US 20160222389A1

(19) **United States**

(12) **Patent Application Publication**

Grossman et al.

(10) **Pub. No.: US 2016/0222389 A1**

(43) **Pub. Date: Aug. 4, 2016**

(54) **MODULATORS OF COMPLEMENT FACTOR B**

(71) Applicant: **IONIS PHARMACEUTICALS, INC.**, Carlsbad, CA (US)

(72) Inventors: **Tamar R. Grossman**, La Jolla, CA (US); **Michael L. McCaleb**, La Jolla, CA (US); **Andrew T. Watt**, San Diego, CA (US); **Susan M. Freier**, San Diego, CA (US)

(73) Assignee: **Ionis Pharmaceuticals, Inc.**, Carlsbad, CA (US)

(21) Appl. No.: **15/021,651**

(22) PCT Filed: **Sep. 12, 2014**

(86) PCT No.: **PCT/US14/55458**

§ 371 (c)(1),
(2) Date: **Mar. 11, 2016**

Related U.S. Application Data

(60) Provisional application No. 61/877,624, filed on Sep. 13, 2013.

Publication Classification

(51) **Int. Cl.**
C12N 15/113 (2006.01)

(52) **U.S. Cl.**
CPC ***C12N 15/1137*** (2013.01); *C12N 2310/11* (2013.01); *C12N 2310/315* (2013.01); *C12N 2310/3231* (2013.01); *C12N 2310/321* (2013.01); *C12N 2310/3341* (2013.01)

(57) **ABSTRACT**

The present embodiments provide methods, compounds, and compositions for treating, preventing, or ameliorating a disease associated with dysregulation of the complement alternative pathway by administering a Complement Factor B (CFB) specific inhibitor to a subject.

MODULATORS OF COMPLEMENT FACTOR B

SEQUENCE LISTING

[0001] The present application is being filed along with a Sequence Listing in electronic format. The Sequence Listing is provided as a file entitled BIOL0183WOSEQ_ST25.txt created Sep. 11, 2014, which is 225 kb in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

FIELD

[0002] The present embodiments provide methods, compounds, and compositions for treating, preventing, or ameliorating a disease associated with dysregulation of the complement alternative pathway by administering a Complement Factor B (CFB) specific inhibitor to a subject.

BACKGROUND

[0003] The complement system is part of the host innate immune system involved in lysing foreign cells, enhancing phagocytosis of antigens, clumping antigen-bearing agents, and attracting macrophages and neutrophils. The complement system is divided into three initiation pathways—the classical, lectin, and alternative pathways—that converge at component C3 to generate an enzyme complex known as C3 convertase, which cleaves C3 into C3a and C3b. C3b associates with C3 convertase mediated by CFB and results in generation of C5 convertase, which cleaves C5 into C5a and C5b, which initiates the membrane attack pathway resulting in the formation of the membrane attack complex (MAC) comprising components C5b, C6, C7, C8, and C9. The membrane-attack complex (MAC) forms transmembrane channels and disrupts the phospholipid bilayer of target cells, leading to cell lysis.

[0004] In the homeostatic state, the alternative pathway is continuously activated at a low "tickover" level as a result of activation of the alternative pathway by spontaneous hydrolysis of C3 and the production of C3b, which generates C5 convertase.

SUMMARY

[0005] The complement system mediates innate immunity and plays an important role in normal inflammatory response to injury, but its dysregulation may cause severe injury. Activation of the alternative complement pathway beyond its constitutive "tickover" level can lead to unrestrained hyperactivity and manifest as diseases of complement dysregulation.

[0006] Certain embodiments provided herein relate to methods of treating, preventing, or ameliorating a disease associated with dysregulation of the complement alternative pathway in a subject by administration of a Complement Factor B (CFB) specific inhibitor. Several embodiments provided herein are drawn to a method of inhibiting expression of CFB in a subject having, or at risk of having, a disease associated with dysregulation of the complement alternative pathway by administering a CFB specific inhibitor to the subject. In certain embodiments, a method of reducing or inhibiting accumulation of C3 deposits in the eye of a subject having, or at risk of having, a disease associated with dysregulation of the complement alternative pathway comprises administering a CFB specific inhibitor to the subject. In several embodiments, a method of reducing or inhibiting accumulation of C3 deposits in the kidney of a subject having, or at risk of having, a disease associated with dysregulation of the complement alternative pathway comprises administering a CFB specific inhibitor to the subject.

DETAILED DESCRIPTION

[0007] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed. Herein, the use of the singular includes the plural unless specifically stated otherwise. As used herein, the use of "or" means "and/or" unless stated otherwise. Furthermore, the use of the term "including" as well as other forms, such as "includes" and "included", is not limiting. Also, terms such as "element" or "component" encompass both elements and components comprising one unit and elements and components that comprise more than one subunit, unless specifically stated otherwise.

[0008] The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. All documents, or portions of documents, cited in this application, including, but not limited to, patents, patent applications, articles, books, and treatises, are hereby expressly incorporated by reference for the portions of the document discussed herein, as well as in their entirety.

