acids are predominantly of a class called "Th1" (examples are IL-12 and IFN-γ). Cytokine production by helper $CD4^+$ (and also in $CD8^+$) T cells frequently fall into one of two phenotypes, Th1 and Th2, in both murine and human systems (Romagnani, 1991, Immunol Today 12: 256-257, Mosmann, 1989, Annu Rev Immunol, 7: 145-173). Th1 cells produce interleukin 2 (IL-2), tumor necrosis factor (TNFα) and interferon gamma (IFNγ) and they are responsible primarily for cell-mediated immunity such as delayed type hypersensitivity. Th2 cells produce interleukins, IL-4, IL-5, IL-6, IL-9, IL-10 and IL-13 and are primarily involved in providing optimal help for humoral immune responses such as IgE and IgG4 antibody isotype switching (Mosmann, 1989, Annu Rev Immunol, 7: 145-173).

[0093] The types of antibodies associated with a Th1 response are generally more protective because they have high neutralization and opsonization capabilities. Th2 responses involve predominately antibodies and these have less protective effect against infection and some Th2 isotypes (e.g., IgE) are associated with allergy. Strongly polarized Th1 and Th2 responses not only play different roles in protection, they can promote different immunopathological reactions. Th1-type responses are involved organ specific autoimmunity such as experimental autoimmune uveoretinitis (Dubey et al, 1991, Eur Cytokine Network 2: 147-152), experimental autoimmune encephalitis (EAE) (Beraud et al, 1991, Cell Immunol 133: 379-389) and insulin dependent diabetes mellitus (Hahn et al, 1987, *Eur. J. Immunol.* 18: 2037-2042), in contact dermatitis (Kapsenberg et al, Immunol Today 12: 392-395), and in some chronic inflammatory disorders. In contrast Th2-type responses are responsible for triggering allergic atopic disorders (against common environmental allergens) such as allergic asthma (Walker et al, 1992, Am Rev Resp Dis 148: 109-115) and atopic dermatitis (van der Heijden et al, 1991, J Invest Derm 97: 389-394), are thought to exacerbate infection with tissue-dwelling protozoa such as helminths (Finkelman et al, 1991, Immunoparasitol Today 12: A62-66) and *Leishmania major* (Caceres-Dittmar et al, 1993, Clin Exp Immunol 91: 500-505), are preferentially induced in certain primary immunodeficiencies such as hyper-IgE syndrome (Del Prete et al, 1989, J Clin Invest 84: 1830-1835) and Omenn's syndrome (Schandene et al, 1993, Eur J Immunol 23: 56-60), and are associated with reduced ability to suppress HIV replication (Barker et al, 1995, Proc Soc Nat Acad Sci USA 92: 11135-11139).

[0094] Thus, in general, it appears that allergic diseases are mediated by Th2 type immune responses. Based on the ability of the immunostimulatory nucleic acid to shift the immune response in a subject from a Th2 (which is associated with production of IgE antibodies and allergy and asthma) to a Th1 response (which is protective against allergic and asthmatic reactions), an effective dose for inducing an immune response of a immunostimulatory nucleic acid can be administered to a subject to treat or prevent an allergy or asthma.

[0095] Th2 cytokines, especially IL-4 and IL-5 are elevated in the airways of asthmatic subjects. These cytokines promote important aspects of the asthmatic inflammatory response, including IgE isotype switching, eosinophil chemotaxis and activation, and mast cell growth. Th1 cytokines, especially IFN-γ and IL-12, can suppress the formation of Th2 clones and production of Th2 cytokines. Thus, the immunostimulatory nucleic acid has significant therapeutic utility in the treatment of allergic conditions and asthma.

[0096] An "allergen" as used herein is a molecule capable of provoking an immune response characterized by production of IgE. Thus, in the context of this invention, the term allergen means a specific type of antigen which can trigger an allergic response which is mediated by IgE antibody. The method and preparations of this invention extend to a broad class of such allergens and fragments of allergens or haptens acting as allergens. Allergens include but are not limited to Environmental Aeroallergens; plant pollens such as Ragweed/hayfever; Weed pollen allergens; Grass pollen allergens; Johnson grass; Tree pollen allergens; Ryegrass; House dust mite allergens; Storage mite allergens; Japanese cedar pollen/hay fever Mold spore allergens; Animal allergens (cat, dog, guinea pig, hamster, gerbil, rat, mouse); Food Allergens (e.g., Crustaceans; nuts, such as peanuts; citrus fruits); Insect Allergens (Other than mites listed above); Venoms: (Hymenoptera, yellow jacket, honey bee, wasp, hornet, fire ant); Other environmental insect allergens from cockroaches, fleas, mosquitoes, etc.; Bacteria such as streptococcal antigens; Parasites such as *Ascaris* antigen; Viral Antigens; Fungal spores; Drug Allergens; Antibiotics; penicillins and related compounds; other antibiotics; Whole Proteins such as hormones (insulin), enzymes (Streptokinase); all drugs and their metabolites capable of acting as incomplete antigens or haptens; Industrial Chemicals and metabolites capable of acting as haptens and stimulating the immune system (Examples are the acid anhydrides (such as trimellitic anhydride) and the isocyanates (such as toluene diisocyanate)); Occupational Allergens such as flour (ie. Baker's asthma), castor bean, coffee bean, and industrial chemicals described above; flea allergens; and human proteins in non-human animals.

[0097] Allergens include but are not limited to cells, cell extracts, proteins, polypeptides, peptides, polysaccharides, polysaccharide conjugates, peptide and non-peptide mimics of polysaccharides and other molecules, small molecules, lipids, glycolipids, and carbohydrates. Many allergens, however, are protein or polypeptide in nature, as proteins and polypeptides are generally more antigenic than carbohydrates or fats.

[0098] Examples of specific natural, animal and plant allergens include but are not limited to proteins specific to the following genuses: *Canine* (*Canis familiaris*); *Dermatophagoides* (e.g. *Dermatophagoides farinae*); *Felis* (*Felis domesticus*); *Ambrosia* (*Ambrosia artemiisfolia; Lolium* (e.g. *Lolium perenne* or *Lolium multiflorum*); *Cryptomeria* (*Cryptomeria japonica*); *Alternaria* (*Alternaria alternata*); *Alder; Alnus* (*Alnus gultinoasa*); *Betula* (*Betula verrucosa*); *Quercus* (*Quercus alba*); *Olea* (*Olea europa*); *Artemisia* (*Artemisia vulgaris*); *Plantago* (e.g. *Plantago lanceolata*); *Parietaria* (e.g. *Parietaria officinalis* or *Parietaria judaica*); *Blattella* (e.g. *Blattella germanica*); *Apis* (e.g. *Apis multiflorum*); *Cupressus* (e.g. *Cupressus sempervirens, Cupressus arizonica* and *Cupressus macrocarpa*); *Juniperus* (e.g. *Juniperus sabinoides, Juniperus virginiana, Juniperus communis* and *Juniperus ashei*); *Thuya* (e.g. *Thuya orientalis*); *Chamaecyparis* (e.g. *Chamaecyparis obtusa*); *Periplaneta* (e.g. *Periplaneta americana*); *Agropyron* (e.g. *Agropyron repens*); *Secale* (e.g. *Secale cereale*); *Triticum* (e.g. *Triticum aestivum*); *Dactylis* (e.g. *Dactylis glomerata*); *Festuca* (e.g. *Festuca elatior*); *Poa* (e.g. *Poa pratensis* or *Poa compressa*); *Avena* (e.g. *Avena sativa*); *Holcus* (e.g. *Holcus lanatus*); *Anthoxanthum* (e.g. *Anthoxanthum odoratum*); *Arrhenatherum* (e.g. *Arrhenatherum elatius*); *Agrostis* (e.g. *Agrostis alba*); *Phleum* (e.g. *Phleum pratense*); *Phalaris* (e.g. *Phalaris arundinacea*); *Paspalum* (e.g. *Paspalum notatum*); *Sorghum* (e.g. *Sorghum halepensis*); and *Bromus* (e.g. *Bromus inermis*).

[0099] A "subject having asthma" is a subject that has a disorder of the respiratory system characterized by inflammation, narrowing of the airways and increased reactivity of the airways to inhaled agents. Asthma is frequently, although not exclusively associated with atopic or allergic symptoms. An "initiator" as used herein refers to a composition or environmental condition which triggers asthma. Initiators include, but are not limited to, allergens, cold temperatures, exercise, viral infections, SO_2.

[0100] In another aspect the invention provides methods for treating or preventing asthma or allergy in a hypo-responsive subject. As used herein, a hypo-responsive subject is one who has previously failed to respond to a treatment directed at treating or preventing asthma or allergy or one who is at risk of not responding to such a treatment. The treatment directed at treating or preventing asthma or allergy may be an asthma/allergy medicament, in which case the hypo-responsive subject is one who is hypo-responsive to an asthma/allergy medicament.

[0101] Other subjects who are hypo-responsive include those who are refractory to an asthma/allergy medicament. As used herein, the term "refractory" means resistant or failure to yield to treatment. Such subjects may be those who never responded to an asthma/allergy medicament (i.e., subjects who are non-responders), or alternatively, they may be those who at one time responded to an asthma/allergy medicament, but have since that time have become refractory to the medicament. In some embodiments, the subject is one who is refractory to a subset of medicaments. A subset of medicaments is at least one medicament. In some embodiments, a subset refers to 2, 3, 4, 5, 6, 7, 8, 9, or 10 medicaments.

[0102] In other embodiments, hypo-responsive subjects are elderly subjects, regardless of whether they have or have not previously responded to a treatment directed at treating or preventing asthma or allergy. Elderly subjects, even those who have previously responded to such treatment, are considered to be at risk of not responding to a future administration of this treatment. Similarly, neonatal subjects are also considered to be at risk of not responding to treatment directed at treating or preventing asthma or allergy.

[0103] In some embodiments, an immunostimulatory nucleic acid is administered to the hypo-responsive subject without the further administration of an asthma/allergy medicament. In yet other embodiments, an asthma/allergy medicament is administered to the hypo-responsive subject, in which case it may be administered substantially simultaneously (i.e., concurrently) with, or following the administration of the immunostimulatory nucleic acid.

[0104] An "asthma/allergy medicament" as used herein is a composition of matter which reduces the symptoms, inhibits the asthmatic or allergic reaction, or prevents the development of an allergic or asthmatic reaction. Various types of medicaments for the treatment of asthma and allergy are described in the Guidelines For The Diagnosis and Management of Asthma, Expert Panel Report 2, NIH Publication No. 97/4051, Jul. 19, 1997, the entire contents of which are incorporated herein by reference. The summary of the medicaments as described in the NIH publication is presented below.

[0105] In most embodiments the asthma/allergy medicament is useful to some degree for treating both asthma and allergy. Some asthma/allergy medicaments are preferably used in combination with the immunostimulatory nucleic acids to treat asthma. These are referred to as asthma medicaments. Asthma medicaments include, but are not limited, PDE-4 inhibitors, bronchodilator/beta-2 agonists, K+ channel openers, VLA-4 antagonists, neurokin antagonists, TXA2 synthesis inhibitors, xanthanines, arachidonic acid antagonists, 5 lipoxygenase inhibitors, thromboxin A2 receptor antagonists, thromboxane A2 antagonists, inhibitor of 5-lipox activation proteins, and protease inhibitors.

[0106] Bronchodilator/beta-2 agonists are a class of compounds which cause bronchodilation or smooth muscle relaxation. Bronchodilator/beta-2 agonists include, but are not limited to, salmeterol, salbutamol, albuterol, terbutaline, D2522/formoterol, fenoterol, bitolterol, pirbuerol methylxanthines and orciprenaline. Long-acting β_2 agonists and bronchodilators are compounds which are used for long-term prevention of symptoms in addition to the anti-inflammatory therapies. They function by causing bronchodilation, or smooth muscle relaxation, following adenylate cyclase activation and increase in cyclic AMP producing functional antagonism of bronchoconstriction. These compounds also inhibit mast cell mediator release, decrease vascular permeability and increase mucociliary clearance. Long-acting β_2 agonists include, but are not limited to, salmeterol and albuterol. These compounds are usually used in combination

with corticosteroids and generally are not used without any inflammatory therapy. They have been associated with side effects such as tachycardia, skeletal muscle tremor, hypokalemia, and prolongation of QTc interval in overdose.

[0107] Methylxanthines, including for instance theophylline, have been used for long-term control and prevention of symptoms. These compounds cause bronchodilation resulting from phosphodiesterase inhibition and likely adenosine antagonism. It is also believed that these compounds may effect eosinophilic infiltration into bronchial mucosa and decrease T-lymphocyte numbers in the epithelium. Dose-related acute toxicities are a particular problem with these types of compounds. As a result, routine serum concentration must be monitored in order to account for the toxicity and narrow therapeutic range arising from individual differences in metabolic clearance. Side effects include tachycardia, nausea and vomiting, tachyarrhythmias, central nervous system stimulation, headache, seizures, hematemesis, hyperglycemia and hypokalemia. Short-acting β_2 agonists/bronchodilators relax airway smooth muscle, causing the increase in air flow. These types of compounds are a preferred drug for the treatment of acute asthmatic systems. Previously, short-acting β_2 agonists had been prescribed on a regularly-scheduled basis in order to improve overall asthma symptoms. Later reports, however, suggested that regular use of this class of drugs produced significant diminution in asthma control and pulmonary function (Sears, et al. *Lancet;* 336:1391-6, 1990). Other studies showed that regular use of some types of β_2 agonists produced no harmful effects over a four-month period but also produced no demonstrable effects (Drazen, et al., *N. Eng. J. Med.;* 335:841-7, 1996). As a result of these studies, the daily use of short-acting β_2 agonists is not generally recommended. Short-acting β_2 agonists include, but are not limited to, albuterol, bitolterol, pirbuterol, and terbutaline. Some of the adverse effects associated with the mastration of short-acting β_2 agonists include tachycardia, skeletal muscle tremor, hypokalemia, increased lactic acid, headache, and hyperglycemia.

[0108] Other asthma/allergy medicaments are preferably used in combination with the immunostimulatory nucleic acids to treat allergy. These are referred to as allergy medicaments. Allergy medicaments include, but are not limited to, anti-histamines, steroids, and prostaglandin inducers. Anti-histamines are compounds which counteract histamine released by mast cells or basophils. These compounds are well known in the art and commonly used for the treatment of allergy. Anti-histamines include, but are not limited to, loratidine, cetirizine, buclizine, ceterizine analogues, fexofenadine, terfenadine, desloratadine, norastemizole, epinastine, ebastine, ebastine, astemizole, levocabastine, azelastine, tranilast, terfenadine, mizolastine, betatastine, CS 560, and HSR 609. Prostaglandin inducers are compounds which induce prostaglandin activity. Prostaglandins function by regulating smooth muscle relaxation. Prostaglandin inducers include, but are not limited to, S-5751.

[0109] The asthma/allergy medicaments useful in combination with the immunostimulatory nucleic acids also include steroids and immunomodulators.

[0110] The steroids include, but are not limited to, beclomethasone, fluticasone, tramcinolone, budesonide, corticosteroids and budesonide. The combination of immunostimulatory nucleic acids and steroids are particularly well suited to the treatment of young subjects (e.g., children). To date, the use of steroids in children has been limited by the observation that some steroid treatments have been reportedly associated with growth retardation. Thus, according to the present invention, the immunostimulatory nucleic acids can be used in combination with growth retarding steroids, and can thereby provide a "steroid sparing effect." The combination of the two agents can result in lower required doses of steroids.

[0111] Corticosteroids are used long-term to prevent development of the symptoms, and suppress, control, and reverse inflammation arising from an initiator. Some corticosteroids can be administered by inhalation and others are administered systemically. The corticosteroids that are inhaled have an anti-inflammatory function by blocking late-reaction allergen and reducing airway hyper-responsiveness. These drugs also inhibit cytokine production, adhesion protein activation, and inflammatory cell migration and activation.

[0112] Corticosteroids include, but are not limited to, beclomethasome dipropionate, budesonide, flunisolide, fluticaosone, propionate, and triamcinoone acetonide. Although dexamethasone is a corticosteroid having anti-inflammatory action, it is not regularly used for the treatment of asthma/allergy in an inhaled form because it is highly absorbed, it has long-term suppressive side effects at an effective dose. Dexamethasone, however, can be used according to the invention for the treating of asthma/allergy because when administered in combination with immunostimulatory nucleic acids it can be administered at a low dose to reduce the side effects. Additionally, the immunostimulatory nucleic acid can be administered to reduce the side effects of dexamethasone at higher concentrations. Some of the side effects associated with corticosteroid include cough, dysphonia, oral thrush (candidiasis), and in higher doses, systemic effects, such as adrenal suppression, osteoporosis, growth suppression, skin thinning and easy bruising. (Barnes & Peterson, *Am. Rev. Respir. Dis.;* 148:S1-S26, 1993; and Kamada et al., *Am. J. Respir. Crit. Care Med.;* 153:1739-48, 1996)

[0113] Systemic corticosteroids include, but are not limited to, methylprednisolone, prednisolone and prednisone. Cortosteroids are used generally for moderate to severe exacerbations to prevent the progression, reverse inflammation and speed recovery. These anti-inflammatory compounds include, but are not limited to, methylprednisolone, prednisolone, and prednisone. Cortosteroids are associated with reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, mood alteration, hypertension, peptic ulcer, and rarely asceptic necrosis of femur. These compounds are useful for short-term (3-10 days) prevention of the inflammatory reaction in inadequately controlled persistent asthma. They also function in a long-term prevention of symptoms in severe persistent asthma to suppress and control and actually reverse inflammation. The side effects associated with systemic corticosteroids are even greater than those associated with inhaled corticosteroids. Side effects include, for instance, reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, mood alteration, hypertension, peptic ulcer and asceptic necrosis of femur, which are

associated with short-term use. Some side effects associated with longer term use include adrenal axis suppression, growth suppression, dermal thinning, hypertension, diabetes, Cushing's syndrome, cataracts, muscle weakness, and in rare instances, impaired immune function. It is recommended that these types of compounds be used at their lowest effective dose (guidelines for the diagnosis and management of asthma; expert panel report to; NIH Publication No. 97-4051; July 1997). The inhaled corticosteroids are believed to function by blocking late reaction to allergen and reducing airway hyper-responsiveness. Their also believed to reverse β_2-receptor downregulation and to inhibit microvascular leakage.

[0114] The immunomodulators include, but are not limited to, the group consisting of anti-inflammatory agents, leukotriene antagonists, IL-4 muteins, soluble IL-4 receptors, immunosuppressants (such as tolerizing peptide vaccine), anti-IL-4 antibodies, IL-4 antagonists, anti-IL-5 antibodies, soluble IL-13 receptor-Fc fusion proteins, anti-IL-9 antibodies, CCR3 antagonists, CCR5 antagonists, VLA-4 inhibitors, and, and downregulators of IgE.

[0115] Leukotriene modifiers are often used for long-term control and prevention of symptoms in mild persistent asthma. Leukotriene modifiers function as leukotriene receptor antagonists by selectively competing for LTD-4 and LTE-4 receptors. These compounds include, but are not limited to, zafirlukast tablets and zileuton tablets. Zileuton tablets function as 5-lipoxygenase inhibitors. These drugs have been associated with the elevation of liver enzymes and some cases of reversible hepatitis and hyperbilirubinemia. Leukotrienes are biochemical mediators that are released from mast cells, eosinophils, and basophils that cause contraction of airway smooth muscle and increase vascular permeability, mucous secretions and activate inflammatory cells in the airways of patients with asthma.

[0116] Other immunomodulators include neuropeptides that have been shown to have immunomodulating properties. Functional studies have shown that substance P, for instance, can influence lymphocyte function by specific receptor mediated mechanisms. Substance P also has been shown to modulate distinct immediate hypersensitivity responses by stimulating the generation of arachidonic acid-derived mediators from mucosal mast cells. J. McGillies, et al., Substance P and Immunoregulation, Fed. Proc. 46:196-9 (1987). Substance P is a neuropeptide first identified in 1931 by Von Euler and Gaddum. An unidentified depressor substance in certain tissue extracts, J. Physiol. (London) 72:74-87 (1931). Its amino acid sequence, Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH.sub.2 (Sequence Id. No. 1) was reported by Chang et al. in 1971. Amino acid sequence of substance P, Nature (London) New Biol. 232:86-87 (1971). The immunoregulatory activity of fragments of substance P has been studied by Siemion, et al. Immunoregulatory Activity of Substance P Fragments, Molec. Immunol. 27:887-890 (1990).

[0117] Another class of compounds is the down-regulators of IgE. These compounds include peptides or other molecules with the ability to bind to the IgE receptor and thereby prevent binding of antigen-specific IgE. Another type of downregulator of IgE is a monoclonal antibody directed against the IgE receptor-binding region of the human IgE molecule. Thus, one type of downregulator of IgE is an anti-IgE antibody or antibody fragment. Anti-IgE is being developed by Genentech. One of skill in the art could prepare functionally active antibody fragments of binding peptides which have the same function. Other types of IgE downregulators are polypeptides capable of blocking the binding of the IgE antibody to the Fc receptors on the cell surfaces and displacing IgE from binding sites upon which IgE is already bound.

[0118] One problem associated with downregulators of IgE is that many molecules don't have a binding strength to the receptor corresponding to the very strong interaction between the native IgE molecule and its receptor. The molecules having this strength tend to bind irreversibly to the receptor. However, such substances are relatively toxic since they can bind covalently and block other structurally similar molecules in the body. Of interest in this context is that the .alpha. chain of the IgE receptor belongs to a larger gene family where i.e. several of the different IgG Fc receptors are contained. These receptors are absolutely essential for the defense of the body against i.e. bacterial infections. Molecules activated for covalent binding are, furthermore, often relatively unstable and therefore they probably have to be administered several times a day and then in relatively high concentrations in order to make it possible to block completely the continuously renewing pool of IgE receptors on mast cells and basophilic leukocytes.

[0119] These types of asthma/allergy medicaments are sometimes classified as long-term control medications or quick-relief medications. Long-term control medications include compounds such as corticosteroids (also referred to as glucocorticoids), methylprednisolone, prednisolone, prednisone, cromolyn sodium, nedocromil, long-acting β_2-agonists, methylxanthines, and leukotriene modifiers. Quick relief medications are useful for providing quick relief of symptoms arising from allergic or asthmatic responses. Quick relief medications include short-acting β_2 agonists, anticholinergics and systemic corticosteroids.

[0120] Chromolyn sodium and medocromil are used as long-term control medications for preventing primarily asthma symptoms arising from exercise or allergic symptoms arising from allergens. These compounds are believed to block early and late reactions to allergens by interfering with chloride channel function. They also stabilize mast cell membranes and inhibit activation and release of mediators from eosinophils and epithelial cells. A four to six week period of administration is generally required to achieve a maximum benefit.

[0121] Anticholinergics are generally used for the relief of acute bronchospasm. These compounds are believed to function by competitive inhibition of muscarinic cholinergic receptors. Anticholinergics include, but are not limited to, ipratrapoium bromide. These compounds reverse only cholinerigically-mediated bronchospasm and do not modify any reaction to antigen. Side effects include drying of the mouth and respiratory secretions, increased wheezing in some individuals, blurred vision if sprayed in the eyes.

[0122] In addition to standard asthma/allergy medicaments other methods for treating asthma/allergy have been used either alone or in combination with established medicaments. One preferred, but frequently impossible, method of relieving allergies is allergen or initiator avoidance.

Another method currently used for treating allergic disease involves the injection of increasing doses of allergen to induce tolerance to the allergen and to prevent further allergic reactions.

[0123] Allergen injection therapy (allergen immunotherapy) is known to reduce the severity of allergic rhinitis. This treatment has been theorized to involve the production of a different form of antibody, a protective antibody which is termed a "blocking antibody". Cooke, RA et al., Serologic Evidence of Immunity with Coexisting Sensitization in a Type of Human Allergy, Exp. Med. 62:733 (1935). Other attempts to treat allergy involve modifying the allergen chemically so that its ability to cause an immune response in the patient is unchanged, while its ability to cause an allergic reaction is substantially altered.

[0124] These methods, however, can take several years to be effective and are associated with the risk of side effects such as anaphylactic shock. The use of an immunostimulatory nucleic acid and asthma/allergy medicament in combination with an allergen avoids many of the side effects etc.

[0125] Commonly used allergy and asthma drugs which are currently in development or on the market are shown in Tables 2 and 3 respectively.

TABLE 2

Allergy Drugs in Development or on the Market

MARKETER	BRAND NAME (GENERIC NAME)	MECHANISM
Schering-Plough	Claritin + Claritin D (loratidine)	Anti-histamine
	Vancenase (beclomethasone)	Steroid
UCB	Reactine (cetirizme) (US)	Anti-histamine
	Zyrtec (cetirizine) (ex US)	
	Longifene (buclizine)	Anti-histamine
	UCB 28754 (ceterizine alalogue)	Anti-histamine
Glaxo	Beconase (beclomethasone	Steroid
	Flonase (fluticasone)	Steroid
Aventis	Allegra (fexofenadine)	Anti-histamine
	Seldane (terfenadine)	Anti-histamine
Pfizer	Reactine (cetirizine) (US)	Anti-histamine
	Zyrtec/Reactine (cetirizine) (ex US) (both licensed from UCB)	
Sepracor	Allegra (fexofenadine)	Anti-histamine
	Desloratadine (lic to Schering-Plough)	Anti-histamine
	Cetirizine (−) (lic to UCB)	Anti-histamine
	Norastemizole (option to J & J not exercised, Oct. 17,1999)	Anti-histamine
B. Ingeiheim	Alesion (epinastine)	Anti-histamine
Aventis	Kestin (ebastine) (US)	Anti-histamine
	Bastel (ebastine) (Eu/Ger)	
	Nasacort (tramcinolone)	Steroid
Johnson & Johnson	Hismanol (astemizole)	Anti-histamine
	Livostin/Livocarb (levocabastine)	Anti-histamine
AstraZeneca	Rhinocort (budesonide) (Astra)	Steroid
Merck	Rhinocort (budesonide)	Steroid
Eisai	Azeptin (azelastine)	Anti-histamine
Kissei	Rizaben (tranilast)	Anti-histamine
Shionogi	Triludan (terfenadine)	Anti-histamine
	S-S751	Prostaglandin inducer
Schwarz	Zolim (mizolastine)	Anti-histamine
Daiichi	Zyrtec (cetirizine)	Anti-histamine
Tanabe Seiyaku	Talion/TAU-284 (betatastine)	Anti-histamine
Sanlcyo**	CS 560 (Hypersensitizaion therapy for cedar pollen allergy)	Other
Asta Medica	Azelastine-MDPI (azelastine)	Anti-histamine
BASF	HSR 609	Anti-histamine
SR Pharma	SRL 172	Immunomodulation
Peptide Therapeutics	Allergy vaccine (allergy (hayfever, anaphylaxis, atopic asthma)	Downregulates specific IgE
	Tolerizing peptide vaccine (rye grass peptide (T cell epitope))	Immuno-suppressant
Coley Pharmaceutical Group	CpG DNA	Immunomodulation
Genetech	Anti-IgE	Down-regulator of IgE
SR Pharma	SRL 172	Immunomodulation

[0126]

TABLE 3

Asthma Drugs in Development or on the Market

MARKETER	BRAND NAME (GENERIC NAME)	MECHANISM
Glaxo	Serevent (salmeterol)	Bronchodilator/beta-2 agonist
	Flovent (fluticasone)	Steroid
	Flixotide (fluticasone)	
	Becotide (betamethasone)	Steroid
	Ventoim (salbutamol)	Bronchodilator/beta-2 agonist
	Seretide (salmeterol + fluticasone)	Beta agonist + steroid
	GW215864	Steroid, hydolysable
	GW250495	Steroid, hydolysable
	GW328267	Adenosine A2 agonist
AstraZeneca	Bambec (bambuterol) (Astra)	
	Pulmicort (budesonide) (Astra)	Steroid
	Bricanyl Turbuhaler (terbutaline) (Astra)	Bronchodilator/beta-2 agonist
	Accolate (zafirlukast) (Zeneca)	Leukotriene antagonist Slo-Phyllin (theophylline)
	Inspiryl (salbutamol) (Astra)	Bronchodilator/beta-2 agonist
	Oxis Turbuhaler (D2522/formoterol)	Bronchodilator/beta-2 agonist
	Symbicort (pulmicort-oxis combination)	Steroid
	Roflepanide (Astra)	Steroid
	Bronica (seratrodast)	TXA2 synthesis inhibitor
	ZD 4407 (Zeneca)	5 lipoxygenase inhibitor
B. Ingeiheim	Atrovent (ipratropium)	Bronchodilator/anti-cholinergic
	Berodual (ipratropium + fenoterol) Bronchodilator/anti-cholinergic	
	Berotec (fenoterol)	Bronchodilator/beta-2 agonist
	Alupent (orciprenaline)	Bronchodilator/beta-2 agonist
	Ventilat (oxitropium)	Bronchodilator/anti-cholinergic
	Spiropent (clenbuterol)	Bronchodilator/beta-2 agonist
	Inhacort (flunisolide)	Steroid
	B1679/tiotropium bromide	
	RPR 106541	Steroid
	BIIX 1	Potassium channel
	B11L284	LTB-4 antagonist
Schering-Plough	Proventil (salbutamol)	Bronchodilator/beta-2 agonist
	Vanceril (becbomethasone)	Steroid
	Mometasone furoate	Steroid
	Theo-Dur (theophylline (w/Astra)	
	Uni-Dur (theophylline)	
	Asmanex (mometasone)	Steroid
	CDP 835 (lic from Ceiltech)	Anti-IL-5 Mab
RPR	Intal (disodium cromoglycate)	Anti-inflammatory
(Aventis)	Intal/Aarane (disodium cromoglycate)	
	Tilade (nedocromil sodium)	Anti-inflammatory
	Azmacort (triamcinolone acetonide) Steroid	
	RP 73401	PDE-4 inhibitor
Novartis	Zaditen (ketotifen)	Anti-inflammatory
	Azmacort (triamcinolone)	Steriod
	Foradil (formoterol) (lic fromYamanouchi)	Bronchodilator/beta-2 agonist
	E25	Anti-IgE
	KCO 912	K + channel opener
Merck	Singulair (montelukast)	Leukotriene antagonist
	Pulmicort Turbuhaler (budesonide)	Steriod
	Slo-Phylim (theophylline)	
	Symbicort (Pulmicort-Oxis combination)	Steriod
	Oxis Turbuhaler (D2522/formoterol)	Bronchodilator/beta-2 agonist
	Roflepanide	Steroid
	VLA-4 antagonist (lic from Biogen)	VLA-4 antagonist
ONO	Onon (pranlukast)	Leukotriene antagonist
	Vega (ozagrel)	TXA2 synthesis inhibitor
Fujisawa	Intal (chromoglycate)	Anti-inflammatory
	FK 888	Neurokin antagonist
Forest Labs	Aerobid (flunisolide)	Steroid
IVAX	Ventolin (salbutamol)	Bronchodilator/beta-2 agonist
	Becotide (beclomethasone Easi-Breathe)	Steroid
	Serevent (salmeterol)	Bronchodilator/beta-2 agonist
	Flixotide (fluticasone)	Steroid
	Budesonide Dry Powder Inhaler	Steroid
	Salbutamol Dry Powder Inhaler	Bronchodilator/beta-2 agonist

TABLE 3-continued

Asthma Drugs in Development or on the Market

MARKETER	BRAND NAME (GENERIC NAME)	MECHANISM
Alza	Volmax (salbutamol)	Bronchodilator/beta-2 agonist
Altana	Euphyllin (theophylline)	Xanthanine
	Ciclesonide	Arachidonic acid antagonist
	BY 217	PDE 4 inhibitor
	BY 9010N (ciclesonide)	Steroid (nasal)
Tanabe Seiyaku	Flucort (fluocinolone acetonide	Steroid
Kissei	Domenan (ozagrel)	TXA2 synthesis inhibitor
Abbott	Zyflo (zileuton) (4×/day dosing, not competitive w/ Singulair or Accolate, no further interest in this area)	5 lipoxygenase inhibitor
Asta Medica	Aerobec (beclomethasone dipropionate) (w/3M)	
	Allergodil (azelastine)	
	Allergospasmin (sodium cromoglycate reproterol)	
	Bronchospasmin (reproterol)	
	Salbulair (salbutamol sulphate) (w/3M)	
	TriNasal (triamcinolone)	Steroid
	Formoterol-MDPI	Beta 2 adrenoceptor agonist
	Budesonide-MDPI	
UCB	Atenos/Respecal (tulobuerol)	Bronchodilator/beta-2 agonist
Recordati	Theodur (theophylline)	Xanthine
Medeva	Clickhalers Asmasal, Asmabec (salbutamol beclomethasone diproprionate, dry inhaler)	Steroid
Eisai	E 6123	PAF receptor antagonist
Sankyo	Zaditen (ketotifen)	Anti-inflammatory
	CS 615	Leukotriene antagonist
Shionogi	Anboxan/S 1452 (domitroban)	Thromboxin A2 receptor antagonist
Yamanouchi	YM 976	PDE 4 inhibitor
	YM 158	Leukotriene D4/thromboxan 2 dual antagonist
3M Pharma	Exirel (pirbuterol)	
Hoechst (Aventis)	Autoinhalers (3M albuterol projects)	Bronchodilator/beta-2 agonist
SmithKline Beecham	Ariflo	PDE-4 inhibitor
	SB 240563	Anti-IL5 MAb (humanized)
	SB 240683	Anti-IL4 Mab
	IDEC 151/clenoliximab	Anti-CD4 MAb, primatised
Roche	Anti-IgE (GNE)/CGO51901	Down-regulator of IgE
Sepracor	Fomoterol (R, R)	Beta 2 adrenoceptor agonist
	Xopenex (levalbuterol)	Bet 2 adrenoceptor agonist
Bayer	BAY U 3405 (ramatroban)	Thromboxane A2 antagonist
	BAY 16-9996 (once monthly dosing)	IL4 mutein
	BAY 19-8004	PDE-4 inhibitor
SR Pharma	SRL 172	Immunomodulation
Immunex	Nuvance	Soluble IL-4 receptor (immunomodulator)
Biogen	Anti-VLA-4	Immunosuppressant
Vanguard	VML 530	Inhibitor of 5-lipox activation protein
Recordati	Respix (zafirlukast)	Leukotriene antagonist
Genentech	Anti-IgE MAb	Down-regulator of IgE
Warner Lambert	CI-1018	PDE 4 inhibitor
Celltech/ Chiroscience	CDP 835/SCH 55700 (anti-IL-5) (lic to Schering-Plough)	IL-5 antagonist Mab
	D 4418 (w/Schering-Plough)	PDE 4 inhibitor
	CDP 840 (Celltech)	PDE 4 inhibitor
AHP	Pda-641 (asthma steroid replacement)	
Peptide Therapeutics	RAPID Technology Platform	Protease inhibitors
Coley Pharmaceutical Group	CpG DNA	Immunomodulation

[0127] In some cases the subject is exposed to an allergen in addition to being treated with the immunostimulatory nucleic acid and the asthma/allergy medicament. In this case the subject is said to be exposed to the allergen. As used herein, the term "exposed to" refers to either the active step of contacting the subject with an allergen or the passive exposure of the subject to the allergen in vivo. Methods for the active exposure of a subject to an allergen are well-known in the art. In general, an allergen is administered directly to the subject by any means such as intravenous,

intramuscular, oral, transdermal, mucosal, intranasal, intratracheal, or subcutaneous administration. The allergen can be administered systemically or locally. Methods for administering the allergen and the immunostimulatory nucleic acid/asthma/allergy medicament are described in more detail below. A subject is passively exposed to an allergen if an allergen becomes available for exposure to the immune cells in the body. A subject may be passively exposed to an allergen, for instance, by entry of an allergen into the body when the allergen is present in the environment surrounding the subject, i.e. pollen.

[0128] The methods in which a subject is passively exposed to an allergen can be particularly dependent on timing of administration of the immunostimulatory nucleic acid and the asthma/allergy medicament. For instance, in a subject at risk of developing an allergic or asthmatic response, the subject may be administered the immunostimulatory nucleic acid and the asthma/allergy medicament on a regular basis when that risk is greatest, i.e., during pollen allergy season. Additionally the immunostimulatory nucleic acid and the asthma/allergy medicament may be administered to travelers before they travel to a destination where they are at risk of exposure to a particular allergen.

[0129] As used herein, the term "prevent", "prevented", or "preventing" when used with respect to the treatment of an allergic or asthmatic disorder refers to a prophylactic treatment which increases the resistance of a subject to an allergen or initiator or, in other words, decreases the likelihood that the subject will develop an allergic or asthmatic response to the allergen or initiator as well as a treatment after the allergic or asthmatic disorder has begun in order to fight the allergy/asthma, e.g., reduce or eliminate it altogether or prevent it from becoming worse.

[0130] The term "substantially purified" as used herein refers to a molecular species which is substantially free of other proteins, lipids, carbohydrates or other materials with which it is naturally associated. One skilled in the art can purify allergenic polypeptides using standard techniques for protein purification. The substantially pure polypeptide will often yield a single major band on a non-reducing polyacrylamide gel. In the case of partially glycosylated polypeptides or those that have several start codons, there may be several bands on a non-reducing polyacrylamide gel, but these will form a distinctive pattern for that polypeptide. The purity of the allergenic polypeptide can also be determined by amino-terminal amino acid sequence analysis.

[0131] The allergen and/or polypeptide asthma/allergy medicament may be in the form of a polypeptide when administered to the subject or it may be encoded by a nucleic acid vector. If the nucleic acid vector is administered to the subject the protein is expressed in vivo. Minor modifications of the primary amino acid sequences of polypeptide allergens may also result in a polypeptide which has substantially equivalent allergenic activity as compared to the unmodified counterpart polypeptide. Such modifications may be deliberate, as by site-directed mutagenesis, or may be spontaneous.

[0132] The nucleic acid encoding the allergen or asthma/allergy medicament is operatively linked to a gene expression sequence which directs the expression of the protein within a eukaryotic cell. The "gene expression sequence" is any regulatory nucleotide sequence, such as a promoter sequence or promoter-enhancer combination, which facilitates the efficient transcription and translation of the protein which it is operatively linked. The gene expression sequence may, for example, be a mammalian or viral promoter, such as a constitutive or inducible promoter. Constitutive mammalian promoters include, but are not limited to, the promoters for the following genes: hypoxanthine phosphoribosyl transferase (HPTR), adenosine deaminase, pyruvate kinase, b-actin promoter and other constitutive promoters. Exemplary viral promoters which function constitutively in eukaryotic cells include, for example, promoters from the cytomegalovirus (CMV), simian virus (e.g., SV40), papilloma virus, adenovirus, human immunodeficiency virus (HIV), Rous sarcoma virus, cytomegalovirus, the long terminal repeats (LTR) of Moloney leukemia virus and other retroviruses, and the thymidine kinase promoter of herpes simplex virus. Other constitutive promoters are known to those of ordinary skill in the art. The promoters useful as gene expression sequences of the invention also include inducible promoters. Inducible promoters are expressed in the presence of an inducing agent. For example, the metallothionein promoter is induced to promote transcription and translation in the presence of certain metal ions. Other inducible promoters are known to those of ordinary skill in the art.

[0133] In general, the gene expression sequence shall include, as necessary, 5' non-transcribing and 5' non-translating sequences involved with the initiation of transcription and translation, respectively, such as a TATA box, capping sequence, CAAT sequence, and the like. Especially, such 5' non-transcribing sequences will include a promoter region which includes a promoter sequence for transcriptional control of the operably joined antigen nucleic acid. The gene expression sequences optionally include enhancer sequences or upstream activator sequences as desired.

[0134] As used herein, the nucleic acid sequence encoding the protein and the gene expression sequence are said to be "operably linked" when they are covalently linked in such a way as to place the expression or transcription and/or translation of the antigen coding sequence under the influence or control of the gene expression sequence. Two DNA sequences are said to be operably linked if induction of a promoter in the 5' gene expression sequence results in the transcription of the gene sequence and if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region to direct the transcription of the antigen sequence, or (3) interfere with the ability of the corresponding RNA transcript to be translated into a protein. Thus, a gene expression sequence would be operably linked to a specific nucleic acid sequence if the gene expression sequence were capable of effecting transcription of that nucleic acid sequence such that the resulting transcript is translated into the desired protein or polypeptide.

[0135] The immunostimulatory nucleic acids may also be delivered to the subject in the form of a plasmid vector. In some embodiments, one plasmid vector could include both the immunostimulatory nucleic acid and a nucleic acid encoding a protein asthma/allergy medicament and/or an allergen. In other embodiments, separate plasmids could be used. In yet other embodiments, no plasmids could be used.

[0136] The compositions of the invention may be delivered to the immune system or other target cells alone or in association with a vector. In its broadest sense, a "vector" is any vehicle capable of facilitating the transfer of the compositions to the target cells. The vector generally transports the nucleic acid to the immune cells with reduced degradation relative to the extent of degradation that would result in the absence of the vector.

[0137] In general, the vectors useful in the invention are divided into two classes: biological vectors and chemical/physical vectors. Biological vectors and chemical/physical vectors are useful for delivery/uptake of nucleic acids, asthma/allergy medicaments, and/or allergens to/by a target cell.

[0138] Biological vectors include, but are not limited to, plasmids, phagemids, viruses, other vehicles derived from viral or bacterial sources that have been manipulated by the insertion or incorporation of nucleic acid sequences, and free nucleic acid fragments which can be attached to nucleic acid sequences. Viral vectors are a preferred type of biological vector and include, but are not limited to, nucleic acid sequences from the following viruses: retroviruses, such as: Moloney murine leukemia virus; Harvey murine sarcoma virus; murine mammary tumor virus; Rous sarcoma virus; adenovirus; adeno-associated virus; SV40-type viruses; polyoma viruses; Epstein-Barr viruses; papilloma viruses; herpes viruses; vaccinia viruses; polio viruses; and RNA viruses such as any retrovirus. One can readily employ other viral vectors not named but known in the art.

[0139] Preferred viral vectors are based on non-cytopathic eukaryotic viruses in which non-essential genes have been replaced with a nucleic acid of interest. Non-cytopathic viruses include retroviruses, the life cycle of which involves reverse transcription of genomic viral RNA into DNA with subsequent proviral integration into host cellular DNA. Retroviruses have been approved for human gene therapy trials. In general, the retroviruses are replication-deficient (i.e., capable of directing synthesis of the desired proteins, but incapable of manufacturing an infectious particle). Such genetically altered retroviral expression vectors have general utility for the high-efficiency transduction of genes in vivo. Standard protocols for producing replication-deficient retroviruses (including the steps of incorporation of exogenous genetic material into a plasmid, transfection of a packaging cell lined with plasmid, production of recombinant retroviruses by the packaging cell line, collection of viral particles from tissue culture media, and infection of the target cells with viral particles) are provided in Kriegler, M., "Gene Transfer and Expression, A Laboratory Manual," W.H. Freeman Co., New York (1990) and Murry, E. J. Ed. "Methods in Molecular Biology," vol. 7, Humana Press, Inc., Cliffton, N.J. (1991).