[0009] Unless otherwise indicated, the following terms have the following meanings:

[0010] "2'-O-methoxyethyl" (also 2'-MOE and 2'-O(CH_2)$_2$—OCH_3) refers to an O-methoxy-ethyl modification at the 2' position of a furanose ring. A 2'-O-methoxyethyl modified sugar is a modified sugar.

[0011] "2'-MOE nucleoside" (also 2'-O-methoxyethyl nucleoside) means a nucleoside comprising a 2'-MOE modified sugar moiety.

[0012] "2'-substituted nucleoside" means a nucleoside comprising a substituent at the 2'-position of the furanosyl ring other than H or OH. In certain embodiments, 2' substituted nucleosides include nucleosides with bicyclic sugar modifications.

[0013] "3' target site" refers to the nucleotide of a target nucleic acid which is complementary to the 3'-most nucleotide of a particular antisense compound.

[0014] "5' target site" refers to the nucleotide of a target nucleic acid which is complementary to the 5'-most nucleotide of a particular antisense compound.

[0015] "5-methylcytosine" means a cytosine modified with a methyl group attached to the 5 position. A 5-methylcytosine is a modified nucleobase.

[0016] "About" means within ±10% of a value. For example, if it is stated, "the compounds affected at least about 70% inhibition of CFB", it is implied that CFB levels are inhibited within a range of 60% and 80%.

[0017] "Administration" or "administering" refers to routes of introducing an antisense compound provided herein to a subject to perform its intended function. An example of a route of administration that can be used includes, but is not limited to parenteral administration, such as subcutaneous, intravenous, or intramuscular injection or infusion.

[0018] "Amelioration" refers to a lessening of at least one indicator, sign, or symptom of an associated disease, disorder, or condition. In certain embodiments, amelioration includes a delay or slowing in the progression of one or more indicators

of a condition or disease. The severity of indicators may be determined by subjective or objective measures, which are known to those skilled in the art.

[0019] "Animal" refers to a human or non-human animal, including, but not limited to, mice, rats, rabbits, dogs, cats, pigs, and non-human primates, including, but not limited to, monkeys and chimpanzees.

[0020] "Antisense activity" means any detectable or measurable activity attributable to the hybridization of an antisense compound to its target nucleic acid. In certain embodiments, antisense activity is a decrease in the amount or expression of a target nucleic acid or protein encoded by such target nucleic acid.

[0021] "Antisense compound" means an oligomeric compound that is capable of undergoing hybridization to a target nucleic acid through hydrogen bonding. Examples of antisense compounds include single-stranded and double-stranded compounds, such as, antisense oligonucleotides, siRNAs, shRNAs, ssRNAs, and occupancy-based compounds.

[0022] "Antisense inhibition" means reduction of target nucleic acid levels in the presence of an antisense compound complementary to a target nucleic acid compared to target nucleic acid levels in the absence of the antisense compound.

[0023] "Antisense mechanisms" are all those mechanisms involving hybridization of a compound with target nucleic acid, wherein the outcome or effect of the hybridization is either target degradation or target occupancy with concomitant stalling of the cellular machinery involving, for example, transcription or splicing.

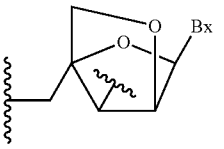
[0024] "Antisense oligonucleotide" means a single-stranded oligonucleotide having a nucleobase sequence that permits hybridization to a corresponding region or segment of a target nucleic acid.

[0025] "Base complementarity" refers to the capacity for the precise base pairing of nucleobases of an antisense oligonucleotide with corresponding nucleobases in a target nucleic acid (i.e., hybridization), and is mediated by Watson-Crick, Hoogsteen or reversed Hoogsteen hydrogen binding between corresponding nucleobases.

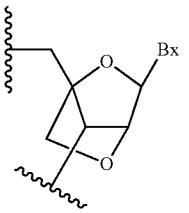
[0026] "Bicyclic sugar moiety" means a modified sugar moiety comprising a 4 to 7 membered ring (including but not limited to a furanosyl) comprising a bridge connecting two atoms of the 4 to 7 membered ring to form a second ring, resulting in a bicyclic structure. In certain embodiments, the 4 to 7 membered ring is a sugar ring. In certain embodiments the 4 to 7 membered ring is a furanosyl. In certain such embodiments, the bridge connects the 2'-carbon and the 4'-carbon of the furanosyl.

[0027] "Bicyclic nucleic acid" or "BNA" or "BNA nucleosides" means nucleic acid monomers having a bridge connecting two carbon atoms between the 4' and 2' position of the nucleoside sugar unit, thereby forming a bicyclic sugar. Examples of such bicyclic sugar include, but are not limited to A) α-L-Methyleneoxy (4'-CH_2—O-2') LNA, (B) β-D-Methyleneoxy (4'-CH_2—O-2') LNA, (C) Ethyleneoxy (4'-$(CH_2)_2$—O-2') LNA, (D) Aminooxy (4'-CH_2—O—N(R)-2') LNA and (E) Oxyamino (4'-CH_2—N(R)—O-2') LNA, as depicted below.