[0140] Another preferred virus for certain applications is the adeno-associated virus, a double-stranded DNA virus. The adeno-associated virus can be engineered to be replication-deficient and is capable of infecting a wide range of cell types and species. It further has advantages, such as heat and lipid solvent stability; high transduction frequencies in cells of diverse lineages; and lack of superinfection inhibition thus allowing multiple series of transductions. Reportedly, the adeno-associated virus can integrate into human insertional mutagenesis and variability of inserted gene expression. In addition, wild-type adeno-associated virus infections have been followed in tissue culture for greater than 100 passages in the absence of selective pressure, implying that the adeno-associated virus genomic integration is a relatively stable event. The adeno-associated virus can also function in an extrachromosomal fashion.

[0141] Other biological 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. These 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, pRC/CMV, SV40, 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.

[0142] It has recently been discovered that gene carrying plasmids 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. B cells, dendritic cells, likely 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 allergen, immunostimulatory nucleic acid and/or other therapeutic agent.

[0143] In addition to the biological vectors, chemical/physical vectors may be used to deliver a nucleic acid, asthma/allergy medicament, and/or allergen to a target cell and facilitate uptake thereby. As used herein, a "chemical/physical vector" refers to a natural or synthetic molecule, other than those derived from bacteriological or viral sources, capable of delivering the nucleic acid, asthma/allergy medicament, and/or allergen to a cell.

[0144] A preferred chemical/physical vector of the invention is a colloidal dispersion system. Colloidal dispersion systems include lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system of the invention is a liposome. Liposomes are artificial membrane vessels which are useful as a delivery vector in vivo or in vitro. It has been shown that large unilamellar vessels (LUV), which range in size from 0.2-4.0 μm can encapsulate large macromolecules. RNA, DNA, and intact virions can be encapsulated within the aqueous interior and be delivered to cells in a biologically active form (Fraley, et al., *Trends Biochem. Sci.*, (1981) 6:77).

[0145] Liposomes may be targeted to a particular tissue by coupling the liposome to a specific ligand such as a monoclonal antibody, sugar, glycolipid, or protein. Ligands which may be useful for targeting a liposome to an immune cell include, but are not limited to: intact or fragments of

molecules which interact with immune cell specific receptors and molecules, such as antibodies, which interact with the cell surface markers of immune cells. Such ligands may easily be identified by binding assays well known to those of skill in the art. Additionally, the vector may be coupled to a nuclear targeting peptide, which will direct the vector to the nucleus of the host cell.

[0146] Lipid formulations for transfection are commercially available from QIAGEN, for example, as EFFECTENE™ (a non-liposomal lipid with a special DNA condensing enhancer) and SUPERFEC™ (a novel acting dendrimeric technology).

[0147] Liposomes are commercially available from Gibco BRL, for example, as LIPOFECTIN™ and LIPOFECTACE™, which are formed of cationic lipids such as N-[1-(2,3dioleyloxy)-propyl]-N,N,N-trimethylammonium chloride (DOTMA) and dimethyl dioctadecylammonium bromide (DDAB). Methods for making liposomes are well known in the art and have been described in many publications. Liposomes also have been reviewed by Gregoriadis, G. in *Trends in Biotechnology*, (1985) 3:235-241.

[0148] In one embodiment, the vehicle is a biocompatible microparticle or implant that is suitable for implantation or administration to the mammalian recipient. Exemplary bioerodible implants that are useful in accordance with this method are described in PCT International application no. PCT/US/03307 (Publication No. WO95/24929, entitled "Polymeric Gene Delivery System". PCT/US/0307 describes a biocompatible, preferably biodegradable polymeric matrix for containing an exogenous gene under the control of an appropriate promoter. The polymeric matrix can be used to achieve sustained release of the exogenous gene in the patient.

[0149] The polymeric matrix preferably is in the form of a microparticle such as a microsphere (wherein the a nucleic acid, asthma/allergy medicament, and/or allergen is dispersed throughout a solid polymeric matrix) or a microcapsule (wherein the a nucleic acid, asthma/allergy medicament, and/or allergen is stored in the core of a polymeric shell). Other forms of the polymeric matrix for containing the a nucleic acid, asthma/allergy medicament, and/or allergen include films, coatings, gels, implants, and stents. The size and composition of the polymeric matrix device is selected to result in favorable release kinetics in the tissue into which the matrix is introduced. The size of the polymeric matrix further is selected according to the method of delivery which is to be used, typically injection into a tissue or administration of a suspension by aerosol into the nasal and/or pulmonary areas. Preferably when an aerosol route is used the polymeric matrix and the nucleic acid, asthma/allergy medicament, and/or allergen are encompassed in a surfactant vehicle. The polymeric matrix composition can be selected to have both favorable degradation rates and also to be formed of a material which is bioadhesive, to further increase the effectiveness of transfer when the matrix is administered to a nasal and/or pulmonary surface that has sustained an injury. The matrix composition also can be selected not to degrade, but rather, to release by diffusion over an extended period of time.

[0150] In another embodiment the chemical/physical vector is a biocompatible microsphere that is suitable for delivery, such as oral or mucosal delivery. Such microspheres are disclosed in Chickering et al., *Biotech. And Bioeng.*, (1996) 52:96-101 and Mathiowitz et al., *Nature*, (1997) 386:.410-414 and PCT Patent Application WO97/03702.

[0151] Both non-biodegradable and biodegradable polymeric matrices can be used to deliver the nucleic acid, asthma/allergy medicament, and/or allergen to the subject. Biodegradable matrices are preferred. Such polymers may be natural or synthetic polymers. The polymer is selected based on the period of time over which release is desired, generally in the order of a few hours to a year or longer. Typically, release over a period ranging from between a few hours and three to twelve months is most desirable. The polymer optionally is in the form of a hydrogel that can absorb up to about 90% of its weight in water and further, optionally is cross-linked with multi-valent ions or other polymers.

[0152] Bioadhesive polymers of particular interest include bioerodible hydrogels described by H. S. Sawhney, C. P. Pathak and J. A. Hubell in *Macromolecules*, (1993) 26:581-587, the teachings of which are incorporated herein, polyhyaluronic acids, casein, gelatin, glutin, polyanhydrides, polyacrylic acid, alginate, chitosan, poly(methyl methacrylates), poly(ethyl methacrylates), poly(butylmethacrylate), poly(isobutyl methacrylate), poly(hexylmethacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), and poly(octadecyl acrylate).

[0153] Compaction agents also can be used alone, or in combination with, a biological or chemical/physical vector. A "compaction agent", as used herein, refers to an agent, such as a histone, that neutralizes the negative charges on the nucleic acid and thereby permits compaction of the nucleic acid into a fine granule. Compaction of the nucleic acid facilitates the uptake of the nucleic acid by the target cell. The compaction agents can be used alone, i.e., to deliver a nucleic acid in a form that is more efficiently taken up by the cell or, more preferably, in combination with one or more of the above-described vectors.

[0154] Other exemplary compositions that can be used to facilitate uptake by a target cell of the nucleic acid, asthma/allergy medicament, and/or allergen include calcium phosphate and other chemical mediators of intracellular transport, microinjection compositions, electroporation and homologous recombination compositions (e.g., for integrating a nucleic acid into a preselected location within the target cell chromosome).

[0155] The immunostimulatory nucleic acid and/or the asthma/allergy medicament the antigen and/or other therapeutics may be administered alone (e.g. in saline or buffer) or using any delivery vectors known in the art. For instance the following delivery vehicles have been described: Cochleates (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., 1998, Morein et al., 1999); Liposomes (Childers et al., 1999, Michalek et al., 1989, 1992, de Haan 1995a, 1995b); Live bacterial vectors (e.g., *Salmonella, Escherichia coli, Bacillus calmatte-guerin, Shigella, Lactobacillus*) (Hone et al., 1996, Pouwels et al., 1998, Chatfield et al., 1993, Stover et al., 1991, Nugent et al., 1998); Live viral vectors (e.g., Vaccinia, adenovirus,

Herpes Simplex) (Gallichan 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, Jabbal-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 (Tacket et al., 1998, Mason et al., 1998, Haq et al., 1995); Virosomes (Gluck et al., 1992, Mengiardi et al., 1995, Cryz et al., 1998); Virus-like particles (Jiang et al., 1999, Leibl et al., 1998).

[0156] The immunostimulatory nucleic acid and asthma/allergy medicament can be combined with other therapeutic agents such as adjuvants to enhance immune responses even further. The immunostimulatory nucleic acid, asthma/allergy medicament and other therapeutic agent may be administered simultaneously or sequentially. When the other therapeutic agents are administered simultaneously they can be administered in the same or separate formulations, but are administered at the same time. The other therapeutic agents are administered sequentially with one another and with the immunostimulatory nucleic acid and asthma/allergy medicament, when the administration of the other therapeutic agents and the immunostimulatory nucleic acid and asthma/allergy medicament is temporally separated. The separation in time between the administration of these compounds may be a matter of minutes or it may be longer. Other therapeutic agents include but are not limited to non-nucleic acid adjuvants, cytokines, antibodies, antigens, etc.

[0157] A "non-nucleic acid adjuvant" is any molecule or compound except for the immunostimulatory nucleic acids described herein which can stimulate the humoral and/or cellular immune response. Non-nucleic acid adjuvants include, for instance, adjuvants that create a depo effect, immune stimulating adjuvants, adjuvants that create a depo effect and stimulate the immune system and mucosal adjuvants.

[0158] An "adjuvant that creates a depo effect" as used herein is an adjuvant that causes an antigen or allergen to be slowly released in the body, thus prolonging the exposure of immune cells to the antigen or allergen. This class of adjuvants includes but is not limited to alum (e.g., aluminum hydroxide, aluminum phosphate); or emulsion-based formulations including mineral oil, non-mineral oil, water-in-oil or oil-in-water-in oil emulsion, oil-in-water emulsions such as Seppic ISA series of Montanide adjuvants (e.g., Montanide ISA 720, AirLiquide, Paris, France); MF-59 (a squalene-in-water emulsion stabilized with Span 85 and Tween 80; Chiron Corporation, Emeryville, Calif.; and PROVAX (an oil-in-water emulsion containing a stabilizing detergent and a micelle-forming agent; IDEC, Pharmaceuticals Corporation, San Diego, Calif.).

[0159] An "immune stimulating adjuvant" is an adjuvant that causes activation of a cell of the immune system. It may, for instance, cause an immune cell to produce and secrete cytokines. This class of adjuvants includes but is not limited to saponins purified from the bark of the Q. *saponaria* tree, such as QS21 (a glycolipid that elutes in the 21st peak with HPLC fractionation; Aquila Biopharmaceuticals, Inc., Worcester, Mass.); poly[di(carboxylatophenoxy)phosphazene (PCPP polymer; Virus Research Institute, USA); derivatives of lipopolysaccharides such as monophosphoryl lipid A (MPL; Ribi ImmunoChem Research, Inc., Hamilton, Mont.), muramyl dipeptide (MDP; Ribi) andthreonyl-muramyl dipeptide (t-MDP; Ribi); OM-174 (a glucosamine disaccharide related to lipid A; OM Pharma SA, Meyrin, Switzerland); and *Leishmania* elongation factor (a purified *Leishmania* protein; Corixa Corporation, Seattle, Wash.).

[0160] "Adjuvants that create a depo effect and stimulate the immune system" are those compounds which have both of the above- identified functions. This class of adjuvants includes but is not limited to ISCOMS (Immunostimulating complexes which contain mixed saponins, lipids and form virus-sized particles with pores that can hold antigen; CSL, Melbourne, Australia); SB-AS2 (SmithKline Beecham adjuvant system #2 which is an oil-in-water emulsion containing MPL and QS21: SmithKline Beecham Biologicals [SBB], Rixensart, Belgium); SB-AS4 (SmithKline Beecham adjuvant system #4 which contains alum and MPL; SBB, Belgium); non-ionic block copolymers that form micelles such as CRL 1005 (these contain a linear chain of hydrophobic polyoxpropylene flanked by chains of polyoxyethylene; Vaxcel, Inc., Norcross, Ga.); and Syntex Adjuvant Formulation (SAF, an oil-in-water emulsion containing Tween 80 and a nonionic block copolymer; Syntex Chemicals, Inc., Boulder, Colo.).

[0161] A "non-nucleic acid mucosal adjuvant" as used herein is an adjuvant other than an immunostimulatory nucleic acid that is capable of inducing a mucosal immune response in a subject when administered to a mucosal surface in conjunction with an antigen or allergen. Mucosal adjuvants include but are not limited to Bacterial toxins: e.g., Cholera toxin (CT), CT derivatives including but not limited to CT B subunit (CTB) (Wu et al., 1998, Tochikubo et al., 1998); CTD53 (Val to Asp) (Fontana et al., 1995); CTK97 (Val to Lys) (Fontana et al., 1995); CTK104 (Tyr to Lys) (Fontana et al., 1995); CTD53/K63 (Val to Asp, Ser to Lys) (Fontana et al., 1995); CTH54 (Arg to His) (Fontana et al., 1995); CTN107 (His to Asn) (Fontana et al., 1995); CTE114 (Ser to Glu) (Fontana et al., 1995); CTE112K (Glu to Lys) (Yamamoto et al., 1997a); CTS61F (Ser to Phe) (Yamamoto et al., 1997a, 1997b); CTS106 (Pro to Lys) (Douce et al., 1997, Fontana et al., 1995); and CTK63 (Ser to Lys) (Douce et al., 1997, Fontana et al., 1995), Zonula occludens toxin, zot, *Escherichia coli* heat-labile enterotoxin, Labile Toxin (LT), LT derivatives including but not limited to LT B subunit (LTB) (Verweij et al., 1998); LT7K (Arg to Lys) (Komase et al., 1998, Douce et al., 1995); LT61F (Ser to Phe) (Komase et al., 1998); LT112K (Glu to Lys) (Komase et al., 1998); LT118E (Gly to Glu) (Komase et al., 1998); LT146E (Arg to Glu) (Komase et al., 1998); LT192G (Arg to Gly) (Komase et al., 1998); LTK63 (Ser to Lys) (Marchetti et al., 1998, Douce et al., 1997, 1998, Di Tommaso et al., 1996); and LTR72 (Ala to Arg) (Giuliani et al., 1998), Pertussis toxin, PT. (Lycke et al., 1992, Spangler B D, 1992, Freytag and Clemments, 1999, Roberts et al., 1995, Wilson et al., 1995) including PT-9K/129G (Roberts et al., 1995, Cropley et al., 1995); Toxin derivatives (see below) (Holmgren et al., 1993, Verweij et al., 1998, Rappuoli et al., 1995, Freytag and Clements, 1999); Lipid A derivatives (e.g., monophosphoryl lipid A, MPL) (Sasaki et al., 1998, Vancott et al., 1998; Muramyl Dipeptide (MDP) derivatives

(Fukushima et al., 1996, Ogawa et al., 1989, Michalek et al., 1983, Morisaki et al., 1983); Bacterial outer membrane proteins (e.g., outer surface protein A (OspA) lipoprotein of *Borrelia burgdorferi*, outer membrane protine of *Neisseria meningitidis*)(Marinaro et al., 1999, Van de Verg et al., 1996); Oil-in-water emulsions (e.g., MF59) (Barchfield et al., 1999, Verschoor et al., 1999, O'Hagan, 1998); Aluminum salts (Isaka et al., 1998, 1999); and Saponins (e.g., QS21) Aquila Biopharmaceuticals, Inc., Worster, Mass.) (Sasaki et al., 1998, MacNeal et al., 1998), ISCOMS, MF-59 (a squalene-in-water emulsion stabilized with Span 85 and Tween 80; Chiron Corporation, Emeryville, Calif.); the Seppic ISA series of Montanide adjuvants (e.g., Montanide ISA 720; AirLiquide, Paris, France); PROVAX (an oil-in-water emulsion containing a stabilizing detergent and a micell-forming agent; IDEC Pharmaceuticals Corporation, San Diego, Calif.); Syntext Adjuvant Formulation (SAF; Syntex Chemicals, Inc., Boulder, Colo.); poly[di(carboxylatophenoxy)phosphazene (PCPP polymer; Virus Research Institute, USA) and *Leishmania* elongation factor (Corixa Corporation, Seattle, Wash.).

[0162] Immune responses can also be induced or augmented by the co-administration or co-linear expression of cytokines (Bueler & Mulligan, 1996; Chow et al., 1997; Geissler et al., 1997; Iwasaki et al., 1997; Kim et al., 1997) or B-7 co-stimulatory molecules (Iwasaki et al., 1997; Tsuji et al., 1997) with the immunostimulatory nucleic acids and asthma/allergy medicaments. The cytokines can be administered directly with immunostimulatory nucleic acids or may be administered in the form of a nucleic acid vector that encodes the cytokine, such that the cytokine can be expressed in vivo. In one embodiment, the cytokine is administered in the form of a plasmid expression vector. The term "cytokine" is used as a generic name for a diverse group of soluble proteins and peptides which act as humoral regulators at nano- to picomolar concentrations and which, either under normal or pathological conditions, modulate the functional activities of individual cells and tissues. These proteins also mediate interactions between cells directly and regulate processes taking place in the extracellular environment. Examples of cytokines include, but are not limited to IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-10, IL-12, IL-15, IL-18 granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (GCSF), interferon-γ (γ-IFN), IFN-a, tumor necrosis factor (TNF), TGF-β, FLT-3 ligand, and CD40 ligand. Cytokines play a role in directing the T cell response. Helper (CD4+) T cells orchestrate the immune response of mammals through production of soluble factors that act on other immune system cells, including other T cells. Most mature CD4+ T helper cells express one of two cytokine profiles: Th1 or Th2. In some embodiments it is preferred that the cytokine be a Th1 cytokine.

[0163] The term "effective amount" of an immunostimulatory nucleic acid and an asthma/allergy medicament refers to the amount necessary or sufficient to realize a desired biologic effect. For example, an effective amount of an immunostimulatory nucleic acid and an asthma/allergy medicament for treating or preventing asthma or preventing is that amount necessary to prevent the development of IgE in response to an allergen or initiator upon exposure to the allergen or initiator is that amount necessary to cause the shift from Th2 to Th1 response in response to an allergen or initiator.

[0164] 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. The effective amount for any particular application can vary depending on such factors as the disease or condition being treated, the particular immunostimulatory nucleic acid or asthma/allergy medicament being administered (e.g. the type of nucleic acid, i.e. a CpG nucleic acid, the number of unmethylated CpG motifs or their location in the nucleic acid, the degree of modification of the backbone to the oligonucleotide the type of medicament), 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/or asthma/allergy medicament and/or other therapeutic agent without necessitating undue experimentation.

[0165] Depending upon the aspect of the invention, the immunostimulatory nucleic acid and asthma/allergy medicament may be administered in a synergistic amount effective to treat or prevent asthma or allergy. A synergistic amount is that amount which produces a physiological response that is greater than the sum of the individual effects of either the immunostimulatory nucleic acid or the asthma/allergy medicament alone. For instance, in some embodiments of the invention, the physiological effect is a reduction in IgE levels. A synergistic amount is that amount which produces a reduction in IgE that is greater than the sum of the IgE reduced by either the immunostimulatory nucleic acid or the asthma/allergy medicament alone. In other embodiments, the physiological result is a shift from Th2 cytokines, such as IL-4 and Il-5, to Th1 cytokines, such as IFN-γ and IL-12. The synergistic amount in this case is that amount which produces the shift to a Th1 cytokine that is greater than the sum of the shift produced by either the immunostimulatory nucleic acid or the asthma/allergy medicament alone. In other embodiments the physiological result is a decrease in eosinophilia, hyperreactivity, or lung function.

[0166] In some embodiments of the invention, the immunostimulatory nucleic acid is administered in an effective amount for preventing bacterial or viral infection. Immunostimulatory nucleic acids are known to be useful for preventing bacterial and viral infections. Bacterial and viral infections exacerbate and/or induce allergy and/or asthma. In this aspect of the invention, the immunostimulatory nucleic acid is administered to the subject in an amount effective to prevent bacterial and viral infection and the asthma/allergy medicament is administered to the subject when symptoms of allergy or asthma appear. Thus, the immunostimulatory nucleic acid is administered to the subject and then the asthma/allergy medicament is subsequently administered to the subject or they are administered together at the same time. This method is particularly useful in subjects such as children and immunocompromised subjects, or elderly subjects, who are particularly susceptible to bacterial or viral disease.

[0167] In aspects of the invention directed at treating subjects in anticipation of an asthmatic or allergic event or

season (e.g., in anticipation of the hay-fever season), the subjects may be administered an immunostimulatory nucleic acid in an effective amount for preventing the asthma or allergy. In related embodiments of this method, an asthma/allergy medicament is also administered to the subject. In these latter instances, the amount of the immunostimulatory nucleic acid administered may be that amount necessary to reduce the effective dose of the asthma/allergy medicament which is required to treat or prevent the asthma or allergy.

[0168] Thus, in these embodiments, the immunostimulatory nucleic acid potentiates the effect of the asthma/allergy medicament. The ability to potentiate the effect of an asthma/allergy medicament is useful since it allows for a reduction in the administered dose of an asthma/allergy medicament with the same or better therapeutic result. As an example, if the dose of the medicament is lowered, then so too are the side-effects of the medicament such as, for example, drowsiness, nervousness, dizziness or, in some instances, sleeplessness. Similarly, the administration of a lowered dose of the asthma/allergy medicament may make the medicament more compatible with the administration of other medicaments such as those which are currently not simultaneously prescribed or administered with asthma or allergy medicaments. In some instances, these include certain medicaments which are prescribed for depression, psychiatric or emotional conditions or Parkinson's disease and which contain monoamine oxidase inhibitor (MAOI). Similarly, the ability to potentiate the effect of the asthma/allergy medicament, thereby leading to a decreased effective dose, is useful for treating a wide range of subjects who have previously been contraindicated for such treatment, including subjects with heart disease or diabetes, subjects who have difficulty in urinating due to prostate gland enlargement, and subjects who are pregnant or who are nursing (i.e., breast-feeding). Thus, the invention provides a method for administering to a subject a dose of an asthma/allergy medicament which if administered alone, or if administered without previous administration of an immunostimulatory nucleic acid to the same subject, would be ineffective (and would be considered sub-therapeutic).

[0169] Subject doses of the compounds described herein typically range from about 0.1 μg to 10,000 mg, more typically from about 1 μg/day to 8000 mg, and most typically from about 10 μg to 100 μg. Stated in terms of subject body weight, typical dosages range from about 0.1 μg to 20 mg/kg/day, more typically from about 1 to 10 mg/kg/day, and most typically from about 1 to 5 mg/kg/day.

[0170] In some instances, a sub-therapeutic dosage of the immunostimulatory nucleic acid and the asthma/allergy medicament are used. It has been discovered according to the invention, that when the two classes of drugs are used together, they can be administered in sub-therapeutic doses and still produce a desirable therapeutic result, a "sub-therapeutic dose" as used herein refers to a dosage which is less than that dosage which would produce a therapeutic result in the subject, if administered alone. Thus, the sub-therapeutic dose of an asthma/allergy medicament is one which would not produce the desired therapeutic result in the subject. Therapeutic doses of asthma/allergy medicaments are well known in the field of medicine for the treatment of asthma and allergy. 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 asthma and allergy. 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 above.

[0171] In other aspects, the method of the invention involves administering a high dose of an asthma/allergy medicament to a subject, without inducing side effects. Ordinarily, when an asthma/allergy medicament is administered in a high dose, a variety of side effects can occur. (Discussed in more detail above, as well as in the medical literature). As a result of these side effects, the asthma/allergy medicament is not administered in such high doses, no matter what therapeutic benefits are derived. It was discovered, according to the invention, that such high doses of asthma/allergy medicaments which ordinarily induce side effects can be administered without inducing the side effects as long as the subject also receives an immunostimulatory nucleic acid. The type and extent of the side effects ordinarily induced by the asthma/allergy medicament will depend on the particular asthma/allergy medicament used.

[0172] In other embodiments of the invention, the immunostimulatory nucleic acid is administered on a routine schedule. The asthma/allergy medicament may also be administered on a routine schedule, but alternatively, may be administered as symptoms arise. A "routine schedule" as used herein, refers to a predetermined designated period of time. The routine schedule may encompass periods of time which are identical or which differ in length, as long as the schedule is predetermined. For instance, the routine schedule may involve administration of the immunostimulatory nucleic acid on a daily basis, every two days, every three days, every four days, every five days, every six days, a weekly basis, a bi-weekly basis, a monthly basis, a bi-monthly basis or any set number of days or weeks therebetween, every two months, three months, four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, etc. Alternatively, the predetermined routine schedule may involve administration of the immunostimulatory nucleic acid on a daily basis for the first week, followed by a monthly basis for several months, and then every three months after that. Any particular combination would be covered by the routine schedule as long as it is determined ahead of time that the appropriate schedule involves administration on a certain day.

[0173] In some aspects of the invention, the immunostimulatory nucleic acid is administered to the subject in anticipation of an asthmatic or allergic event in order to prevent an asthmatic or allergic event. The asthmatic or allergic event may be, but need not be limited to, an asthma attack, seasonal allergic rhinitis (e.g., hay-fever, pollen, ragweed hypersensitivity) or perennial allergic rhinitis (e.g., hypersensitivity to allergens such as those described herein). In some instances, the immunostimulatory nucleic acid is administered substantially prior to an asthmatic or an allergic event. As used herein, "substantially prior" means at least six months, at least five months, at least four months, at least three months, at least two months, at least one month, at least three weeks, at least two weeks, at least one week, at least 5 days, or at least 2 days prior to the asthmatic or allergic event.

[0174] Similarly, the asthma/allergy medicament may be administered immediately prior to the asthmatic or allergic event (e.g., within 48 hours, within 24 hours, within 12 hours, within 6 hours, within 4 hours, within 3 hours, within 2 hours, within 1 hour, within 30 minutes or within 10 minutes of an asthmatic or allergic event), substantially simultaneously with the asthmatic or allergic event (e.g., during the time the subject is in contact with the allergen or is experiencing the asthma or allergy symptoms) or following the asthmatic or allergic event.

[0175] In some embodiments, the immunostimulatory nucleic acid and the asthma/allergy medicament are both administered to a subject. The timing of administration of both may vary. In some embodiments, it is preferred that the asthma/allergy medicament be administered subsequent to the administration of the immunostimulatory nucleic acid. In some embodiments, the immunostimulatory nucleic acid is administered to the subject prior to as well as either substantially simultaneously with or following the administration of the asthma/allergy medicament. The administration of the immunostimulatory nucleic acid and the asthma/allergy medicament may also be mutually exclusive of each other so that at any given time during the treatment period, only one of these agents is active in the subject. Alternatively, and preferably in some instances, the administration of the two agents overlaps such that both agents are active in the subject at the same time.

[0176] In some embodiments, the immunostimulatory nucleic acid is administered on a weekly or biweekly basis and the asthma/allergy medicament is administered more frequently (e.g., on a daily basis). However, if the dose of immunostimulatory nucleic acid is reduced sufficiently, it is possible that the immunostimulatory nucleic acid is administered as frequently as the asthma/allergy medicament, albeit at a reduced dose.

[0177] In other aspects, the invention relates to kits that are useful in the treatment of asthma and/or allergy. One kit of the invention includes a sustained release vehicle containing an immunostimulatory nucleic acid and a container housing an asthma/allergy medicament and instructions for timing of administration of the immunostimulatory nucleic acid in the asthma/allergy medicament. A sustained release vehicle is used herein in accordance with its prior art meaning of any device which slowly releases the immunostimulatory nucleic acid.

[0178] 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), copolyoxalates, polycaprolactones, polyesteramides, polyorthoesters, polyhydroxybutyric acid, and polyanhydrides. Microcapsules of the foregoing polymers containing drugs are described in, for example, U.S. Pat. No. 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

[0179] 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) diffusional 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.

[0180] The asthma/allergy medicament is housed in at least one container. The container may be a single container housing all of the asthma/allergy medicament together or it may be multiple containers or chambers housing individual dosages of the asthma/allergy medicament, such as a blister pack. The kit also has instructions for timing of administration of the asthma/allergy medicament. The instructions would direct the subject having asthma/allergy or at risk of asthma/allergy to take the asthma/allergy medicament at the appropriate time. For instance, the appropriate time for delivery of the medicament may be as the symptoms occur. Alternatively, the appropriate time for administration of the medicament may be on a routine schedule such as monthly or yearly.

[0181] Another kit of the invention includes at least one container housing an immunostimulatory nucleic acid and at least one container housing an asthma/allergy medicament and instructions for administering the compositions in effective amounts for inducing a synergistic immune response in the subject. The immunostimulatory nucleic acid and asthma/allergy medicament may be housed in single containers or in separate compartments or containers, such as single dose compartments. The instructions in the kit direct the subject to take the immunostimulatory nucleic acid and the asthma/allergy medicament in amounts which will produce a synergistic immune response. The drugs may be administered simultaneously or separately as long as they are administered close enough in time to produce a synergistic response.

[0182] In other aspects of the invention, a composition is provided. The composition includes an immunostimulatory nucleic and an asthma/allergy medicament formulated in a pharmaceutically-acceptable carrier and present in the composition in an effective amount for preventing or treating an immune or inflammatory response associated with exposure to a mediator of asthma or allergy. The effective amount for preventing or treating an immune or inflammatory response is that amount which prevents, inhibits completely or partially the induction of the immune or inflammatory response or prevents an increase in the immune or inflammatory response associated with asthma or allergy. An immune or inflammatory response associated with asthma or allergy includes an induction in IgE, an increase in Th2 cytokines, etc. A mediator of asthma or allergy includes asthma initiators and allergens. An example of a composition is one which comprises an immunostimulatory nucleic acid, such as a CpG nucleic acid, and an asthma/allergy medicament, such as an anti-IgE agent (e.g., an anti-IgE antibody or antibody fragment). Such a composition can be administered to a subject on a routine basis such as monthly, bimonthly, or quarterly.

[0183] For any compound described herein a therapeutically effective amount can be initially determined from cell culture assays. For instance the effective amount of immu-

nostimulatory nucleic acid useful for inducing B cell activation can be assessed using the in vitro assays with respect to stimulation index in comparison to known immunostimulatory acids. The stimulation index can be used to determine an effective amount of the particular oligonucleotide for the particular subject, and the dosage can be adjusted upwards or downwards to achieve the desired levels in the subject. Therapeutically effective amounts can also be determined from animal models. A therapeutically effective dose can also be determined from human data for immunostimulatory nucleic acids which have been tested in humans (human clinical trials have been initiated) and for compounds which are known to exhibit similar pharmacological activities, such as other adjuvants, e.g., LT and other antigens for vaccination purposes. 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. Most of the asthma/allergy medicaments have been identified. These amounts can be adjusted when they are combined with immuno-stimulatory nucleic acids by routine experimentation.

[0184] 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.

[0185] Asthma/allergy medicaments and immunostimulatory nucleic acids can be administered by any ordinary route for administering medications. Preferably, they are inhaled, ingested or administered by local routes (such as nasal drops) or by systemic routes. Systemic routes include oral and parenteral. Inhaled medications are preferred in some embodiments because of the direct delivery to the lung, the site of inflammation, primarily in asthmatic patients. Several types of metered dose inhalers are regularly used for administration by inhalation. These types of devices include metered dose inhalers (MDI), breath-actuated MDI, dry powder inhaler (DPI), spacer/holding chambers in combination with MDI, and nebulizers. As used herein, delivery to the nasal passages or the lungs via nasal drops or inhalation are referred to as local administration. Although it is possible that delivery to the lung (e.g., via inhalation) can eventually result in systemic delivery of the agent, the administration is still considered "local" in the sense that the majority of the agent is initially presented to the lung tissue or the nasal passages, prior to any secondary systemic effects. In some preferred embodiments, the immunostimulatory nucleic acid is administered locally, such as for example by nasal drops or inhalation.

[0186] For use in therapy, an effective amount of the immunostimulatory nucleic acid can be administered to a subject by any mode that delivers the nucleic acid to the desired surface, e.g., mucosal, systemic. "Administering" the pharmaceutical composition of the present invention may be accomplished by any means known to the skilled artisan. Preferred routes of administration include but are not limited to oral, parenteral, intramuscular, intranasal, intratracheal, inhalation, ocular, vaginal, and rectal.

[0187] For oral administration, the compounds (i.e., immunostimulatory nucleic acids, asthma/allergy medicament, other therapeutic agent) can be formulated readily by combining the active compound(s) with pharmaceutically acceptable carriers well known in the art. 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 grinding a 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 internal acid conditions or may be administered without any carriers.

[0188] Dragee cores are 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.

[0189] 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.

[0190] For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

[0191] For administration by inhalation, the compounds for use according to the present invention may be conveniently delivered in the form of an aerosol spray presentation 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. Techniques for preparing aerosol delivery systems are well known to those of skill in the art. Generally, such systems should utilize

components which will not significantly impair the biological properties of the therapeutic, such as the immunostimulatory capacity of the nucleic acids (see, for example, Sciarra and Cutie, "Aerosols," in *Remington's Pharmaceutical Sciences,* 18th edition, 1990, pp 1694-1712; incorporated by reference). Those of skill in the art can readily determine the various parameters and conditions for producing aerosols without resort to undue experimentation.

[0192] The compounds, when it is desirable to deliver them systemically, 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 multi-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 formulatory agents such as suspending, stabilizing and/or dispersing agents.

[0193] 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.

[0194] Alternatively, the active compounds may be in powder form for constitution with a suitable vehicle, e.g., sterile pyrogen-free water, before use.

[0195] 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 cocoa butter or other glycerides.

[0196] 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 hydrophobic 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.

[0197] 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.

[0198] Suitable liquid or solid pharmaceutical preparation forms are, for example, aqueous or saline solutions for inhalation, microencapsulated, encochleated, coated onto microscopic gold particles, contained in liposomes, nebulized, aerosols, pellets for implantation into the skin, or dried onto a sharp object to be scratched into the skin. The pharmaceutical compositions also include granules, powders, tablets, coated tablets, (micro)capsules, suppositories, syrups, emulsions, suspensions, creams, drops or preparations with protracted 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 methods for drug delivery, see Langer, *Science* 249:1527-1533, 1990, which is incorporated herein by reference.

[0199] The immunostimulatory nucleic acids and asthma/allergy medicament may be administered per se (neat) 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, acetic, salicylic, p-toluene sulphonic, tartaric, citric, methane sulphonic, formic, malonic, succinic, naphthalene-2-sulphonic, and benzene sulphonic. 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.

[0200] Suitable buffering agents 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); and 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).

[0201] The pharmaceutical compositions of the invention contain an effective amount of an immunostimulatory nucleic acid and optionally asthma/allergy medicament and/or other therapeutic agents optionally included in a pharmaceutically-acceptable carrier. The term "pharmaceutically-acceptable carrier" means one or more compatible solid or liquid filler, dilutants 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.

[0202] 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 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.

[0203] All references, patents and patent publications that are recited in this application are incorporated in their entirety herein by reference.

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<210> SEQ ID NO 81
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 81

ggggtccagc gtgcgccatg gggg 24

<210> SEQ ID NO 82
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 82

ggggtgtcgt tcagggggg 19

<210> SEQ ID NO 83
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
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<400> SEQUENCE: 83

tccatgtcgt tcctgtcgtt 20

<210> SEQ ID NO 84
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 84

tccatagcgt tcctagcgtt 20

<210> SEQ ID NO 85
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 85

tcgtcgctgt ctccgcttct t 21

<210> SEQ ID NO 86
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 86

gcatgacgtt gagct 15

<210> SEQ ID NO 87
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 87

tctcccagcg tgcgccatat 20

<210> SEQ ID NO 88
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (17)...(17)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 88

tccatgangt tcctgangtt 20

<210> SEQ ID NO 89
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 89

gcatgangtt gagct 15

<210> SEQ ID NO 90
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 90

tccagcgtgc gccata 16

<210> SEQ ID NO 91
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 91

tctcccagcg tgcgccat 18

<210> SEQ ID NO 92
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 92

tccatgagct tcctgagtct 20

<210> SEQ ID NO 93
<211> LENGTH: 15
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 93

gcatgtcgtt gagct 15

<210> SEQ ID NO 94
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 94

tcctgacgtt cctgacgtt 19

<210> SEQ ID NO 95
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 95

gcatgatgtt gagct 15

<210> SEQ ID NO 96
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 96

gcatttcgag gagct 15

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<210> SEQ ID NO 97
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 97

gcatgtagct gagct 15

<210> SEQ ID NO 98
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 98

tccaggacgt tcctagttct 20

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

<400> SEQUENCE: 99

tccaggagct tcctagttct 20

<210> SEQ ID NO 100
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 100

tccaggatgt tcctagttct 20

<210> SEQ ID NO 101
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 101

tccagtctag gcctagttct 20

<210> SEQ ID NO 102
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 102

tccagttcga gcctagttct 20

<210> SEQ ID NO 103
<211> LENGTH: 15
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 103

gcatggcgtt gagct 15

<210> SEQ ID NO 104
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 104

gcatagcgtt gagct 15

<210> SEQ ID NO 105
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 105

gcattgcgtt gagct 15

<210> SEQ ID NO 106
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 106

gcttgcgttg cgttt 15

<210> SEQ ID NO 107
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 107

tctcccagcg ttgcgccata t 21

<210> SEQ ID NO 108
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 108

tctcccagcg tgcgttatat 20

<210> SEQ ID NO 109
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 109

tctccctgcg tgcgccatat 20

<210> SEQ ID NO 110
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 110

tctgcgtgcg tgcgccatat 20

<210> SEQ ID NO 111
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 111

tctcctagcg tgcgccatat 20

<210> SEQ ID NO 112
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 112

tctcccagcg tgcgcctttt 20

<210> SEQ ID NO 113
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: n is a or g or c or t/u
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: d is a or g or t/u; not c
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (9)...(10)
<223> OTHER INFORMATION: h is a or c or t/u; not g

<400> SEQUENCE: 113

gctandcghh agc 13

<210> SEQ ID NO 114
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 114

tcctgacgtt ccc 13

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<210> SEQ ID NO 115
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 115

ggaagacgtt aga 13

<210> SEQ ID NO 116
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 116

tcctgacgtt aga 13

<210> SEQ ID NO 117
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 117

tcagaccagc tggtcgggtg ttcctga 27

<210> SEQ ID NO 118
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 118

tcaggaacac ccgaccagct ggtctga 27

<210> SEQ ID NO 119
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 119

gctagtcgat agc 13

<210> SEQ ID NO 120
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 120

gctagtcgct agc 13

<210> SEQ ID NO 121
<211> LENGTH: 14
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 121

gcttgacgtc tagc 14

<210> SEQ ID NO 122
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 122

gcttgacgtt tagc 14

<210> SEQ ID NO 123
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 123

gcttgacgtc aagc 14

<210> SEQ ID NO 124
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 124

gctagacgtt tagc 14

<210> SEQ ID NO 125
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 125

tccatgacat tcctgatgct 20

<210> SEQ ID NO 126
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 126

gctagacgtc tagc 14

<210> SEQ ID NO 127
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 127

ggctatgtcg ttcctagcc 19

<210> SEQ ID NO 128
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 128

ggctatgtcg atcctagcc 19

<210> SEQ ID NO 129
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 129

ctcatgggtt tctccaccaa g 21

<210> SEQ ID NO 130
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 130

cttggtggag aaacccatga g 21

<210> SEQ ID NO 131
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 131

tccatgacgt tcctagttct 20

<210> SEQ ID NO 132
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 132

ccgcttcctc cagatgagct catg 24

<210> SEQ ID NO 133
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 133

catgagctca tctggaggaa gcgg 24

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<210> SEQ ID NO 134
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 134

ccagatgagc tcatgggttt ctcc 24

<210> SEQ ID NO 135
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 135

ggagaaaccc atgagctcat ctgg 24

<210> SEQ ID NO 136
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 136

agcatcagga acgacatgga 20

<210> SEQ ID NO 137
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 137

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 138
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 138

gcgcgcgcgc gcgcgcgcg 19

<210> SEQ ID NO 139
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 139

ccggccggcc ggccggccgg 20

<210> SEQ ID NO 140
<211> LENGTH: 43
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 140

ttccaatcag ccccacccgc tctggcccca ccctcaccct cca 43

<210> SEQ ID NO 141
<211> LENGTH: 43
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 141

tggagggtga gggtggggcc agagcgggtg gggctgattg gaa 43

<210> SEQ ID NO 142
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 142

tcaaatgtgg gattttccca tgagtct 27

<210> SEQ ID NO 143
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 143

agactcatgg gaaaatccca catttga 27

<210> SEQ ID NO 144
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 144

tgccaagtgc tgagtcacta ataaaga 27

<210> SEQ ID NO 145
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 145

tctttattag tgactcagca cttggca 27

<210> SEQ ID NO 146
<211> LENGTH: 31
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 146

tgcaggaagt ccgggttttc cccaaccccc c 31

<210> SEQ ID NO 147
<211> LENGTH: 31
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 147

ggggggttgg ggaaaacccg gacttcctgc a 31

<210> SEQ ID NO 148
<211> LENGTH: 38
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 148

ggggactttc cgctggggac tttccagggg gactttcc 38

<210> SEQ ID NO 149
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 149

tccatgacgt tcctctccat gacgttcctc tccatgacgt tcctc 45

<210> SEQ ID NO 150
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 150

gaggaacgtc atggagagga acgtcatgga gaggaacgtc atgga 45

<210> SEQ ID NO 151
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 151

ataatagagc ttcaagcaag 20

<210> SEQ ID NO 152
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 152

tccatgacgt tcctgacgtt 20

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<210> SEQ ID NO 153
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 153