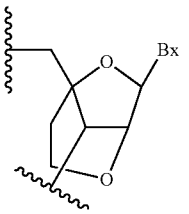
(A)



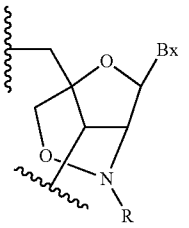
(B)



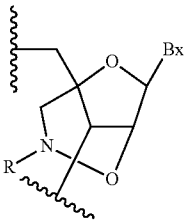
(C)



(D)



(E)



[0028] As used herein, LNA compounds include, but are not limited to, compounds having at least one bridge between the 4' and the 2' position of the sugar wherein each of the bridges independently comprises 1 or from 2 to 4 linked groups independently selected from —$[C(R_1)(R_2)]_n$—, —$C(R_1)$=$C(R_2)$—, —$C(R_1)$=N—, —C(=NR_1)—, —C(=O)—, —C(=S)—, —O—, —$Si(R_1)_2$—, —$S(=O)_x$— and —$N(R_1)$—; wherein: x is 0, 1, or 2; n is 1, 2, 3, or 4; each R_1 and R_2 is, independently, H, a protecting group, hydroxyl, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, a heterocycle radical, a substituted heterocycle radical, heteroaryl, substituted heteroaryl, C_5-C_7 alicyclic radical, substituted C_5-C_7 alicyclic radical, halogen, OJ_1, NJ_1J_2, SJ_1, N_3, $COOJ_1$, acyl (C(=O)—H), substituted acyl, CN, sulfonyl (S(=$O)_2$-J_1), or sulfoxyl (S(=O)-J_1); and each J_1 and J_2 is, independently, H, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12}

alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, acyl (C(=O)—H), substituted acyl, a heterocycle radical, a substituted heterocycle radical, C_1-C_{12} aminoalkyl, substituted C_1-C_{12} aminoalkyl or a protecting group.

[0029] Examples of 4'-2' bridging groups encompassed within the definition of LNA include, but are not limited to one of formulae: —$[C(R_1)(R_2)]_n$—, —$[C(R_1)(R_2)]_n$—O —, —$C(R_1R_2)$—$N(R_1)$—O— or —$C(R_1R_2)$—O—$N(R_1)$—. Furthermore, other bridging groups encompassed with the definition of LNA are 4'-CH_2-2',4'-$(CH_2)_2$-2', 4'-$(CH_2)_3$-2', 4'-CH_2—O-2', 4'-$(CH_2)_2$—O-2', 4'-CH_2—O—$N(R_1)$-2' and 4'-CH_2—$N(R_1)$—O-2'-bridges, wherein each R_1 and R_2 is, independently, H, a protecting group or C_1-C_{12} alkyl.

[0030] Also included within the definition of LNA according to the invention are LNAs in which the 2'-hydroxyl group of the ribosyl sugar ring is connected to the 4' carbon atom of the sugar ring, thereby forming a methyleneoxy (4'-CH_2—O-2') bridge to form the bicyclic sugar moiety. The bridge can also be a methylene (—CH_2—) group connecting the 2' oxygen atom and the 4' carbon atom, for which the term methyleneoxy (4'-CH_2—O-2') LNA is used. Furthermore; in the case of the bicylic sugar moiety having an ethylene bridging group in this position, the term ethyleneoxy (4'-CH_2CH_2—O-2') LNA is used. α-L-methyleneoxy (4'-CH_2-0-2'), an isomer of methyleneoxy (4'-CH_2—O-2') LNA is also encompassed within the definition of LNA, as used herein.

[0031] "Cap structure" or "terminal cap moiety" means chemical modifications, which have been incorporated at either terminus of an antisense compound.

[0032] "cEt" or "constrained ethyl" means a bicyclic sugar moiety comprising a bridge connecting the 4'-carbon and the 2'-carbon, wherein the bridge has the formula: 4'-$CH(CH_3)$—O-2'.

[0033] "Constrained ethyl nucleoside" (also cEt nucleoside) means a nucleoside comprising a bicyclic sugar moiety comprising a 4'-$CH(CH_3)$—O-2' bridge.

[0034] "Complement Factor B (CFB)" means any nucleic acid or protein of CFB. "CFB nucleic acid" means any nucleic acid encoding CFB. For example, in certain embodiments, a CFB nucleic acid includes a DNA sequence encoding CFB, an RNA sequence transcribed from DNA encoding CFB (including genomic DNA comprising introns and exons), including a non-protein encoding (i.e. non-coding) RNA sequence, and an mRNA sequence encoding CFB. "CFB mRNA" means an mRNA encoding a CFB protein.

[0035] "CFB specific inhibitor" refers to any agent capable of specifically inhibiting CFB RNA and/or CFB protein expression or activity at the molecular level. For example, CFB specific inhibitors include nucleic acids (including antisense compounds), peptides, antibodies, small molecules, and other agents capable of inhibiting the expression of CFB RNA and/or CFB protein.