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 154
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 154

tccaggactt tcctcaggtt 20

<210> SEQ ID NO 155
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 155

tcttgcgatg ctaaaggacg tcacattgca caatcttaat aaggt 45

<210> SEQ ID NO 156
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 156

accttattaa gattgtgcaa tgtgacgtcc tttagcatcg caaga 45

<210> SEQ ID NO 157
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 157

tcctgacgtt cctggcggtc ctgtcgct 28

<210> SEQ ID NO 158
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 158

tcctgtcgct cctgtcgct 19

<210> SEQ ID NO 159
<211> LENGTH: 15
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 159

tcctgacgtt gaagt 15

<210> SEQ ID NO 160
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 160

tcctgtcgtt gaagt 15

<210> SEQ ID NO 161
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 161

tcctggcgtt gaagt 15

<210> SEQ ID NO 162
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 162

tcctgccgtt gaagt 15

<210> SEQ ID NO 163
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 163

tccttacgtt gaagt 15

<210> SEQ ID NO 164
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 164

tcctaacgtt gaagt 15

<210> SEQ ID NO 165
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 165

tcctcacgtt gaagt 15

<210> SEQ ID NO 166
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 166

tcctgacgat gaagt 15

<210> SEQ ID NO 167
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 167

tcctgacgct gaagt 15

<210> SEQ ID NO 168
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 168

tcctgacggt gaagt 15

<210> SEQ ID NO 169
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 169

tcctgacgta gaagt 15

<210> SEQ ID NO 170
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 170

tcctgacgtc gaagt 15

<210> SEQ ID NO 171
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 171

tcctgacgtg gaagt 15

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<210> SEQ ID NO 172
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 172

tcctgagctt gaagt 15

<210> SEQ ID NO 173
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 173

gggggacgtt ggggg 15

<210> SEQ ID NO 174
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 174

tcctgacgtt ccttc 15

<210> SEQ ID NO 175
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 175

tctcccagcg agcgagcgcc at 22

<210> SEQ ID NO 176
<211> LENGTH: 32
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 176

tcctgacgtt cccctggcgg tcccctgtcg ct 32

<210> SEQ ID NO 177
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 177

tcctgtcgct cctgtcgctc ctgtcgct 28

<210> SEQ ID NO 178
<211> LENGTH: 15
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 178

tcctggcggg gaagt 15

<210> SEQ ID NO 179
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 179

tcctgangtt gaagt 15

<210> SEQ ID NO 180
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 180

tcntgacgtt gaagt 15

<210> SEQ ID NO 181
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 181

tcctagcgtt gaagt 15

<210> SEQ ID NO 182
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 182

tccagacgtt gaagt 15

<210> SEQ ID NO 183
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 183

tcctgacggg gaagt 15

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<210> SEQ ID NO 184
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 184

tcctggcggt gaagt 15

<210> SEQ ID NO 185
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 185

ggctccgggg agggaatttt tgtctat 27

<210> SEQ ID NO 186
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 186

atagacaaaa attccctccc cggagcc 27

<210> SEQ ID NO 187
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 187

tccatgagct tccttgagtc t 21

<210> SEQ ID NO 188
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 188

tcgtcgctgt ctccgcttct t 21

<210> SEQ ID NO 189
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 189

tcgtcgctgt ctccgcttct t 21

<210> SEQ ID NO 190
<211> LENGTH: 23
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 190

tcgagacatt gcacaatcat ctg 23

<210> SEQ ID NO 191
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 191

cagattgtgc aatgtctcga 20

<210> SEQ ID NO 192
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 192

tccatgtcgt tcctgatgcg 20

<210> SEQ ID NO 193
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 193

gcgatgtcgt tcctgatgct 20

<210> SEQ ID NO 194
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 194

gcgatgtcgt tcctgatgcg 20

<210> SEQ ID NO 195
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 195

tccatgtcgt tccgcgcgcg 20

<210> SEQ ID NO 196
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 196

tccatgtcgt tcctgccgct 20

<210> SEQ ID NO 197
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 197

tccatgtcgt tcctgtagct 20

<210> SEQ ID NO 198
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 198

gcggcgggcg gcgcgcgccc 20

<210> SEQ ID NO 199
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 199

atcaggaacg tcatgggaag c 21

<210> SEQ ID NO 200
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 200

tccatgagct tcctgagtct 20

<210> SEQ ID NO 201
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 201

tcaacgtt 8

<210> SEQ ID NO 202
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 202

tcaagctt 8

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<210> SEQ ID NO 203
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 203

tcctgtcgtt cctgtcgtt 19

<210> SEQ ID NO 204
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 204

tccatgtcgt ttttgtcgtt 20

<210> SEQ ID NO 205
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 205

tcctgtcgtt ccttgtcgtt 20

<210> SEQ ID NO 206
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 206

tccttgtcgt tcctgtcgtt 20

<210> SEQ ID NO 207
<211> LENGTH: 29
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 207

tccattccat gacgttcctg atgcttcca 29

<210> SEQ ID NO 208
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 208

tcctgtcgtt ttttgtcgtt 20

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<210> SEQ ID NO 209
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 209

tcgtcgctgt ctccgcttct t 21

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

<400> SEQUENCE: 210

tcgtcgctgt ctgcccttct t 21

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

<400> SEQUENCE: 211

tcgtcgctgt tgtcgtttct t 21

<210> SEQ ID NO 212
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 212

tcctgtcgtt cctgtcgttg gaacgacagg 30

<210> SEQ ID NO 213
<211> LENGTH: 40
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 213

tcctgtcgtt cctgtcgttt caacgtcagg aacgacagga 40

<210> SEQ ID NO 214
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 214

ggggtctgtc gttttggggg g 21

<210> SEQ ID NO 215
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 215

ggggtctgtg cttttggggg g 21

<210> SEQ ID NO 216
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 216

tccggccgtt gaagt 15

<210> SEQ ID NO 217
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 217

tccggacggt gaagt 15

<210> SEQ ID NO 218
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 218

tcccgccgtt gaagt 15

<210> SEQ ID NO 219
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 219

tccagacggt gaagt 15

<210> SEQ ID NO 220
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 220

tcccgacggt gaagt 15

<210> SEQ ID NO 221
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 221

tccagagctt gaagt 15

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

<400> SEQUENCE: 222

tccatgtngt tcctgtngtt 20

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

<400> SEQUENCE: 223

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 224
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 224

ggggttgacg ttttgggggg 20

<210> SEQ ID NO 225
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 225

tccaggactt ctctcaggtt 20

<210> SEQ ID NO 226
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 226

ttttttttt ttttttttt 20

<210> SEQ ID NO 227
<211> LENGTH: 20
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 227

tccatgccgt tcctgccgtt 20

<210> SEQ ID NO 228
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 228

tccatggcgg gcctggcggg 20

<210> SEQ ID NO 229
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 229

tccatgacgt tcctgccgtt 20

<210> SEQ ID NO 230
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 230

tccatgacgt tcctggcggg 20

<210> SEQ ID NO 231
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 231

tccatgacgt tcctgcgttt 20

<210> SEQ ID NO 232
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 232

tccatgacgg tcctgacggt 20

<210> SEQ ID NO 233
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 233

tccatgcgtg cgtgcgtttt 20

<210> SEQ ID NO 234
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 234

tccatgcgtt gcgttgcgtt 20

<210> SEQ ID NO 235
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 235

tccattccat tctaggcctg agtcttccat 30

<210> SEQ ID NO 236
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 236

tccatagcgt tcctagcgtt 20

<210> SEQ ID NO 237
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 237

tccatgtcgt tcctgtcgtt 20

<210> SEQ ID NO 238
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 238

tccatagcga tcctagcgat 20

<210> SEQ ID NO 239
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 239

tccattgcgt tccttgcgtt 20

<210> SEQ ID NO 240
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 240

tccatagcgg tcctagcggt 20

<210> SEQ ID NO 241
<211> LENGTH: 29
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 241

tccatgattt tcctgcagtt cctgatttt 29

<210> SEQ ID NO 242
<211> LENGTH: 29
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 242

tccatgacgt tcctgcagtt cctgacgtt 29

<210> SEQ ID NO 243
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 243

ggcggcggcg gcggcggcgg 20

<210> SEQ ID NO 244
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 244

tccacgacgt tttcgacgtt 20

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

<400> SEQUENCE: 245

tcgtcgttgt cgttgtcgtt 20

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<210> SEQ ID NO 246
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 246

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 247
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 247

tcgtcgttgt cgttttgtcg tt 22

<210> SEQ ID NO 248
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 248

gcgtgcgttg tcgttgtcgt t 21

<210> SEQ ID NO 249
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (10)...(10)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (15)...(15)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 249

cnggcnggcn gggcnccgg 19

<210> SEQ ID NO 250
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 250

gcggcgggcg gcgcgcgccc 20

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<210> SEQ ID NO 251
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: I
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: I
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (14)...(14)
<223> OTHER INFORMATION: I

<400> SEQUENCE: 251

agncccgnga acgnattcac 20

<210> SEQ ID NO 252
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 252

tgtcgtttgt cgtttgtcgt t 21

<210> SEQ ID NO 253
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 253

tgtcgttgtc gttgtcgttg tcgtt 25

<210> SEQ ID NO 254
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 254

tgtcgttgtc gttgtcgttg tcgtt 25

<210> SEQ ID NO 255
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 255

tcgtcgtcgt cgtt 14

<210> SEQ ID NO 256
<211> LENGTH: 13
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 256

tgtcgttgtc gtt 13

<210> SEQ ID NO 257
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 257

ccccccccc ccccccccc 20

<210> SEQ ID NO 258
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 258

tctagcgttt ttagcgttcc 20

<210> SEQ ID NO 259
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 259

tgcatccccc aggccaccat 20

<210> SEQ ID NO 260
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 260

tcgtcgtcgt cgtcgtcgtc gtt 23

<210> SEQ ID NO 261
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 261

tcgtcgttgt cgttgtcgtt 20

<210> SEQ ID NO 262
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 262

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 263
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 263

tcgtcgttgt cgttttgtcg tt 22

<210> SEQ ID NO 264
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 264

ggggagggag gaacttctta aaattccccc agaatgttt 39

<210> SEQ ID NO 265
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 265

aaacattctg ggggaatttt aagaagttcc tccctcccc 39

<210> SEQ ID NO 266
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 266

atgtttactt cttaaaattc ccccagaatg ttt 33

<210> SEQ ID NO 267
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 267

aaacattctg ggggaatttt aagaagtaaa cat 33

<210> SEQ ID NO 268
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 268

atgtttacta gacaaaattc ccccagaatg ttt 33

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<210> SEQ ID NO 269
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 269

aaacattctg ggggaatttt gtctagtaaa cat 33

<210> SEQ ID NO 270
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 270

aaaattgacg ttttaaaaaa 20

<210> SEQ ID NO 271
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 271

ccccttgacg ttttcccccc 20

<210> SEQ ID NO 272
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 272

ttttcgttgt ttttgtcgtt 20

<210> SEQ ID NO 273
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 273

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 274
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 274

ctgcagcctg ggac 14

<210> SEQ ID NO 275
<211> LENGTH: 25
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 275

acccgtcgta attatagtaa aaccc 25

<210> SEQ ID NO 276
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 276

ggtacctgtg gggacattgt g 21

<210> SEQ ID NO 277
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 277

agcaccgaac gtgagagg 18

<210> SEQ ID NO 278
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 278

tccatgccgt tcctgccgtt 20

<210> SEQ ID NO 279
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 279

tccatgacgg tcctgacggt 20

<210> SEQ ID NO 280
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 280

tccatgccgg tcctgccggt 20

<210> SEQ ID NO 281
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 281

tccatgcgcg tcctgcgcgt 20

<210> SEQ ID NO 282
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 282

ctggtctttc tggtttttt ctgg 24

<210> SEQ ID NO 283
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 283

tcaggggtgg ggggaacctt 20

<210> SEQ ID NO 284
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 284

tccatgangt tcctagttct 20

<210> SEQ ID NO 285
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 285

tccatgatgt tcctagttct 20

<210> SEQ ID NO 286
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 286

cccgaagtca tttcctctta acctgg 26

<210> SEQ ID NO 287
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 287

ccaggttaag aggaaatgac ttcggg 26

<210> SEQ ID NO 288
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 288

tcctggnggg gaagt 15

<210> SEQ ID NO 289
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (9)...(9)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (12)...(12)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (14)...(14)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (16)...(16)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 289

gnggngggng gngngngccc 20

<210> SEQ ID NO 290
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 290

tccatgtgct tcctgatgct 20

<210> SEQ ID NO 291
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 291

tccatgtcct tcctgatgct 20

<210> SEQ ID NO 292
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 292

tccatgtcgt tcctagttct 20

<210> SEQ ID NO 293
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 293

tccaagtagt tcctagttct 20

<210> SEQ ID NO 294
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 294

tccatgtagt tcctagttct 20

<210> SEQ ID NO 295
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 295

tcccgcgcgt tccgcgcgtt 20

<210> SEQ ID NO 296
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 296

tcctggcggt cctggcggtt 20

<210> SEQ ID NO 297
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 297

tcctggaggg gaagt 15

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<210> SEQ ID NO 298
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 298

tcctgggggg gaagt 15

<210> SEQ ID NO 299
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 299

tcctggtggg gaagt 15

<210> SEQ ID NO 300
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 300

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 301
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 301

ctggtctttc tggttttttt ctgg 24

<210> SEQ ID NO 302
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 302

tccatgacgt tcctgacgtt 20

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

<400> SEQUENCE: 303

tccaggactt ctctcaggtt 20

<210> SEQ ID NO 304
<211> LENGTH: 24
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (13)...(13)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (21)...(21)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 304

tngtngtttt gtngttttgt ngtt 24

<210> SEQ ID NO 305
<211> LENGTH: 29
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 305

tcgtcgtttt gtcgttttgt cgttttttt 29

<210> SEQ ID NO 306
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 306

gctatgacgt tccaaggg 18

<210> SEQ ID NO 307
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 307

tcaacgtt 8

<210> SEQ ID NO 308
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 308

tccaggactt tcctcaggtt 20

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<210> SEQ ID NO 309
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 309

ctctctgtag gcccgcttgg 20

<210> SEQ ID NO 310
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 310

ctttccgttg gacccctggg 20

<210> SEQ ID NO 311
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 311

gtccgggcca ggccaaagtc 20

<210> SEQ ID NO 312
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 312

gtgcgcgcga gcccgaaatc 20

<210> SEQ ID NO 313
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: I
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (17)...(17)
<223> OTHER INFORMATION: I

<400> SEQUENCE: 313

tccatgangt tcctgangtt 20

<210> SEQ ID NO 314
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 314

aatagtcgcc ataacaaaac 20

<210> SEQ ID NO 315
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 315

aatagtcgcc atggcggggc 20

<210> SEQ ID NO 316
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Biotin moiety attached at 5' end of sequence.

<400> SEQUENCE: 316

tttttccatg tcgttcctga tgcttttt 28

<210> SEQ ID NO 317
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 317

tcctgtcgtt gaagtttttt 20

<210> SEQ ID NO 318
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 318

gctagcttta gagctttaga gctt 24

<210> SEQ ID NO 319
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 319

tgctgcttcc cccccccccc 20

<210> SEQ ID NO 320
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 320

tcgacgttcc ccccccccc 20

<210> SEQ ID NO 321
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 321

tcgtcgttcc ccccccccc 20

<210> SEQ ID NO 322
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 322

tcgtcgttcc ccccccccc 20

<210> SEQ ID NO 323
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 323

tcgccgttcc ccccccccc 20

<210> SEQ ID NO 324
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 324

tcgtcgatcc ccccccccc 20

<210> SEQ ID NO 325
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 325

tcctgacgtt gaagt 15

<210> SEQ ID NO 326
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 326

tcctgccgtt gaagt 15

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<210> SEQ ID NO 327
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 327

tcctgacggt gaagt 15

<210> SEQ ID NO 328
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 328

tcctgagctt gaagt 15

<210> SEQ ID NO 329
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 329

tcctggcggg gaagt 15

<210> SEQ ID NO 330
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 330

aaaatctgtg cttttaaaaa a 21

<210> SEQ ID NO 331
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 331

gatccagtca cagtgacctg gcagaatctg gat 33

<210> SEQ ID NO 332
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 332

gatccagatt ctgccaggtc actgtgactg gat 33

<210> SEQ ID NO 333
<211> LENGTH: 33
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 333

gatccagtca cagtgactca gcagaatctg gat 33

<210> SEQ ID NO 334
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 334

gatccagatt ctgctgagtc actgtgactg gat 33

<210> SEQ ID NO 335
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (16)...(16)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 335

tcgtcgttcc cccccncccc 20

<210> SEQ ID NO 336
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 336

tngtngttcc cccccccccc 20

<210> SEQ ID NO 337
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 337

tngtcgttcc cccccccccc 20

<210> SEQ ID NO 338
<211> LENGTH: 20
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 338

tcgtngttcc ccccccccc 20

<210> SEQ ID NO 339
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 339

tcgtcgctcc ccccccccc 20

<210> SEQ ID NO 340
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 340

tcgtcggtcc ccccccccc 20

<210> SEQ ID NO 341
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 341

tcggcgttcc ccccccccc 20

<210> SEQ ID NO 342
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 342

ggccttttcc ccccccccc 20

<210> SEQ ID NO 343
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 343

tcgtcgtttt gacgttttgt cgtt 24

<210> SEQ ID NO 344
<211> LENGTH: 24
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 344

tcgtcgtttt gacgttttga cgtt 24

<210> SEQ ID NO 345
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 345

ccgtcgttcc cccccccccc 20

<210> SEQ ID NO 346
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 346

gcgtcgttcc cccccccccc 20

<210> SEQ ID NO 347
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 347

tcgtcattcc cccccccccc 20

<210> SEQ ID NO 348
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 348

acgtcgttcc cccccccccc 20

<210> SEQ ID NO 349
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 349

ctgtcgttcc cccccccccc 20

<210> SEQ ID NO 350
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Biotin moiety attached at 5' end of sequence.

<400> SEQUENCE: 350

tttttcgtcg ttccccccccc cccc 24

<210> SEQ ID NO 351
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (18)...(20)
<223> OTHER INFORMATION: Biotin moiety attached at 3' end of sequence.

<400> SEQUENCE: 351

tcgtcgttcc ccccccccc 20

<210> SEQ ID NO 352
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (22)...(24)
<223> OTHER INFORMATION: Biotin moiety attached at 3' end of sequence.

<400> SEQUENCE: 352

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 353
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 353

tccagttcct tcctcagtct 20

<210> SEQ ID NO 354
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 354

tngtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 355
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 355

tcctggaggg gaagt 15

<210> SEQ ID NO 356
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 356

tcctgaaaag gaagt 15

<210> SEQ ID NO 357
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 357

tcgtcgttcc ccccccc 17

<210> SEQ ID NO 358
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (13)...(13)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (21)...(21)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 358

tngtngtttt gtngttttgt ngtt 24

<210> SEQ ID NO 359
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 359

ggggtcaagc ttgaggggg 20

<210> SEQ ID NO 360
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 360

tgctgcttcc ccccccccc 20

<210> SEQ ID NO 361
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 361

tcgtcgtcgt cgtt 14

<210> SEQ ID NO 362
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 362

tcgtcgtcgt cgtt 14

<210> SEQ ID NO 363
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 363

tcgtcgtcgt cgtt 14

<210> SEQ ID NO 364
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 364

tcaacgttga 10

<210> SEQ ID NO 365
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 365

tcaacgtt 8

<210> SEQ ID NO 366
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 366

atagttttcc atttttttac 20

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<210> SEQ ID NO 367
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 367

aatagtcgcc atcgcgcgac 20

<210> SEQ ID NO 368
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 368

aatagtcgcc atcccgggac 20

<210> SEQ ID NO 369
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 369

aatagtcgcc atcccccccc 20

<210> SEQ ID NO 370
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 370

tgctgctttt gtgcttttgt gctt 24

<210> SEQ ID NO 371
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 371

ctgtgctttc tgtgtttttc tgtg 24

<210> SEQ ID NO 372
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 372

ctaatctttc taatttttttt ctaa 24

<210> SEQ ID NO 373
<211> LENGTH: 26
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 373

tcgtcgttgg tgtcgttggt gtcgtt 26

<210> SEQ ID NO 374
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 374

tcgtcgttgg ttgtcgtttt ggtt 24

<210> SEQ ID NO 375
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 375

accatggacg agctgtttcc cctc 24

<210> SEQ ID NO 376
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 376

tcgtcgtttt gcgtgcgttt 20

<210> SEQ ID NO 377
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 377

ctgtaagtga gcttggagag 20

<210> SEQ ID NO 378
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 378

gagaacgctg gaccttcc 18

<210> SEQ ID NO 379
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 379

cgggcgactc agtctatcgg 20

<210> SEQ ID NO 380
<211> LENGTH: 37
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 380

gttctcagat aaagcggaac cagcaacaga cacagaa 37

<210> SEQ ID NO 381
<211> LENGTH: 37
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 381

ttctgtgtct gttgctggtt ccgctttatc tgagaac 37

<210> SEQ ID NO 382
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 382

cagacacaga agcccgatag acg 23

<210> SEQ ID NO 383
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 383

agacagacac gaaacgaccg 20

<210> SEQ ID NO 384
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 384

gtctgtccca tgatctcgaa 20

<210> SEQ ID NO 385
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 385

gctggccagc ttacctcccg 20

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<210> SEQ ID NO 386
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 386

ggggcctcta tacaacctgg g 21

<210> SEQ ID NO 387
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 387

ggggtccctg agactgcc 18

<210> SEQ ID NO 388
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 388

gagaacgctg gaccttccat 20

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

<400> SEQUENCE: 389

tccatgtcgg tcctgatgct 20

<210> SEQ ID NO 390
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 390

ctcttgcgac ctggaaggta 20

<210> SEQ ID NO 391
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 391

aggtacagcc aggactacga 20

<210> SEQ ID NO 392
<211> LENGTH: 24
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 392

accatggacg acctgtttcc cctc 24

<210> SEQ ID NO 393
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 393

accatggatt acctttttcc cctt 24

<210> SEQ ID NO 394
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 394

atggaaggtc cagcgttctc 20

<210> SEQ ID NO 395
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 395

agcatcagga ccgacatgga 20

<210> SEQ ID NO 396
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 396

ctctccaagc tcacttacag 20

<210> SEQ ID NO 397
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 397

tccctgagac tgccccacct t 21

<210> SEQ ID NO 398
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 398

gccaccaaaa cttgtccatg 20

<210> SEQ ID NO 399
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 399

gtccatggcg tgcgggatga 20

<210> SEQ ID NO 400
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 400

cctctataca acctgggac 19

<210> SEQ ID NO 401
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 401

cgggcgactc agtctatcgg 20

<210> SEQ ID NO 402
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 402

gcgctaccgg tagcctgagt 20

<210> SEQ ID NO 403
<211> LENGTH: 35
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 403

cgactgccga acaggatatc ggtgatcagc actgg 35

<210> SEQ ID NO 404
<211> LENGTH: 35
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 404

ccagtgctga tcaccgatat cctgttcggc agtcg 35

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<210> SEQ ID NO 405
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 405

ccaggttgta tagaggc 17

<210> SEQ ID NO 406
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 406

tctcccagcg tacgccat 18

<210> SEQ ID NO 407
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 407

tctcccagcg tgcgtttt 18

<210> SEQ ID NO 408
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 408

tctcccgacg tgcgccat 18

<210> SEQ ID NO 409
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 409

tctcccgtcg tgcgccat 18

<210> SEQ ID NO 410
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 410

ataatcgtcg ttcaagcaag 20

<210> SEQ ID NO 411
<211> LENGTH: 23
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 411

tcgtcgtttt gtcgttttgt cgt 23

<210> SEQ ID NO 412
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 412

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 413
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 413

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 414
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: n is a or c or g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: n is a or c or g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (11)...(11)
<223> OTHER INFORMATION: n is a or c or g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (16)...(16)
<223> OTHER INFORMATION: n is a or c or g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (19)...(19)
<223> OTHER INFORMATION: n is a or c or g or t/u
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (24)...(24)
<223> OTHER INFORMATION: n is a or c or g or t/u

<400> SEQUENCE: 414

tcntcgtntt ntcgtnttnt cgtn 24

<210> SEQ ID NO 415
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 415

tctcccagcg tcgccat 17

<210> SEQ ID NO 416
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 416

tctcccatcg tcgccat 17

<210> SEQ ID NO 417
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 417

ataatcgtgc gttcaagaaa g 21

<210> SEQ ID NO 418
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 418

ataatcgacg ttccccccc 20

<210> SEQ ID NO 419
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 419

tctatcgacg ttcaagcaag 20

<210> SEQ ID NO 420
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 420

tcctgacggg gagt 14

<210> SEQ ID NO 421
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 421

tccatgacgt tcctgatcc 19

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<210> SEQ ID NO 422
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 422

tccatgacgt tcctgatcc 19

<210> SEQ ID NO 423
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 423

tccatgacgt tcctgatcc 19

<210> SEQ ID NO 424
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 424

tcctggcgtg gaagt 15

<210> SEQ ID NO 425
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 425

tccatgacgt tcctgatcc 19

<210> SEQ ID NO 426
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 426

tcgtcgctgt tgtcgtttct t 21

<210> SEQ ID NO 427
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 427

agcagcttta gagctttaga gctt 24

<210> SEQ ID NO 428
<211> LENGTH: 24
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 428

ccccccccccc ccccccccccc cccc 24

<210> SEQ ID NO 429
<211> LENGTH: 32
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 429

tcgtcgtttt gtcgttttgt cgttttgtcg tt 32

<210> SEQ ID NO 430
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 430

tcgtcgtttt ttgtcgtttt ttgtcgtt 28

<210> SEQ ID NO 431
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 431

tcgtcgtttt ttttttttt 20

<210> SEQ ID NO 432
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 432

tttttcaacg ttgatttttt 20

<210> SEQ ID NO 433
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 433

ttttttttttt ttttttttttt tttt 24

<210> SEQ ID NO 434
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ggggtcgtcg ttttgggggg 20

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tcgtcgtttt gtcgttttgg gggg 24

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tcgtcgctgt ctccgcttct tcttgcc 27

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tcgtcgctgt ctccg 15

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ctgtaagtga gcttggagag 20

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gagaacgctg gaccttccat 20

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ccaggttgta tagaggc 17

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gctagacgtt agcgtga 17

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ggagctcttc gaacgccata 20

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tctccatgat ggttttatcg 20

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aaggtggggc agtctcaggg a 21

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atcggaggac tggcgcgccg 20

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ttaggacaag gtctagggtg 20

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accacaacga gaggaacgca 20

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ggcagtgcag gctcaccggg 20

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<400> SEQUENCE: 449

gaaccttcca tgctgtt 17

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gctagacgtt agcgtga 17

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gcttggaggg cctgtaagtg 20

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gtagccttcc ta 12

<210> SEQ ID NO 453
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<400> SEQUENCE: 453

cggtagcctt ccta 14

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cacggtagcc ttccta 16

<210> SEQ ID NO 455
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<400> SEQUENCE: 455

agcacggtag ccttccta 18

<210> SEQ ID NO 456
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gaacgctgga ccttccat 18

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gaccttccat 10

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tggaccttcc at 12

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gctggacctt ccat 14

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acgctggacc ttccat 16

<210> SEQ ID NO 461
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taagctctgt caacgccagg 20

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<400> SEQUENCE: 462

gagaacgctg gaccttccat gt 22

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<400> SEQUENCE: 463

tccatgtcgg tcctgatgct 20

<210> SEQ ID NO 464
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<400> SEQUENCE: 464

ttcatgcctt gcaaaatggc g 21

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<400> SEQUENCE: 465

tgctagctgt gcctgtacct 20

<210> SEQ ID NO 466
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<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 466

agcatcagga ccgacatgga 20

<210> SEQ ID NO 467
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<212> TYPE: DNA
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<400> SEQUENCE: 467

gaccttccat gtcggtcctg at 22

<210> SEQ ID NO 468
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 468

acaaccacga gaacgggaac 20

<210> SEQ ID NO 469
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 469

gaaccttcca tgctgttccg 20

<210> SEQ ID NO 470
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 470

caatcaatct gaggagaccc 20

<210> SEQ ID NO 471
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<212> TYPE: DNA
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<400> SEQUENCE: 471

tcagctctgg tacttttca 20

<210> SEQ ID NO 472
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 472

tggttacggt ctgtcccatg 20

<210> SEQ ID NO 473
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 473

gtctatcgga ggactggcgc 20

<210> SEQ ID NO 474
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 474

cattttacgg gcgggcgggc 20

<210> SEQ ID NO 475
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 475

gaggggacca ttttacgggc 20

<210> SEQ ID NO 476
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 476

tgtccagccg aggggaccat 20

<210> SEQ ID NO 477
<211> LENGTH: 20
<212> TYPE: DNA
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<400> SEQUENCE: 477

cgggcttacg gcggatgctg 20

<210> SEQ ID NO 478
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 478

tggaccttct atgtcggtcc 20

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<210> SEQ ID NO 479
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 479

tgtcccatgt ttttagaagc 20

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<212> TYPE: DNA
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<400> SEQUENCE: 480

gtggttacgg tcgtgcccat 20

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<212> TYPE: DNA
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<400> SEQUENCE: 481

cctccaaatg aaagaccccc 20

<210> SEQ ID NO 482
<211> LENGTH: 20
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<400> SEQUENCE: 482

ttgtactctc catgatggtt 20

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
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<400> SEQUENCE: 483

ttccatgctg ttccggctgg 20

<210> SEQ ID NO 484
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 484

gaccttctat gtcggtcctg 20

<210> SEQ ID NO 485
<211> LENGTH: 20
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<213> ORGANISM: Artificial sequence
<220> FEATURE:
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<400> SEQUENCE: 485

gagaccgctc gaccttcgat 20

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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 486

ttgccccata ttttagaaac 20

<210> SEQ ID NO 487
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
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<400> SEQUENCE: 487

ttgaaactga ggtgggac 18

<210> SEQ ID NO 488
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 488

ctatcggagg actggcgcgc c 21

<210> SEQ ID NO 489
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 489

cttggagggc ctcccggcgg 20

<210> SEQ ID NO 490
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
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gctgaacctt ccatgctgtt 20

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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 491

tagaaacagc attcttcttt tagggcagca ca 32

<210> SEQ ID NO 492
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 492

agatggttct cagataaagc ggaa 24

<210> SEQ ID NO 493
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 493

ttccgcttta tctgagaacc atct 24

<210> SEQ ID NO 494
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
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<400> SEQUENCE: 494

gtcccaggtt gtatagaggc tgc 23

<210> SEQ ID NO 495
<211> LENGTH: 20
<212> TYPE: DNA
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<400> SEQUENCE: 495

gcgccagtcc tccgatagac 20

<210> SEQ ID NO 496
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 496

atcggaggac tggcgcgccg 20

<210> SEQ ID NO 497
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<212> TYPE: DNA
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<400> SEQUENCE: 497

ggtctgtccc atatttttag 20

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<212> TYPE: DNA
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<400> SEQUENCE: 498

tttttcaacg ttgaggggg 20

<210> SEQ ID NO 499
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<212> TYPE: DNA
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tttttcaagc gttgattttt t 21

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<212> TYPE: DNA
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<400> SEQUENCE: 500

ggggtcaacg ttgatttttt 20

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 501

ggggttttca acgttttgag ggggg 25

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<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 502

ggttacggtc tgtcccatat 20

<210> SEQ ID NO 503
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 503

ctgtcccata tttttagaca 20

<210> SEQ ID NO 504
<211> LENGTH: 20
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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 504

accatcctga ggccattcgg 20

<210> SEQ ID NO 505
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 505

cgtctatcgg gcttctgtgt ctg 23

<210> SEQ ID NO 506
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 506

ggccatccca cattgaaagt t 21

<210> SEQ ID NO 507
<211> LENGTH: 22
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 507

ccaaatatcg gtggtcaagc ac 22

<210> SEQ ID NO 508
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 508

gtgcttgacc accgatattt gg 22

<210> SEQ ID NO 509
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 509

gtgctgatca ccgatatcct gttcgg 26

<210> SEQ ID NO 510
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 510

ggccaacttt caatgtggga tggcctc 27

<210> SEQ ID NO 511
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 511

ttccgccgaa tggcctcagg atggtac 27

<210> SEQ ID NO 512
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 512

tatagtccct gagactgccc caccttctca acaacc 36

<210> SEQ ID NO 513
<211> LENGTH: 27
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 513

gcagcctcta tacaacctgg gacggga 27

<210> SEQ ID NO 514
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 514

ctatcggagg actggcgcgc cg 22

<210> SEQ ID NO 515
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 515

tatcggagga ctggcgcgcc g 21

<210> SEQ ID NO 516
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 516

gatcggagga ctggcgcgcc g 21

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<210> SEQ ID NO 517
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 517

ccgaacagga tatcggtgat cagcac 26

<210> SEQ ID NO 518
<211> LENGTH: 24
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 518

ttttggggtc aacgttgagg gggg 24

<210> SEQ ID NO 519
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 519

ggggtcaacg ttgaggggg 20

<210> SEQ ID NO 520
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<212> TYPE: DNA
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<400> SEQUENCE: 520

cgcgcgcgcg cgcgcgcgcg 20

<210> SEQ ID NO 521
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<212> TYPE: DNA
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<400> SEQUENCE: 521

ggggcatgac gttcgggggg 20

<210> SEQ ID NO 522
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<400> SEQUENCE: 522

ggggcatgac gttcaaaaaa 20

<210> SEQ ID NO 523
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<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 523

ggggcatgag cttcgggggg 20

<210> SEQ ID NO 524
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 524

ggggcatgac gttcgggggg 20

<210> SEQ ID NO 525
<211> LENGTH: 20
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 525

aaaacatgac gttcaaaaaa 20

<210> SEQ ID NO 526
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 526

aaaacatgac gttcgggggg 20

<210> SEQ ID NO 527
<211> LENGTH: 20
<212> TYPE: DNA
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<400> SEQUENCE: 527

ggggcatgac gttcaaaaaa 20

<210> SEQ ID NO 528
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 528

accatggacg atctgtttcc cctc 24

<210> SEQ ID NO 529
<211> LENGTH: 24
<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 529

gccatggacg aactgttccc cctc 24

<210> SEQ ID NO 530
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ccccccccccc ccccccccccc 20

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gggggggggg gggggggggg 20

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gctgtaaaat gaatcggccg 20

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ttcgggcgga ctcctccatt 20

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tatgccgcgc ccggacttat 20

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ggggtaatcg atcaggggggg 20

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tttgagaacg ctggaccttc 20

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gtcggtcctg atgctgttcc 20

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tcgtcgtcag ttcgctgtcg 20

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ctggaccttc catgtcgg 18

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gctcgttcag cgcgtct 17

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ctggaccttc catgtc 16

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cactgtcctt cgtcga 16

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cgctggacct tccatgtcgg 20

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gctgagctca tgccgtctgc 20

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aacgctggac cttccatgtc 20

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tgcatgccgt acacagctct 20

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ccttccatgt cggtcctgat 20

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tactcttcgg atcccttgcg 20

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ttccatgtcg gtcctgat 18

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ctgattgctc tctcgtga 18

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ggcgttattc ctgactcgcc 20

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cctacgttgt atgcgcccag ct 22

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<400> SEQUENCE: 554

ggggtaatcg atgagggggg 20

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<400> SEQUENCE: 555

ttcgggcgga ctcctccatt 20

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<400> SEQUENCE: 556

ttttttttt ttttttttt 20

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<400> SEQUENCE: 557

ggggggtttt tttttggggg 20

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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 558

tttttggggg gggggttttt 20

<210> SEQ ID NO 559
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 559

ggggggggggg gggggggt 19

<210> SEQ ID NO 560
<211> LENGTH: 20
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 560

aaaaaaaaaa aaaaaaaaaa 20

<210> SEQ ID NO 561
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<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 561

ccccccaaaaa aaaaaccccc 20

<210> SEQ ID NO 562
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 562

aaaaaccccc ccccccaaaaa 20

<210> SEQ ID NO 563
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 563

tttgaattca ggactggtga ggttgag 27

<210> SEQ ID NO 564
<211> LENGTH: 27
<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 564

tttgaatcct cagcggtctc cagtggc 27

<210> SEQ ID NO 565
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 565

aattctctat cggggcttct gtgtctgttg ctggttccgc tttat 45

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 566

ctagataaag cggaaccagc aacagacaca gaagccccga tagag 45

<210> SEQ ID NO 567
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 567

ttttctagag aggtgcacaa tgctctgg 28

<210> SEQ ID NO 568
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 568

tttgaattcc gtgtacagaa gcgagaagc 29

<210> SEQ ID NO 569
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 569

tttgcggccg ctagacttaa cctgagagat a 31

<210> SEQ ID NO 570
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 570

tttgggccca cgagagacag agacacttc 29

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<211> LENGTH: 29
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 571

tttgggcccg cttctcgctt ctgtacacg 29

<210> SEQ ID NO 572
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 572

gagaacgctg gaccttccat 20

<210> SEQ ID NO 573
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 573

tccatgtcgg tcctgatgct 20

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<210> SEQ ID NO 574
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<212> TYPE: DNA
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<400> SEQUENCE: 574

ctgtcg 6

<210> SEQ ID NO 575
<211> LENGTH: 6
<212> TYPE: DNA
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<400> SEQUENCE: 575

tcgtga 6

<210> SEQ ID NO 576
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 576

cgtcga 6

<210> SEQ ID NO 577
<211> LENGTH: 6
<212> TYPE: DNA
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<400> SEQUENCE: 577

agtgct 6

<210> SEQ ID NO 578
<211> LENGTH: 6
<212> TYPE: DNA
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<400> SEQUENCE: 578

ctgtcg 6

<210> SEQ ID NO 579
<211> LENGTH: 6
<212> TYPE: DNA
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<400> SEQUENCE: 579

agtgct 6

<210> SEQ ID NO 580
<211> LENGTH: 6
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 580

cgtcga 6

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 581

tcgtga 6

<210> SEQ ID NO 582
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 582

gagaacgctc cagcttcgat 20

<210> SEQ ID NO 583
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 583

gctagacgta agcgtga 17

<210> SEQ ID NO 584
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 584

gagaacgctc gaccttccat 20

<210> SEQ ID NO 585
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 585

gagaacgctg gacctatcca t 21

<210> SEQ ID NO 586
<211> LENGTH: 17
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 586

gctagaggtt agcgtga 17

<210> SEQ ID NO 587
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 587

gagaacgctg gacttccat 19

<210> SEQ ID NO 588
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 588

tcacgctaac gtctagc 17

<210> SEQ ID NO 589
<211> LENGTH: 17
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<213> ORGANISM: Artificial sequence
<220> FEATURE:
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<220> FEATURE:
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<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 589

gctagacgtt agcgtga 17

<210> SEQ ID NO 590
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 590

atggaaggtc gagcgttctc 20

<210> SEQ ID NO 591
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 591

gagaacgctg gaccttcgat 20

<210> SEQ ID NO 592
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 592

gagaacgatg gaccttccat 20

<210> SEQ ID NO 593
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 593

gagaacgctg gatccat 17

<210> SEQ ID NO 594
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 594

gagaacgctc cagcactgat 20

<210> SEQ ID NO 595
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 595

tccatgtcgg tcctgctgat 20

<210> SEQ ID NO 596
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 596

atgtcctcgg tcctgatgct 20

<210> SEQ ID NO 597
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 597

gagaacgctc caccttccat 20

<210> SEQ ID NO 598
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 598

gagaacgctg gaccttcgta 20

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<210> SEQ ID NO 599
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 599

atggaaggtc cagcgttctc 20

<210> SEQ ID NO 600
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 600

tcctga 6

<210> SEQ ID NO 601
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 601

tcaacgtt 8

<210> SEQ ID NO 602
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 602

aacgtt 6

<210> SEQ ID NO 603
<211> LENGTH: 8
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 603

aacgttga 8

<210> SEQ ID NO 604
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 604

tcacgctaac ctctagc 17

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<210> SEQ ID NO 605
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 605

gagaacgctg gaccttgcat 20

<210> SEQ ID NO 606
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 606

gctggacctt ccat 14

<210> SEQ ID NO 607
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 607

gagaacgctg gacctcatcc at 22

<210> SEQ ID NO 608
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 608

gagaacgctg gacgctcatc cat 23

<210> SEQ ID NO 609
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 609

aacgttgagg ggcat 15

<210> SEQ ID NO 610
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 610

atgcccctca acgtt 15

<210> SEQ ID NO 611
<211> LENGTH: 10
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 611

tcaacgttga 10

<210> SEQ ID NO 612
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 612

gctggacctt ccat 14

<210> SEQ ID NO 613
<211> LENGTH: 7
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 613

caacgtt 7

<210> SEQ ID NO 614
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 614

acaacgttga 10

<210> SEQ ID NO 615
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 615

tcacgt 6

<210> SEQ ID NO 616
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 616

tcaagctt 8

<210> SEQ ID NO 617
<211> LENGTH: 6
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 617

tcgtca 6

<210> SEQ ID NO 618
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 618

aggatatc 8

<210> SEQ ID NO 619
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 619

tagacgtc 8

<210> SEQ ID NO 620
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 620

gacgtcat 8

<210> SEQ ID NO 621
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 621

ccatcgat 8

<210> SEQ ID NO 622
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 622

atcgatgt 8

<210> SEQ ID NO 623
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 623

atgcatgt 8

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<210> SEQ ID NO 624
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 624

ccatgcat 8

<210> SEQ ID NO 625
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 625

agcgctga 8

<210> SEQ ID NO 626
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<212> TYPE: DNA
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<400> SEQUENCE: 626

tcagcgct 8

<210> SEQ ID NO 627
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<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 627

ccttcgat 8

<210> SEQ ID NO 628
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 628

gtgccggggt ctccgggc 18

<210> SEQ ID NO 629
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<212> TYPE: DNA
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<400> SEQUENCE: 629

gctgtggggc ggctcctg 18

<210> SEQ ID NO 630
<211> LENGTH: 8
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
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<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 630

tcaacgtt 8

<210> SEQ ID NO 631
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence
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<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to FITC moiety.

<400> SEQUENCE: 631

tcaacgtt 8

<210> SEQ ID NO 632
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
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<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to FITC moiety.