[0036] "Chemically distinct region" refers to a region of an antisense compound that is in some way chemically different than another region of the same antisense compound. For example, a region having 2'-O-methoxyethyl nucleotides is chemically distinct from a region having nucleotides without 2'-O-methoxyethyl modifications.

[0037] "Chimeric antisense compounds" means antisense compounds that have at least 2 chemically distinct regions, each position having a plurality of subunits.

[0038] "Complementarity" means the capacity for pairing between nucleobases of a first nucleic acid and a second nucleic acid.

[0039] "Comprise," "comprises" and "comprising" will be understood to imply the inclusion of a stated step or element or group of steps or elements but not the exclusion of any other step or element or group of steps or elements.

[0040] "Contiguous nucleobases" means nucleobases immediately adjacent to each other.

[0041] "Deoxyribonucleotide" means a nucleotide having a hydrogen at the 2' position of the sugar portion of the nucleotide. Deoxyribonucleotides may be modified with any of a variety of substituents.

[0042] "Designing" or "Designed to" refer to the process of designing an oligomeric compound that specifically hybridizes with a selected nucleic acid molecule.

[0043] "Effective amount" means the amount of active pharmaceutical agent sufficient to effectuate a desired physiological outcome in an individual in need of the agent. The effective amount may vary among individuals depending on the health and physical condition of the individual to be treated, the taxonomic group of the individuals to be treated, the formulation of the composition, assessment of the individual's medical condition, and other relevant factors.

[0044] "Efficacy" means the ability to produce a desired effect.

[0045] "Expression" includes all the functions by which a gene's coded information is converted into structures present and operating in a cell. Such structures include, but are not limited to the products of transcription and translation.

[0046] "Fully complementary" or "100% complementary" means each nucleobase of a first nucleic acid has a complementary nucleobase in a second nucleic acid. In certain embodiments, a first nucleic acid is an antisense compound and a target nucleic acid is a second nucleic acid.

[0047] "Gapmer" means a chimeric antisense compound in which an internal region having a plurality of nucleosides that support RNase H cleavage is positioned between external regions having one or more nucleosides, wherein the nucleosides comprising the internal region are chemically distinct from the nucleoside or nucleosides comprising the external regions. The internal region may be referred to as the "gap" and the external regions may be referred to as the "wings."

[0048] "Hybridization" means the annealing of complementary nucleic acid molecules. In certain embodiments, complementary nucleic acid molecules include, but are not limited to, an antisense compound and a nucleic acid target. In certain embodiments, complementary nucleic acid molecules include, but are not limited to, an antisense oligonucleotide and a nucleic acid target.

[0049] "Identifying an animal having, or at risk for having, a disease, disorder and/or condition" means identifying an animal having been diagnosed with the disease, disorder and/or condition or identifying an animal predisposed to develop the disease, disorder and/or condition. Such identification may be accomplished by any method including evaluating an individual's medical history and standard clinical tests or assessments.

[0050] "Immediately adjacent" means there are no intervening elements between the immediately adjacent elements.

[0051] "Individual" means a human or non-human animal selected for treatment or therapy.

[0052] "Inhibiting the expression or activity" refers to a reduction, blockade of the expression or activity and does not necessarily indicate a total elimination of expression or activity.

[0053] "Internucleoside linkage" refers to the chemical bond between nucleosides.

[0054] "Lengthened" antisense oligonucleotides are those that have one or more additional nucleosides relative to an antisense oligonucleotide disclosed herein.

[0055] "Linked deoxynucleoside" means a nucleic acid base (A, G, C, T, U) substituted by deoxyribose linked by a phosphate ester to form a nucleotide.

[0056] "Linked nucleosides" means adjacent nucleosides linked together by an internucleoside linkage.

[0057] "Mismatch" or "non-complementary nucleobase" refers to the case when a nucleobase of a first nucleic acid is not capable of pairing with the corresponding nucleobase of a second or target nucleic acid.

[0058] "Modified internucleoside linkage" refers to a substitution or any change from a naturally occurring internucleoside bond (i.e. a phosphodiester internucleoside bond).

[0059] "Modified nucleobase" means any nucleobase other than adenine, cytosine, guanine, thymidine, or uracil. An "unmodified nucleobase" means the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U).

[0060] "Modified nucleoside" means a nucleoside having, independently, a modified sugar moiety and/or modified nucleobase.

[0061] "Modified nucleotide" means a nucleotide having, independently, a modified sugar moiety, modified internucleoside linkage, or modified nucleobase.

[0062] "Modified oligonucleotide" means an oligonucleotide comprising at least one modified internucleoside linkage, a modified sugar, and/or a modified nucleobase.

[0063] "Modified sugar" means substitution and/or any change from a natural sugar moiety.

[0064] "Modulating" refers to changing or adjusting a feature in a cell, tissue, organ or organism. For example, modulating CFB mRNA can mean to increase or decrease the level of CFB mRNA and/or CFB protein in a cell, tissue, organ or organism. A "modulator" effects the change in the cell, tissue, organ or organism. For example, a CFB antisense compound can be a modulator that decreases the amount of CFB mRNA and/or CFB protein in a cell, tissue, organ or organism.