<400> SEQUENCE: 632

aacgttga 8

<210> SEQ ID NO 633
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 633

tcaacgt 7

<210> SEQ ID NO 634
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<400> SEQUENCE: 634

aacgttg 7

<210> SEQ ID NO 635
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 635

cgacga 6

<210> SEQ ID NO 636
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<400> SEQUENCE: 636

tcaacgtt 8

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<400> SEQUENCE: 637

tcgga 5

<210> SEQ ID NO 638
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 638

agaacgtt 8

<210> SEQ ID NO 639
<211> LENGTH: 8
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 639

tcatcgat 8

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<400> SEQUENCE: 640

taaacgtt 8

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<400> SEQUENCE: 641

ccaacgtt 8

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gctcga 6

<210> SEQ ID NO 643
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<400> SEQUENCE: 643

cgacgt 6

<210> SEQ ID NO 644
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<400> SEQUENCE: 644

cgtcgt 6

<210> SEQ ID NO 645
<211> LENGTH: 6
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<400> SEQUENCE: 645

acgtgt 6

<210> SEQ ID NO 646
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<212> TYPE: DNA
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<400> SEQUENCE: 646

cgttcg 6

<210> SEQ ID NO 647
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 647

gagcaagctg gaccttccat 20

<210> SEQ ID NO 648
<211> LENGTH: 6
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 648

cgcgta 6

<210> SEQ ID NO 649
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cgtacg 6

<210> SEQ ID NO 650
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<400> SEQUENCE: 650

tcaccggt 8

<210> SEQ ID NO 651
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<400> SEQUENCE: 651

caagagatgc taacaatgca 20

<210> SEQ ID NO 652
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 652

acccatcaat agctctgtgc 20

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<400> SEQUENCE: 653

ccatcgat 8

<210> SEQ ID NO 654
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 654

tcgacgtc 8

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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 655

ctagcgct 8

<210> SEQ ID NO 656
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<212> TYPE: DNA
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<400> SEQUENCE: 656

taagcgct 8

<210> SEQ ID NO 657
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 657

tcgcgaattc gcg 13

<210> SEQ ID NO 658
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<400> SEQUENCE: 658

atggaaggtc cagcgttct 19

<210> SEQ ID NO 659
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 659

actggacgtt agcgtga 17

<210> SEQ ID NO 660
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 660

cgcctggggc tggtctgg 18

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<210> SEQ ID NO 661
<211> LENGTH: 18
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 661

gtgtcggggt ctccgggc 18

<210> SEQ ID NO 662
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<400> SEQUENCE: 662

gtgccggggt ctccgggc 18

<210> SEQ ID NO 663
<211> LENGTH: 18
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 663

cgccgtcgcg gcggttgg 18

<210> SEQ ID NO 664
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 664

gaagttcacg ttgaggggca t 21

<210> SEQ ID NO 665
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 665

atctggtgag ggcaagctat g 21

<210> SEQ ID NO 666
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 666

gttgaaaccc gagaacatca t 21

<210> SEQ ID NO 667
<211> LENGTH: 8
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 667

gcaacgtt 8

<210> SEQ ID NO 668
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 668

gtaacgtt 8

<210> SEQ ID NO 669
<211> LENGTH: 8
<212> TYPE: DNA
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<400> SEQUENCE: 669

cgaacgtt 8

<210> SEQ ID NO 670
<211> LENGTH: 8
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 670

gaaacgtt 8

<210> SEQ ID NO 671
<211> LENGTH: 8
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 671

caaacgtt 8

<210> SEQ ID NO 672
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 672

ctaacgtt 8

<210> SEQ ID NO 673
<211> LENGTH: 8
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 673

ggaacgtt 8

<210> SEQ ID NO 674
<211> LENGTH: 8
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 674

tgaacgtt 8

<210> SEQ ID NO 675
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 675

acaacgtt 8

<210> SEQ ID NO 676
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 676

ttaacgtt 8

<210> SEQ ID NO 677
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 677

aaaacgtt 8

<210> SEQ ID NO 678
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 678

ataacgtt 8

<210> SEQ ID NO 679
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 679

aacgttct 8

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<210> SEQ ID NO 680
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 680

tccgatcg 8

<210> SEQ ID NO 681
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 681

tccgtacg 8

<210> SEQ ID NO 682
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 682

gctagacgct agcgtga 17

<210> SEQ ID NO 683
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 683

gagaacgctg gacctcatca tccat 25

<210> SEQ ID NO 684
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 684

gagaacgcta gaccttctat 20

<210> SEQ ID NO 685
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 685

actagacgtt agtgtga 17

<210> SEQ ID NO 686
<211> LENGTH: 22
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 686

cacaccttgg tcaatgtcac gt 22

<210> SEQ ID NO 687
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 687

tctccatcct atggttttat cg 22

<210> SEQ ID NO 688
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 688

cgctggacct tccat 15

<210> SEQ ID NO 689
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 689

caccaccttg gtcaatgtca cgt 23

<210> SEQ ID NO 690
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 690

gctagacgtt agctgga 17

<210> SEQ ID NO 691
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 691

agtgcgattg cagatcg 17

<210> SEQ ID NO 692
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 692

ttttcgtttt gtggttttgt ggtt 24

<210> SEQ ID NO 693
<211> LENGTH: 23
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 693

ttttcgtttg tcgttttgtc gtt 23

<210> SEQ ID NO 694
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 694

tttttgtttt gtggttttgt ggtt 24

<210> SEQ ID NO 695
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 695

accgcatgga ttctaggcca 20

<210> SEQ ID NO 696
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 696

gctagacgtt agcgt 15

<210> SEQ ID NO 697
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 697

aacgctggac cttccat 17

<210> SEQ ID NO 698
<211> LENGTH: 8
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c

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<400> SEQUENCE: 698

tcaangtt 8

<210> SEQ ID NO 699
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 699

ccttcgat 8

<210> SEQ ID NO 700
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 700

actagacgtt agtgtga 17

<210> SEQ ID NO 701
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 701

gctagaggtt agcgtga 17

<210> SEQ ID NO 702
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 702

atggactctc cagcgttctc 20

<210> SEQ ID NO 703
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 703

atcgactctc gagcgttctc 20

<210> SEQ ID NO 704
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 704

gctagacgtt agc 13

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<210> SEQ ID NO 705
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 705

gctagacgt 9

<210> SEQ ID NO 706
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 706

agtgcgattc gagatcg 17

<210> SEQ ID NO 707
<211> LENGTH: 8
<212> TYPE: DNA
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<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 707

tcagngct 8

<210> SEQ ID NO 708
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 708

ctgattgctc tctcgtga 18

<210> SEQ ID NO 709
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 709

tnaacgtt 8

<210> SEQ ID NO 710
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:

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<221> NAME/KEY: modified_base
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 710

gagaangctg gaccttccat 20

<210> SEQ ID NO 711
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 711

gctagacgtt aggctga 17

<210> SEQ ID NO 712
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 712

gctacttagc gtga 14

<210> SEQ ID NO 713
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 713

gctaccttag cgtga 15

<210> SEQ ID NO 714
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 714

atcgacttcg agcgttctc 19

<210> SEQ ID NO 715
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 715

atgcactctg cagcgttctc 20

<210> SEQ ID NO 716
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 716

agtgactctc cagcgttctc 20

<210> SEQ ID NO 717
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 717

gccagatgtt agctgga 17

<210> SEQ ID NO 718
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 718

atcgactcga gcgttctc 18

<210> SEQ ID NO 719
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 719

atcgatcgag cgttctc 17

<210> SEQ ID NO 720
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 720

gagaacgctc gaccttcgat 20

<210> SEQ ID NO 721
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 721

gctagacgtt agctgga 17

<210> SEQ ID NO 722
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 722

atcgactctc gagcgttctc 20

<210> SEQ ID NO 723
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 723

tagacgttag cgtga 15

<210> SEQ ID NO 724
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 724

cgactctcga gcgttctc 18

<210> SEQ ID NO 725
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 725

ggggtcgacc ttggaggggg g 21

<210> SEQ ID NO 726
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 726

gctaacgtta gcgtga 16

<210> SEQ ID NO 727
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 727

cgtcgtcgt 9

<210> SEQ ID NO 728
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (14)...(14)
<223> OTHER INFORMATION: m5c

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<400> SEQUENCE: 728

gagaacgctg gacnttccat 20

<210> SEQ ID NO 729
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (18)...(18)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 729

atcgacctac gtgcgttntc 20

<210> SEQ ID NO 730
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 730

atngacctac gtgcgttctc 20

<210> SEQ ID NO 731
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 731

gctagangtt agcgt 15

<210> SEQ ID NO 732
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (14)...(14)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 732

atcgactctc gagngttctc 20

<210> SEQ ID NO 733
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 733

ggggtaatgc atcaggggg 20

<210> SEQ ID NO 734
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 734

ggctgtattc ctgactgccc 20

<210> SEQ ID NO 735
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 735

ccatgctaac ctctagc 17

<210> SEQ ID NO 736
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 736

gctagatgtt agcgtga 17

<210> SEQ ID NO 737
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 737

cgtaccttac ggtga 15

<210> SEQ ID NO 738
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 738

tccatgctgg tcctgatgct 20

<210> SEQ ID NO 739
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 739

atcgactctc tcgagcgttc tc 22

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<210> SEQ ID NO 740
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 740

gctagagctt agcgtga 17

<210> SEQ ID NO 741
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 741

atcgactctc gagtgttctc 20

<210> SEQ ID NO 742
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 742

aacgctcgac cttcgat 17

<210> SEQ ID NO 743
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 743

ctcaacgctg gaccttccat 20

<210> SEQ ID NO 744
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 744

atcgacctac gtgcgttctc 20

<210> SEQ ID NO 745
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 745

gagaatgctg gaccttccat 20

<210> SEQ ID NO 746
<211> LENGTH: 17
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 746

tcacgctaac ctctgac 17

<210> SEQ ID NO 747
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 747

gagaacgctc cagcactgat 20

<210> SEQ ID NO 748
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Biotin moiety attached at 5' end of sequence.

<400> SEQUENCE: 748

gagcaagctg gaccttccat 20

<210> SEQ ID NO 749
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 749

cgctagaggt tagcgtga 18

<210> SEQ ID NO 750
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 750

gctagatgtt aacgt 15

<210> SEQ ID NO 751
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 751

atggaaggtc cacgttctc 19

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<210> SEQ ID NO 752
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 752

gctagatgtt agcgt 15

<210> SEQ ID NO 753
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 753

gctagacgtt agtgt 15

<210> SEQ ID NO 754
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 754

tccatgacgg tcctgatgct 20

<210> SEQ ID NO 755
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 755

tccatggcgg tcctgatgct 20

<210> SEQ ID NO 756
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 756

gctagacgat agcgt 15

<210> SEQ ID NO 757
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 757

gctagtcgat agcgt 15

<210> SEQ ID NO 758
<211> LENGTH: 20
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 758

tccatgacgt tcctgatgct 20

<210> SEQ ID NO 759
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 759

tccatgtcgt tcctgatgct 20

<210> SEQ ID NO 760
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (13)...(13)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 760

gctagacgtt agngt 15

<210> SEQ ID NO 761
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 761

gctaggcgtt agcgt 15

<210> SEQ ID NO 762
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 762

tccatgtngg tcctgatgct 20

<210> SEQ ID NO 763
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (12)...(12)
<223> OTHER INFORMATION: m5c

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<400> SEQUENCE: 763

tccatgtcgg tnctgatgct 20

<210> SEQ ID NO 764
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (3)...(3)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (10)...(10)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (14)...(14)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 764

atngactctn gagngttctc 20

<210> SEQ ID NO 765
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 765

atggaaggtc cagtgttctc 20

<210> SEQ ID NO 766
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 766

gcatgacgtt gagct 15

<210> SEQ ID NO 767
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 767

ggggtcaacg ttgaggggg 20

<210> SEQ ID NO 768
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 768

ggggtcaagt ctgaggggg 20

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<210> SEQ ID NO 769
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 769

cgcgcgcgcg cgcgcgcgcg 20

<210> SEQ ID NO 770
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 770

ccccccccc ccccccccc cccccccc 28

<210> SEQ ID NO 771
<211> LENGTH: 35
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 771

ccccccccc ccccccccc ccccccccc ccccc 35

<210> SEQ ID NO 772
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 772

tccatgtcgc tcctgatcct 20

<210> SEQ ID NO 773
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 773

gctaaacgtt agcgt 15

<210> SEQ ID NO 774
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 774

tccatgtcga tcctgatgct 20

<210> SEQ ID NO 775
<211> LENGTH: 20
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 775

tccatgccgg tcctgatgct 20

<210> SEQ ID NO 776
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 776

aaaatcaacg ttgaaaaaaa 20

<210> SEQ ID NO 777
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 777

tccataacgt tcctgatgct 20

<210> SEQ ID NO 778
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 778

tggaggtccc accgagatcg gag 23

<210> SEQ ID NO 779
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 779

cgtcgtcgtc gtcgtcgtcg t 21

<210> SEQ ID NO 780
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 780

ctgctgctgc tgctgctgct g 21

<210> SEQ ID NO 781
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 781

gagaacgctc cgaccttcga t 21

<210> SEQ ID NO 782
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 782

gctagatgtt agcgt 15

<210> SEQ ID NO 783
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 783

gcatgacgtt gagct 15

<210> SEQ ID NO 784
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)...(10)
<223> OTHER INFORMATION: Conjugated to FITC moiety.

<400> SEQUENCE: 784

tcaatgctga 10

<210> SEQ ID NO 785
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)...(10)
<223> OTHER INFORMATION: Conjugated to FITC moiety.

<400> SEQUENCE: 785

tcaacgttga 10

<210> SEQ ID NO 786
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)...(10)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 786

tcaacgttga 10

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<210> SEQ ID NO 787
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)...(10)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 787

gcaatattgc 10

<210> SEQ ID NO 788
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)...(10)
<223> OTHER INFORMATION: Conjugated to FITC moiety.

<400> SEQUENCE: 788

gcaatattgc 10

<210> SEQ ID NO 789
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 789

agttgcaact 10

<210> SEQ ID NO 790
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 790

tcttcgaa 8

<210> SEQ ID NO 791
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 791

tcaacgtc 8

<210> SEQ ID NO 792
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 792

ccatgtcggt cctgatgct 19

<210> SEQ ID NO 793
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 793

gtttttatat aatttggg 18

<210> SEQ ID NO 794
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 794

tttttgtttg tcgttttgtc gtt 23

<210> SEQ ID NO 795
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 795

ttgggggggg tt 12

<210> SEQ ID NO 796
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 796

ggggttgggg gtt 13

<210> SEQ ID NO 797
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 797

ggtggtgtag gttttgg 17

<210> SEQ ID NO 798
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.
<220> FEATURE:

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<221> NAME/KEY: modified_base
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 798

gagaangctc gaccttcgat 20

<210> SEQ ID NO 799
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 799

tcaacgttaa cgttaacgtt 20

<210> SEQ ID NO 800
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (8)...(8)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 800

gagcaagntg gaccttccat 20

<210> SEQ ID NO 801
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 801

gagaangctc cagcactgat 20

<210> SEQ ID NO 802
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (5)...(5)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)...(10)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

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<400> SEQUENCE: 802

tcaangttga 10

<210> SEQ ID NO 803
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (8)...(10)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 803

gnaatattgc 10

<210> SEQ ID NO 804
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 804

tgctgctttt gtcgttttgt gctt 24

<210> SEQ ID NO 805
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 805

ctgcgttagc aatttaactg tg 22

<210> SEQ ID NO 806
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 806

tccatgacgt tcctgatgct 20

<210> SEQ ID NO 807
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 807

tgcatgccgt gcatccgtac acagctct 28

<210> SEQ ID NO 808
<211> LENGTH: 20
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 808

tgcatgccgt acacagctct 20

<210> SEQ ID NO 809
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 809

tgcatcagct ct 12

<210> SEQ ID NO 810
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 810

tgcgctct 8

<210> SEQ ID NO 811
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 811

ccccccccc ccccccccc 20

<210> SEQ ID NO 812
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 812

ccccccccc cc 12

<210> SEQ ID NO 813
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 813

cccccccc 8

<210> SEQ ID NO 814
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 814

tgcatcagct ct 12

<210> SEQ ID NO 815
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 815

tgcatgccgt acacagctct 20

<210> SEQ ID NO 816
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 816

gagcaagctg gaccttccat 20

<210> SEQ ID NO 817
<211> LENGTH: 32
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 817

tcaacgttaa cgttaacgtt aacgttaacg tt 32

<210> SEQ ID NO 818
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 818

gagaacgctc gaccttcgat 20

<210> SEQ ID NO 819
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 819

gtccccattt cccagaggag gaaat 25

<210> SEQ ID NO 820
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 820

ctagcggctg acgtcatcaa gctag 25

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<210> SEQ ID NO 821
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 821

ctagcttgat gacgtcagcc gctag 25

<210> SEQ ID NO 822
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 822

cggctgacgt catcaa 16

<210> SEQ ID NO 823
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 823

ctgacgtg 8

<210> SEQ ID NO 824
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 824

ctgacgtcat 10

<210> SEQ ID NO 825
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 825

attcgatcgg ggcggggcga g 21

<210> SEQ ID NO 826
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 826

ctcgccccgc cccgatcgaa t 21

<210> SEQ ID NO 827
<211> LENGTH: 15
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 827

gactgacgtc agcgt 15

<210> SEQ ID NO 828
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 828

ctagcggctg acgtcataaa gctagc 26

<210> SEQ ID NO 829
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 829

ctagctttat gacgtcagcc gctagc 26

<210> SEQ ID NO 830
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 830

ctagcggctg agctcataaa gctagc 26

<210> SEQ ID NO 831
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 831

ctagtggctg acgtcatcaa gctag 25

<210> SEQ ID NO 832
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 832

tccaccacgt ggtctatgct 20

<210> SEQ ID NO 833
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 833

gggaatgaaa gattttatta taag 24

<210> SEQ ID NO 834
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 834

tctaaaaacc atctattctt aaccct 26

<210> SEQ ID NO 835
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 835

agctcaacgt catgc 15

<210> SEQ ID NO 836
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 836

ttaacggtgg tagcggtatt ggtc 24

<210> SEQ ID NO 837
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 837

ttaagaccaa taccgctacc accg 24

<210> SEQ ID NO 838
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 838

gatctagtga tgagtcagcc ggatc 25

<210> SEQ ID NO 839
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 839

gatccggctg actcatcact agatc 25

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<210> SEQ ID NO 840
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 840

tccaagacgt tcctgatgct 20

<210> SEQ ID NO 841
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 841

tccatgacgt ccctgatgct 20

<210> SEQ ID NO 842
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 842

tccaccacgt ggctgatgct 20

<210> SEQ ID NO 843
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 843

ccacgtggac ctctagc 17

<210> SEQ ID NO 844
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 844

tcagaccacg tggtcgggtg ttcctga 27

<210> SEQ ID NO 845
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 845

tcaggaacac ccgaccacgt ggtctga 27

<210> SEQ ID NO 846
<211> LENGTH: 18
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 846

catttccacg atttccca 18

<210> SEQ ID NO 847
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 847

ttcctctctg caagagact 19

<210> SEQ ID NO 848
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 848

tgtatctctc tgaaggact 19

<210> SEQ ID NO 849
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 849

ataaagcgaa actagcagca gtttc 25

<210> SEQ ID NO 850
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 850

gaaactgctg ctagtttcgc tttat 25

<210> SEQ ID NO 851
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 851

tgcccaaaga ggaaaatttg tttcatacag 30

<210> SEQ ID NO 852
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 852

ctgtatgaaa caaattttcc tctttgggca 30

<210> SEQ ID NO 853
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 853

ttagggttag ggttagggtt 20

<210> SEQ ID NO 854
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 854

tccatgagct tcctgatgct 20

<210> SEQ ID NO 855
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 855

aaaacatgac gttcaaaaaa 20

<210> SEQ ID NO 856
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 856

aaaacatgac gttcgggggg 20

<210> SEQ ID NO 857
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 857

ggggcatgag cttcgggggg 20

<210> SEQ ID NO 858
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 858

ctaggctgac gtcatcaagc tagt 24

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<210> SEQ ID NO 859
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 859

tctgacgtca tctgacgttg gctgacgtct 30

<210> SEQ ID NO 860
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 860

ggaattagta atagatatag aagtt 25

<210> SEQ ID NO 861
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 861

tttacctttt ataaacataa ctaaaacaaa 30

<210> SEQ ID NO 862
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 862

gcgtttttt ttgcg 15

<210> SEQ ID NO 863
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 863

atatctaatc aaaacattaa caaa 24

<210> SEQ ID NO 864
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 864

tctatcccag gtggttcctg ttag 24

<210> SEQ ID NO 865
<211> LENGTH: 20
<212> TYPE: DNA

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 865

tccatgacgt tcctgatgct 20

<210> SEQ ID NO 866
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(3)
<223> OTHER INFORMATION: Conjugated to biotin moiety.

<400> SEQUENCE: 866

tccatgagct tcctgatgct 20

<210> SEQ ID NO 867
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)...(13)
<223> OTHER INFORMATION: Conjugated to FITC moiety.
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: Has phosphodiester backbone.

<400> SEQUENCE: 867

ttttttttttt ttt 13

<210> SEQ ID NO 868
<211> LENGTH: 13
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (11)...(13)
<223> OTHER INFORMATION: Conjugated to biotin moiety.
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (0)...(0)
<223> OTHER INFORMATION: Has phosphorothioate and phosphodiester
chimeric backbone with phosphodiester on 3' end.

<400> SEQUENCE: 868

ttttttttttt ttt 13

<210> SEQ ID NO 869
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 869

ctagcttgat gagctcagcc gctag 25

<210> SEQ ID NO 870
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 870

ttcagttgtc ttgctgctta gctaa 25

<210> SEQ ID NO 871
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 871

tccatgagct tcctgagtct 20

<210> SEQ ID NO 872
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 872

ctagcggctg acgtcatcaa tctag 25

<210> SEQ ID NO 873
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 873

tgctagctgt gcctgtacct 20

<210> SEQ ID NO 874
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 874

atgctaaagg acgtcacatt gca 23

<210> SEQ ID NO 875
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 875

tgcaatgtga cgtcctttag cat 23

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<210> SEQ ID NO 876
<211> LENGTH: 31
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 876

gtaggggact ttccgagctc gagatcctat g 31

<210> SEQ ID NO 877
<211> LENGTH: 31
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 877

cataggatct cgagctcgga aagtccccta c 31

<210> SEQ ID NO 878
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 878

ctgtcaggaa ctgcaggtaa gg 22

<210> SEQ ID NO 879
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 879

cataacatag gaatatttac tcctcgc 27

<210> SEQ ID NO 880
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 880

ctccagctcc aagaaaggac g 21

<210> SEQ ID NO 881
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 881

gaagtttctg gtaagtcttc g 21

<210> SEQ ID NO 882
<211> LENGTH: 24

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 882

tgctgctttt gtgcttttgt gctt 24

<210> SEQ ID NO 883
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 883

tcgtcgtttt gtggttttgt ggtt 24

<210> SEQ ID NO 884
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 884

tcgtcgtttg tcgttttgtc gtt 23

<210> SEQ ID NO 885
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 885

tcctgacgtt cggcgcgcgc cc 22

<210> SEQ ID NO 886
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 886

tgctgctttt gtgcttttgt gctt 24

<210> SEQ ID NO 887
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 887

tccatgagct tcctgagctt 20

<210> SEQ ID NO 888
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 888

tcgtcgtttc gtcgttttga cgtt 24

<210> SEQ ID NO 889
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 889

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<400> SEQUENCE: 890

tcgcgtgcgt tttgtcgttt tgacgtt 27

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<212> TYPE: DNA
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<400> SEQUENCE: 891

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<400> SEQUENCE: 892

tcctgacggg gaagt 15

<210> SEQ ID NO 893
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tcctggcggt gaagt 15

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<400> SEQUENCE: 895

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<210> SEQ ID NO 896
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<400> SEQUENCE: 896

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gcgacgttcg gcgcgcgccc 20

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gcgacgggcg gcgcgcgccc 20

<210> SEQ ID NO 899
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<400> SEQUENCE: 899

gcggcgtgcg gcgcgcgccc 20

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gcggcggtcg gcgcgcgccc 20

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<212> TYPE: DNA
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<400> SEQUENCE: 904

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<400> SEQUENCE: 906

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<210> SEQ ID NO 907
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<400> SEQUENCE: 907

tgtgtgtgtg tgtgtgtgtg t 21

<210> SEQ ID NO 908
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<220> FEATURE:
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<400> SEQUENCE: 908

ctctctctct ctctctctct ct 22

<210> SEQ ID NO 909
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ggggtcgacg tcgagggggg 20

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<400> SEQUENCE: 910

atatatatat atatatatat at 22

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<400> SEQUENCE: 912

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<220> FEATURE:
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<400> SEQUENCE: 913

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gctagagggg agggt 15

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<400> SEQUENCE: 915

gctagatgtt agggg 15

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<400> SEQUENCE: 916

gcatgagggg gagct 15

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<400> SEQUENCE: 917

atggaaggtc caggggctc 20

<210> SEQ ID NO 918
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<400> SEQUENCE: 918

atggactctg gaggggctc 20

<210> SEQ ID NO 919
<211> LENGTH: 20
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<400> SEQUENCE: 919

atggaaggtc caaggggctc 20

<210> SEQ ID NO 920
<211> LENGTH: 20

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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 920

gagaaggggg gaccttggat 20

<210> SEQ ID NO 921
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<212> TYPE: DNA
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<220> FEATURE:
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gagaaggggg gaccttccat 20

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<211> LENGTH: 20
<212> TYPE: DNA
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gagaaggggc cagcactgat 20

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tccatgtggg gcctgatgct 20

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<212> TYPE: DNA
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<400> SEQUENCE: 924

tccatgaggg gcctgatgct 20

<210> SEQ ID NO 925
<211> LENGTH: 20
<212> TYPE: DNA
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<400> SEQUENCE: 925

tccatgtggg gcctgctgat 20

<210> SEQ ID NO 926
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 926

atggactctc cggggttctc 20

<210> SEQ ID NO 927
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 927

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<210> SEQ ID NO 928
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 928

atggactctg gaggggtctc 20

<210> SEQ ID NO 929
<211> LENGTH: 20
<212> TYPE: DNA
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<400> SEQUENCE: 929

atggaggctc catggggctc 20

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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 930

atggactctg gggggttctc 20

<210> SEQ ID NO 931
<211> LENGTH: 20
<212> TYPE: DNA
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<400> SEQUENCE: 931

tccatgtggg tggggatgct 20

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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 932

tccatgcggg tggggatgct 20

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<210> SEQ ID NO 933
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 933

tccatggggg tcctgatgct 20

<210> SEQ ID NO 934
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 934

tccatggggt ccctgatgct 20

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<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 935

tccatggggt gcctgatgct 20

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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 936

tccatggggt tcctgatgct 20

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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 937

tccatcgggg gcctgatgct 20

<210> SEQ ID NO 938
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 938

gctagaggga gtgt 14

<210> SEQ ID NO 939
<211> LENGTH: 18

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 939

ttttttttttt tttttttt 18

<210> SEQ ID NO 940
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
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<221> NAME/KEY: misc_difference
<222> LOCATION: (2)...(2)
<223> OTHER INFORMATION: m is a or c
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (18)...(18)
<223> OTHER INFORMATION: m is a or c

<400> SEQUENCE: 940

gmggtcaacg ttgagggmgg g 21

<210> SEQ ID NO 941
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 941

ggggagttcg ttgaggggggg g 21

<210> SEQ ID NO 942
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 942

tcgtcgtttc ccccccccc 20

<210> SEQ ID NO 943
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 943

ttgggggggtt ttttttttttt ttttt 25

<210> SEQ ID NO 944
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 944

tttaaatttt aaaatttaaa ata 23

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<210> SEQ ID NO 945
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 945

ttggtttttt tggtttttttt ttgg 24

<210> SEQ ID NO 946
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 946

tttccctttt ccccttttcc cctc 24

<210> SEQ ID NO 947
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: misc_difference
<222> LOCATION: (21)...(21)
<223> OTHER INFORMATION: s is g or c

<400> SEQUENCE: 947

ggggtcatcg atgaggggg s 21

<210> SEQ ID NO 948
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 948

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 949
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 949

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<210> SEQ ID NO 950
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 950

tccatgacgt tcctgacgtt 20

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<210> SEQ ID NO 951
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 951

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 952
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 952

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 953
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 953

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 954
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 954

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 955
<211> LENGTH: 20
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 955

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 956
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 956

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 957
<211> LENGTH: 20

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 957

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 958
<211> LENGTH: 20
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 958

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 959
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 959

ggggacgat cgtcgggggg 19

<210> SEQ ID NO 960
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 960

ggggtcgta cgacgggggg 20

<210> SEQ ID NO 961
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 961

tttttttttt tttttttttt tttt 24

<210> SEQ ID NO 962
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 962

aaaaaaaaaa aaaaaaaaaa aaaa 24

<210> SEQ ID NO 963
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 963

ccccccccc ccccccccc cccc 24

<210> SEQ ID NO 964
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 964

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 965
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 965

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 966
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 966

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 967
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 967

tcgtcgtttt gtcgttttgt cgtt 24

<210> SEQ ID NO 968
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 968

ggggtcaacg ttgaggggg 20

<210> SEQ ID NO 969
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 969

ggggtcaacg ttgaggggg 20

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<210> SEQ ID NO 970
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 970

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<210> SEQ ID NO 971
<211> LENGTH: 20
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 971

tgctgcttcc ccccccccc 20

<210> SEQ ID NO 972
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 972

ggggacgtcg acgtgggggg 20

<210> SEQ ID NO 973
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 973

ggggtcgtcg acgaggggggg 20

<210> SEQ ID NO 974
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 974

ggggtcgacg tacgtcgagg gggg 24

<210> SEQ ID NO 975
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 975

ggggaccggt accggtgggg gg 22

<210> SEQ ID NO 976
<211> LENGTH: 19

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 976

gggtcgacgt cgaggggggg 19

<210> SEQ ID NO 977
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 977

ggggtcgacg tcgaggggg 19

<210> SEQ ID NO 978
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 978

ggggaacgtt aacgttgggg gg 22

<210> SEQ ID NO 979
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 979

ggggtcaccg gtgagggggg 20

<210> SEQ ID NO 980
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 980

ggggtcgttc gaacgagggg gg 22

<210> SEQ ID NO 981
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 981

ggggacgttc gaacgtgggg gg 22

<210> SEQ ID NO 982
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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 982

tcaactttga 10

<210> SEQ ID NO 983
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 983

tcaagcttga 10

<210> SEQ ID NO 984
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 984

tcacgatcgt ga 12

<210> SEQ ID NO 985
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 985

tcagcatgct ga 12

<210> SEQ ID NO 986
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 986

gggggagcat gctgggggg 20

<210> SEQ ID NO 987
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 987

gggggggggg gggggggggg 20

<210> SEQ ID NO 988
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 988

ggggacgat atcgtcgggg gg 22

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<210> SEQ ID NO 989
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 989

ggggggacgac gtcgtcgggg gg 22

<210> SEQ ID NO 990
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 990

ggggggacgag ctcgtcgggg gg 22

<210> SEQ ID NO 991
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 991

ggggggacgta cgtcgggggg 20

<210> SEQ ID NO 992
<211> LENGTH: 8
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 992

tcaacgtt 8

<210> SEQ ID NO 993
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 993

tccataccgg tcctgatgct 20

<210> SEQ ID NO 994
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 994

tccataccgg tcctaccggt 20

<210> SEQ ID NO 995
<211> LENGTH: 20

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 995

ggggggacgat cgttgggggg 20

<210> SEQ ID NO 996
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 996

ggggaacgat cgtcgggggg 20

<210> SEQ ID NO 997
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 997

gggggggacga tcgtcggggg g 21

<210> SEQ ID NO 998
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 998

ggggggacgat cgtcgggggg g 21

<210> SEQ ID NO 999
<211> LENGTH: 12
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 999

aaagacgtta aa 12

<210> SEQ ID NO 1000
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1000

aaagagctta aa 12

<210> SEQ ID NO 1001
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (6)...(6)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 1001

aaagangtta aa 12

<210> SEQ ID NO 1002
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1002

aaattcggaa aa 12

<210> SEQ ID NO 1003
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1003

gggggtcatc gatgaggggg g 21

<210> SEQ ID NO 1004
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1004

gggggtcaac gttgaggggg g 21

<210> SEQ ID NO 1005
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1005

atgtagctta ataacaaagc 20

<210> SEQ ID NO 1006
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1006

ggatcccttg agttacttct 20

<210> SEQ ID NO 1007
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 1007

ccattccact tctgattacc 20

<210> SEQ ID NO 1008
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1008

tatgtattat catgtagata 20

<210> SEQ ID NO 1009
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1009

agcctacgta ttcaccctcc 20

<210> SEQ ID NO 1010
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1010

ttcctgcaac tactattgta 20

<210> SEQ ID NO 1011
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1011

atagaaggcc ctacaccagt 20

<210> SEQ ID NO 1012
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1012

ttacaccggt ctatggaggt 20

<210> SEQ ID NO 1013
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1013

ctaaccagat caagtctagg 20

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<210> SEQ ID NO 1014
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1014

cctagacttg atctggttag 20

<210> SEQ ID NO 1015
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1015

tataagcctc gtccgacatg 20

<210> SEQ ID NO 1016
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1016

catgtcggac gaggcttata 20

<210> SEQ ID NO 1017
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1017

tggtggtggg gagtaagctc 20

<210> SEQ ID NO 1018
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1018

gagctactcc cccaccacca 20

<210> SEQ ID NO 1019
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1019

gccttcgatc ttcgttggga 20

<210> SEQ ID NO 1020
<211> LENGTH: 20

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1020

tggacttctc tttgccgtct 20

<210> SEQ ID NO 1021
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1021

atgctgtagc ccagcgataa 20

<210> SEQ ID NO 1022
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1022

accgaatcag cggaaagtga 20

<210> SEQ ID NO 1023
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1023

tccatgacgt tcctgacgtt 20

<210> SEQ ID NO 1024
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1024

ggagaaaccc atgagctcat ctgg 24

<210> SEQ ID NO 1025
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1025

accacagacc agcaggcaga 20

<210> SEQ ID NO 1026
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 1026

gagcgtgaac tgcgcgaaga 20

<210> SEQ ID NO 1027
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1027

tcggtaccct tgcagcggtt 20

<210> SEQ ID NO 1028
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1028

ctggagccct agccaaggat 20

<210> SEQ ID NO 1029
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1029

gcgactccat caccagcgat 20

<210> SEQ ID NO 1030
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1030

cctgaagtaa gaaccagatg t 21

<210> SEQ ID NO 1031
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1031

ctgtgttatc tgacatacac c 21

<210> SEQ ID NO 1032
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1032

aattagcctt aggtgattgg g 21

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<210> SEQ ID NO 1033
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1033

acatctggtt cttacttcag g 21

<210> SEQ ID NO 1034
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1034

ataagtcata ttttgggaac tac 23

<210> SEQ ID NO 1035
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1035

cccaatcacc taaggctaat t 21

<210> SEQ ID NO 1036
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1036

ggggtcgtcg acgaggggg 20

<210> SEQ ID NO 1037
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1037

ggggtcgttc gaacgagggg gg 22

<210> SEQ ID NO 1038
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1038

ggggacgttc gaacgtgggg gg 22

<210> SEQ ID NO 1039
<211> LENGTH: 15

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (9)...(9)
<223> OTHER INFORMATION: n is 5-methylcytosine.

<400> SEQUENCE: 1039

tcctggcgng gaagt 15

<210> SEQ ID NO 1040
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1040

ggggaacgac gtcgttgggg gg 22

<210> SEQ ID NO 1041
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1041

ggggaacgta cgtcgggggg 20

<210> SEQ ID NO 1042
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1042

ggggaacgta cgtacgttgg gggg 24

<210> SEQ ID NO 1043
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1043

ggggtcaccg gtgagggggg 20

<210> SEQ ID NO 1044
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1044

ggggtcgacg tacgtcgagg gggg 24

<210> SEQ ID NO 1045
<211> LENGTH: 22

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1045

ggggaccggt accggtgggg gg 22

<210> SEQ ID NO 1046
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1046

gggtcgacgt cgaggggggg 19

<210> SEQ ID NO 1047
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1047

ggggtcgacg tcgagggg 18

<210> SEQ ID NO 1048
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1048

ggggaacgtt aacgttgggg gg 22

<210> SEQ ID NO 1049
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1049

ggggacgtcg acgtggggg 19

<210> SEQ ID NO 1050
<211> LENGTH: 34
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1050

gcactcttcg aagctacagc cggcagcctc tgat 34

<210> SEQ ID NO 1051
<211> LENGTH: 32
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 1051

cggctcttcc atgaggtctt tgctaatctt gg 32

<210> SEQ ID NO 1052
<211> LENGTH: 35
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1052

cggctcttcc atgaaagtct ttggacgatg tgagc 35

<210> SEQ ID NO 1053
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1053

tcctgcaggt taagt 15

<210> SEQ ID NO 1054
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1054

gggggtcgtt cgttgggggg 20

<210> SEQ ID NO 1055
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1055

gggggatgat tgttgggggg 20

<210> SEQ ID NO 1056
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (7)...(7)
<223> OTHER INFORMATION: m5c
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (11)...(11)
<223> OTHER INFORMATION: m5c

<400> SEQUENCE: 1056

gggggangat ngttgggggg 20

<210> SEQ ID NO 1057
<211> LENGTH: 20

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1057

ggggggagcta gcttgggggg 20

<210> SEQ ID NO 1058
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1058

ggttcttttg gtccttgtct 20

<210> SEQ ID NO 1059
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1059

ggttcttttg gtcctcgtct 20

<210> SEQ ID NO 1060
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1060

ggttcttttg gtccttatct 20

<210> SEQ ID NO 1061
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1061

ggttcttggt ttccttgtct 20

<210> SEQ ID NO 1062
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1062

tggtcttttg gtccttgtct 20

<210> SEQ ID NO 1063
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<400> SEQUENCE: 1063

ggttcaaatg gtccttgtct 20

<210> SEQ ID NO 1064
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1064

gggtcttttg ggccttgtct 20

<210> SEQ ID NO 1065
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1065

tccaggactt ctctcaggtt tttt 24

<210> SEQ ID NO 1066
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1066

tccaaaactt ctctcaaatt 20

<210> SEQ ID NO 1067
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1067

tactactttt atacttttat actt 24

<210> SEQ ID NO 1068
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1068

tgtgtgtgtg tgtgtgtgtg tgtg 24

<210> SEQ ID NO 1069
<211> LENGTH: 25
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1069

ttgttgttgt tgtttgttgt tgttg 25

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<210> SEQ ID NO 1070
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1070

ggctccgggg agggaatttt tgtctat 27

<210> SEQ ID NO 1071
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1071

gggacgatcg tcgggggg 19

<210> SEQ ID NO 1072
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1072

gggtcgtcga cgaggggggg 20

<210> SEQ ID NO 1073
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence

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<220> FEATURE:
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<400> SEQUENCE: 1083

tcctgaaggg gaagt 15

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
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<400> SEQUENCE: 1084

tcctggcggg caagt 15

<210> SEQ ID NO 1085
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
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<400> SEQUENCE: 1085

tcctggcggg taagt 15

<210> SEQ ID NO 1086
<211> LENGTH: 15
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<223> OTHER INFORMATION: Synthetic sequence

<400> SEQUENCE: 1086

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<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
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<210> SEQ ID NO 1088
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<211> LENGTH: 15
<212> TYPE: DNA
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<400> SEQUENCE: 1090

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<210> SEQ ID NO 1091
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<212> TYPE: DNA
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<400> SEQUENCE: 1091

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<210> SEQ ID NO 1092
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<212> TYPE: DNA
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<220> FEATURE:
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<400> SEQUENCE: 1092

ggggcccccc ccccgggggg 20

<210> SEQ ID NO 1093
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<400> SEQUENCE: 1093

ggggttgttg ttgttggggg g 21

We claim:

1-36. (canceled)

37. A method for treating or preventing airway remodeling in a hypo-responsive subject having asthma, the method comprising administering to the subject an immunostimulatory nucleic acid in an amount effective to treat or prevent the airway remodeling.

38. A method for treating or preventing lung fibrosis in a hypo-responsive subject having asthma, the method comprising administering to the subject an immunostimulatory nucleic acid in an amount effective to treat or prevent the lung fibrosis.

39. The method of claim 37 or claim 38, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

40. The method of claim 37 or claim 38, wherein the CpG nucleic acid is represented by at least the formula 5'$X_1X_2CGX_3X_4$3', wherein X_1, X_2, X_3, and X_4 are nucleotides.

41. The method of claim 37 or claim 38, wherein X_2 is adenine, guanine, cytosine, or thymine.

42. The method of claim 37 or claim 38, wherein X_2 is thymine.

43. The method of claim 37 or claim 38, wherein X_3 is cytosine, guanine, adenine, or thymine.

44. The method of claim 37 or claim 38, wherein X_2 is adenine, guanine, or thymine and wherein X_3 is cytosine, adenine, or thymine.

45. The method of claim 37 or claim 38, wherein the immunostimulatory nucleic acid is an isolated CpG nucleic acid represented by at least the formula 5' $N_1X_1X_2CGX_3X_4N_2$3', wherein X_1, X_2, X_3, and X_4 are nucleotides, N is any nucleotide, and N_1 and N_2 are nucleic acid sequences composed of 0-25 nucleotides each.

46. The method of claim 37 or claim 38, wherein X_1X_2 are nucleotides selected from the group consisting of: GpT, GpG, GpA, ApA, ApT, ApG, CpT, CpA, CpG, TpA, TpT, and TpG; and X_3X_4 are nucleotides selected from the group consisting of: TpT, ApT, TpG, ApG, CpG, TpC, ApC, CpC, TpA, ApA, and CpA.

47. The method of claim 37 or claim 38, wherein X_1X_2 is GpA or GpT and wherein X_3X_4 is TpT.

48. The method of claim 37 or claim 38, wherein X_1 or X_2 or both X_1 and X_2 are purines and wherein X_3 or X_4 or both X_3 and X_4 are pyrimidines.

49. The method of claim 37 or claim 38, wherein X_1X_2 is GpA and wherein X_3 or X_4 or both X_3 and X_4 are pyrimidines.

50. The method of claim 37 or claim 38, wherein X_1X_2 is selected from the group consisting of: TpA, ApA, ApC, ApG, and GpG.

51. The method of claim 37 or claim 38, wherein X_3X_4 is selected from the group consisting of: TpT, TpA, TpG, ApA, ApG, ApC, and CpA.

52. The method of claim 37 or claim 38, wherein X_1X_2 is selected from the group consisting of: TpT, TpG, ApT, GpC, CpC, CpT, TpC, GpT and CpG.

53. The method of claim 37 or claim 38, wherein the immunostimulatory nucleic acid has a sequence provided as AATAGTCGCCATCGCGCGAC (SEQ ID NO:367).

54. The method of claim 37 or claim 38, wherein the immunostimulatory nucleic acid is administered to the subject by a route selected from intranasal, intratracheal, and inhalation.

55. The method of claim 37 or claim 38, wherein the immunostimulatory nucleic acid is administered intranasally.

56. The method of claim 37 or claim 38, wherein the immunostimulatory nucleic acid is administered systemically.

57. The method of claim 37 or claim 38, further comprising administering an anti-inflammatory agent.

58. The method of claim 37 or claim 38, further comprising administering a corticosteroid.

59. The method of claim 58, wherein the corticosteroid is selected from the group consisting of methylprednisolone, prednisolone, and prednisone.

60. A pharmaceutical formulation for treatment of lung fibrosis, comprising:

a therapeutically effective amount of an immunostimulatory CpG nucleic acid in an aerosol spray for administration by inhalation.

61. The pharmaceutical formulation of claim 60, wherein the immunostimulatory CpG nucleic acid is delivered from a pressurized pack or nebulizer with the use of a propellant.

62. The pharmaceutical formulation of claim 60, wherein the immunostimulatory nucleic acid is formulated in a metered dose inhaler.

63. The method of any one of claims **37**, **38**, or **60**, wherein the immunostimulatory nucleic acid has a modified backbone.

64. The method of claim 63, wherein the modified backbone is a phosphate modified backbone.

65. The method of claim 63, wherein the modified backbone is a phosphorothioate modified backbone.

* * * * *