[0065] "Monomer" refers to a single unit of an oligomer. Monomers include, but are not limited to, nucleosides and nucleotides, whether naturally occuring or modified.

[0066] "Motif" means the pattern of unmodified and modified nucleosides in an antisense compound.

[0067] "Natural sugar moiety" means a sugar moiety found in DNA (2'-H) or RNA (2'-OH).

[0068] "Naturally occurring internucleoside linkage" means a 3' to 5' phosphodiester linkage.

[0069] "Non-complementary nucleobase" refers to a pair of nucleobases that do not form hydrogen bonds with one another or otherwise support hybridization.

[0070] "Nucleic acid" refers to molecules composed of monomeric nucleotides. A nucleic acid includes, but is not limited to, ribonucleic acids (RNA), deoxyribonucleic acids (DNA), single-stranded nucleic acids, and double-stranded nucleic acids.

[0071] "Nucleobase" means a heterocyclic moiety capable of pairing with a base of another nucleic acid.

[0072] "Nucleobase complementarity" refers to a nucleobase that is capable of base pairing with another nucleobase. For example, in DNA, adenine (A) is complementary to thymine (T). For example, in RNA, adenine (A) is complementary to uracil (U). In certain embodiments, complementary nucleobase refers to a nucleobase of an antisense compound that is capable of base pairing with a nucleobase of its target nucleic acid. For example, if a nucleobase at a certain position of an antisense compound is capable of hydrogen bonding with a nucleobase at a certain position of a target nucleic acid, then the position of hydrogen bonding between the oligonucleotide and the target nucleic acid is considered to be complementary at that nucleobase pair.

[0073] "Nucleobase sequence" means the order of contiguous nucleobases independent of any sugar, linkage, and/or nucleobase modification.

[0074] "Nucleoside" means a nucleobase linked to a sugar.

[0075] "Nucleoside mimetic" includes those structures used to replace the sugar or the sugar and the base and not necessarily the linkage at one or more positions of an oligomeric compound such as for example nucleoside mimetics having morpholino, cyclohexenyl, cyclohexyl, tetrahydropyranyl, bicyclo or tricyclo sugar mimetics, e.g., non furanose sugar units. Nucleotide mimetic includes those structures used to replace the nucleoside and the linkage at one or more positions of an oligomeric compound such as for example peptide nucleic acids or morpholinos (morpholinos linked by —N(H)—C(═O)—O— or other non-phosphodiester linkage). Sugar surrogate overlaps with the slightly broader term nucleoside mimetic but is intended to indicate replacement of the sugar unit (furanose ring) only. The tetrahydropyranyl rings provided herein are illustrative of an example of a sugar surrogate wherein the furanose sugar group has been replaced with a tetrahydropyranyl ring system. "Mimetic" refers to groups that are substituted for a sugar, a nucleobase, and/or internucleoside linkage. Generally, a mimetic is used in place of the sugar or sugar-internucleoside linkage combination, and the nucleobase is maintained for hybridization to a selected target.

[0076] "Nucleotide" means a nucleoside having a phosphate group covalently linked to the sugar portion of the nucleoside.

[0077] "Oligomeric compound" means a polymer of linked monomeric subunits which is capable of hybridizing to at least a region of a nucleic acid molecule.

[0078] "Oligonucleoside" means an oligonucleotide in which the internucleoside linkages do not contain a phosphorus atom.

[0079] "Oligonucleotide" means a polymer of linked nucleosides each of which can be modified or unmodified, independent one from another.

[0080] "Parenteral administration" means administration through injection or infusion. Parenteral administration includes subcutaneous administration, intravenous administration, intramuscular administration, intraarterial administration, intraperitoneal administration, or intracranial administration, e.g. intrathecal or intracerebroventricular administration.

[0081] "Pharmaceutical composition" means a mixture of substances suitable for administering to an individual. For example, a pharmaceutical composition may comprise one or more active pharmaceutical agents and a sterile aqueous solution.

[0082] "Pharmaceutically acceptable salts" means physiologically and pharmaceutically acceptable salts of antisense compounds, i.e., salts that retain the desired biological activity of the parent oligonucleotide and do not impart undesired toxicological effects thereto.

[0083] "Phosphorothioate linkage" means a linkage between nucleosides where the phosphodiester bond is modified by replacing one of the non-bridging oxygen atoms with a sulfur atom. A phosphorothioate linkage is a modified internucleoside linkage.

[0084] "Portion" means a defined number of contiguous (i.e., linked) nucleobases of a nucleic acid. In certain embodiments, a portion is a defined number of contiguous nucleobases of a target nucleic acid. In certain embodiments, a portion is a defined number of contiguous nucleobases of an antisense compound

[0085] "Prevent" refers to delaying or forestalling the onset, development or progression of a disease, disorder, or condition for a period of time from minutes to indefinitely. Prevent also means reducing the risk of developing a disease, disorder, or condition.

[0086] "Prophylactically effective amount" refers to an amount of a pharmaceutical agent that provides a prophylactic or preventative benefit to an animal.

[0087] "Region" is defined as a portion of the target nucleic acid having at least one identifiable structure, function, or characteristic.

[0088] "Ribonucleotide" means a nucleotide having a hydroxy at the 2' position of the sugar portion of the nucleotide. Ribonucleotides may be modified with any of a variety of substituents.

[0089] "Segments" are defined as smaller or sub-portions of regions within a target nucleic acid.

[0090] "Side effects" means physiological disease and/or conditions attributable to a treatment other than the desired effects. In certain embodiments, side effects include injection site reactions, liver function test abnormalities, renal function abnormalities, liver toxicity, renal toxicity, central nervous system abnormalities, myopathies, and malaise. For example, increased aminotransferase levels in serum may indicate liver toxicity or liver function abnormality. For example, increased bilirubin may indicate liver toxicity or liver function abnormality.

[0091] "Sites," as used herein, are defined as unique nucleobase positions within a target nucleic acid.

[0092] "Slows progression" means decrease in the development of the said disease.

[0093] "Specifically hybridizable" refers to an antisense compound having a sufficient degree of complementarity between an antisense oligonucleotide and a target nucleic acid to induce a desired effect, while exhibiting minimal or no effects on non-target nucleic acids under conditions in which specific binding is desired, i.e., under physiological conditions in the case of in vivo assays and therapeutic treatments. "Stringent hybridization conditions" or "stringent conditions" refer to conditions under which an oligomeric compound will hybridize to its target sequence, but to a minimal number of other sequences.

[0094] "Subject" means a human or non-human animal selected for treatment or therapy.

[0095] "Target" refers to a protein, the modulation of which is desired.

[0096] "Target gene" refers to a gene encoding a target.

[0097] "Targeting" means the process of design and selection of an antisense compound that will specifically hybridize to a target nucleic acid and induce a desired effect.

[0098] "Target nucleic acid," "target RNA," "target RNA transcript" and "nucleic acid target" all mean a nucleic acid capable of being targeted by antisense compounds.

[0099] "Target region" means a portion of a target nucleic acid to which one or more antisense compounds is targeted.

[0100] "Target segment" means the sequence of nucleotides of a target nucleic acid to which an antisense compound is targeted. "5' target site" refers to the 5'-most nucleotide of a target segment. "3' target site" refers to the 3'-most nucleotide of a target segment.

[0101] "Therapeutically effective amount" means an amount of a pharmaceutical agent that provides a therapeutic benefit to an individual.

[0102] "Treat" refers to administering a pharmaceutical composition to an animal in order to effect an alteration or improvement of a disease, disorder, or condition in the animal. In certain embodiments, one or more pharmaceutical compositions can be administered to the animal.

[0103] "Unmodified" nucleobases mean the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U).

[0104] "Unmodified nucleotide" means a nucleotide composed of naturally occuring nucleobases, sugar moieties, and internucleoside linkages. In certain embodiments, an unmodified nucleotide is an RNA nucleotide (i.e. β-D-ribonucleosides) or a DNA nucleotide (i.e. β-D-deoxyribonucleoside).

Certain Embodiments

[0105] Certain embodiments provide methods, compounds and compositions for inhibiting Complement Factor B (CFB) expression.

[0106] Certain embodiments provide antisense compounds targeted to a CFB nucleic acid. In certain embodiments, the CFB nucleic acid has the sequence set forth in GENBANK Accession No. NM_001710.5 (incorporated herein as SEQ ID NO: 1), GENBANK Accession No. NT_007592.15 truncated from nucleotides 31852000 to 31861000 (incorporated herein as SEQ ID NO: 2), GENBANK Accession No NW_001116486.1 truncated from nucleotides 536000 to 545000 (incorporated herein as SEQ ID NO: 3), GENBANK Accession No. XM_001113553.2 (incorporated herein as SEQ ID NO: 4), or GENBANK Accession No. NM_008198.2 (incorporated herein as SEQ ID NO: 5).

[0107] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808.

[0108] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 9 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808.

[0109] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 10 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808.

[0110] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 11 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808.

[0111] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence com-

prising at least 12 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808.

[0112] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 6-808.

[0113] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of the nucleobase sequence of any one of SEQ ID NOs: 6-808.

[0114] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides complementary within nucleobases 30-49, 48-63, 150-169, 151-170, 152-171, 154-169, 154-173, 156-171, 156-175, 157-176, 158-173, 158-177, 480-499, 600-619, 638-657, 644-663, 738-757, 1089-1108, 1135-1154, 1141-1160, 1147-1166, 1150-1169, 1153-1172, 1159-1178, 1162-1181, 1165-1184, 1171-1186, 1171-1190, 1173-1188, 1173-1192, 1175-1190, 1175-1194, 1177-1196, 1183-1202, 1208-1227, 1235-1254, 1298-1317, 1304-1323, 1310-1329, 1316-1335, 1319-1338, 1322-1341, 1328-1347, 1349-1368, 1355-1374, 1393-1412, 1396-1415, 1399-1418, 1405-1424, 1421-1440, 1621-1640, 1646-1665, 1646-1665, 1647-1666, 1689-1708, 1749-1768, 1763-1782, 1912-1931, 2073-2092, 2085-2104, 2166-2185, 2172-2191, 2189-2208, 2191-2210, 2193-2212, 2195-2210, 2195-2214, 2196-2215, 2197-2212, 2197-2216, 2202-2221, 2223-2238, 2223-2242, 2225-2240, 2226-2245, 2227-2242, 2227-2246, 2238-2257, 2241-2260, 2267-2286, 2361-2380, 2388-2407, 2397-2416, 2448-2467, 2453-2472, 2455-2474, 2457-2472, 2457-2476, 2459-2474, 2459-2478, 2461-2476, 2461-2480, 2532-2551, 2550-2569, 2551-2566, 2551-2570, 2552-2568, 2552-2570, 2552-2571, 2553-2568, 2553-2570, 2553-2571, 2553-2572, 2554-2571, 2554-2572, 2554-2573, 2555-2570, 2555-2572, 2555-2574, 2556-2573, 2556-2574, 2556-2575, 2557-2573, 2557-2574, 2557-2575, 2557-2576, 2558-2575, 2558-2576, 2558-2577, 2559-2576, 2559-2577, 2559-2578, 2560-2577, 2560-2578, 2560-2579, 2561-2576, 2561-2578, 2561-2579, 2561-2580, 2562-2577, 2562-2579, 2562-2581, 2563-2578, 2563-2580, 2563-2582, 2564-2581, 2564-2583, 2565-2584, 2566-2583, 2566-2585, 2567-2582, 2567-2584, 2567-2586, 2568-2583, 2568-2585, 2568-2587, 2569-2586, 2569-2588, 2570-2585, 2570-2587, 2570-2589, 2571-2586, 2571-2588, 2571-2590, 2572-2589, 2572-2590, 2572-2591, 2573-2590, 2573-2592, 2574-2590, 2574-2591, 2574-2593, 2575-2590, 2575-2591, 2575-2592, 2575-2594, 2576-2593, 2576-2595, 2577-2594, 2577-2595, 2577-2596, 2578-2594, 2578-2596, 2578-2597, 2579-2598, 2580-2596, 2580-2597, 2580-2598, 2580-2599, 2581-2597, 2581-2598, 2581-2599, 2581-2600, 2582-2598, 2582-2599, 2582-2600, 2582-2601, 2583-2599, 2583-2600, 2583-2601, 2583-2602, 2584-2600, 2584-2601, 2584-2602, 2584-2603, 2585-2601, 2585-2603, 2585-2604, 2586-2601, 2586-2602, 2586-2604, 2586-2605, 2587-2602, 2587-2603, 2587-2605, 2587-2606, 2588-2603, 2588-2604, 2588-2605, 2588-2606, 2588-2607, 2589-2604, 2589-2605, 2589-2606, 2589-2607, 2589-2608, 2590-2605, 2590-2606, 2590-2607, 2590-2608, 2590-2609, 2590-2609, 2591-2607, 2591-2608, 2591-2609, 2591-2610, 2592-2607, 2592-2608, 2592-2609, 2592-2610, 2592-2611, 2593-2608, 2593-2609, 2593-2610, 2593-2612, 2594-2609, 2594-2610, 2594-2611, 2594-2612, 2594-2613, 2595-2610, 2595-2611, 2595-2612, 2595-2613, 2595-2614, 2596-2611, 2596-2612, 2596-2613, 2596-2614, 2596-2615, 2597-2612, 2597-2612, 2597-2613, 2597-2614, 2597-2615, 2597-2616, 2598-2613, 2598-2614, 2598-2615, 2598-2616, 2598-2617, 2599-2614, 2599-2615, 2599-2616, 2599-2617, 2599-2618, 2600-2615, 2600-2616, 2600-2617, 2600-2618, 2600-2619, 2601-2616, 2601-2617, 2601-2618, 2601-2619, 2601-2620, 2602-2617, 2602-2618, 2602-2619, 2602-2620, 2602-2621, 2603-2618, 2603-2619, 2603-2620, 2603-2621, 2603-2622, 2604-2619, 2604-2620, 2604-2621, 2604-2622, 2604-2623, 2605-2620, 2605-2621, 2605-2622, 2605-2623, 2605-2624, 2606-2621, 2606-2622, 2606-2623, 2606-2624, 2606-2625, 2607-2622, 2607-2623, 2607-2624, 2607-2625, 2607-2626, 2608-2623, 2608-2624, 2608-2625, 2608-2626, 2608-2627, 2609-2624, 2609-2625, 2609-2626, 2609-2627, 2609-2628, 2610-2625, 2610-2626, 2610-2627, 2610-2628, 2610-2629, 2611-2626, 2611-2627, 2611-2628, 2611-2629, 2611-2630, 2612-2627, 2612-2628, 2612-2629, 2612-2630, 2612-2631, 2613-2628, 2613-2629, 2613-2630, 2613-2631, 2614-2629, 2614-2630, 2614-2631, 2615-2630, 2615-2631, or 2616-2631 of SEQ ID NO: 1, wherein said modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to SEQ ID NO: 1.

[0115] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising a portion of at least 8 contiguous nucleobases complementary to an equal length portion of nucleobases 30-49, 48-63, 150-169, 151-170, 152-171, 154-169, 154-173, 156-171, 156-175, 157-176, 158-173, 158-177, 480-499, 600-619, 638-657, 644-663, 738-757, 1089-1108, 1135-1154, 1141-1160, 1147-1166, 1150-1169, 1153-1172, 1159-1178, 1162-1181, 1165-1184, 1171-1186, 1171-1190, 1173-1188, 1173-1192, 1175-1190, 1175-1194, 1177-1196, 1183-1202, 1208-1227, 1235-1254, 1298-1317, 1304-1323, 1310-1329, 1316-1335, 1319-1338, 1322-1341, 1328-1347, 1349-1368, 1355-1374, 1393-1412, 1396-1415, 1399-1418, 1405-1424, 1421-1440, 1621-1640, 1646-1665, 1646-1665, 1647-1666, 1689-1708, 1749-1768, 1763-1782, 1912-1931, 2073-2092, 2085-2104, 2166-2185, 2172-2191, 2189-2208, 2191-2210, 2193-2212, 2195-2210, 2195-2214, 2196-2215, 2197-2212, 2197-2216, 2202-2221, 2223-2238, 2223-2242, 2225-2240, 2226-2245, 2227-2242, 2227-2246, 2238-2257, 2241-2260, 2267-2286, 2361-2380, 2388-2407, 2397-2416, 2448-2467, 2453-2472, 2455-2474, 2457-2472, 2457-2476, 2459-2474, 2459-2478, 2461-2476, 2461-2480, 2532-2551, 2550-2569, 2551-2566, 2551-2570, 2552-2568, 2552-2570, 2552-2571, 2553-2568, 2553-2570, 2553-2571, 2553-2572, 2554-2571, 2554-2572, 2554-2573, 2555-2570, 2555-2572, 2555-2574, 2556-2573, 2556-2574, 2556-2575, 2557-2573, 2557-2574, 2557-2575, 2557-2576, 2558-2575, 2558-2576, 2558-2577, 2559-2576, 2559-2577, 2559-2578, 2560-2577, 2560-2578, 2560-2579, 2561-2576, 2561-2578, 2561-2579, 2561-2580, 2562-2577, 2562-2579, 2562-2581, 2563-2578, 2563-2580, 2563-2582, 2564-2581, 2564-2583, 2565-2584, 2566-2583, 2566-2585, 2567-2582, 2567-2584, 2567-2586, 2568-2583, 2568-2585, 2568-2587, 2569-2586, 2569-2588, 2570-2585, 2570-2587, 2570-2589, 2571-2586, 2571-2588, 2571-2590, 2572-2589, 2572-2590, 2572-2591, 2573-2590, 2573-2592, 2574-2590, 2574-2591, 2574-2593, 2575-2590, 2575-2591, 2575-2592, 2575-2594, 2576-2593, 2576-2595, 2577-2594, 2577-2595, 2577-2596, 2578-2594, 2578-2596, 2578-2597, 2579-2598, 2580-2596, 2580-2597, 2580-2598, 2580-2599, 2581-2597, 2581-2598, 2581-2599, 2581-2600, 2582-2598, 2582-2599, 2582-2600, 2582-2601, 2583-2599, 2583-2600, 2583-2601, 2583-2602, 2584-2600, 2584-2601, 2584-2602, 2584-2603, 2585-2601, 2585-2603, 2585-2604, 2586-2601, 2586-2602, 2586-2604, 2586-2605, 2587-2602, 2587-2603, 2587-2605,

2587-2606, 2588-2603, 2588-2604, 2588-2605, 2588-2606, 2588-2607, 2589-2604, 2589-2605, 2589-2606, 2589-2607, 2589-2608, 2590-2605, 2590-2606, 2590-2607, 2590-2608, 2590-2609, 2590-2609, 2591-2607, 2591-2608, 2591-2609, 2591-2610, 2592-2607, 2592-2608, 2592-2609, 2592-2610, 2592-2611, 2593-2608, 2593-2609, 2593-2610, 2593-2612, 2594-2609, 2594-2610, 2594-2611, 2594-2612, 2594-2613, 2595-2610, 2595-2611, 2595-2612, 2595-2613, 2595-2614, 2596-2611, 2596-2612, 2596-2613, 2596-2614, 2596-2615, 2597-2612, 2597-2612, 2597-2613, 2597-2614, 2597-2615, 2597-2616, 2598-2613, 2598-2614, 2598-2615, 2598-2616, 2598-2617, 2599-2614, 2599-2615, 2599-2616, 2599-2617, 2599-2618, 2600-2615, 2600-2616, 2600-2617, 2600-2618, 2600-2619, 2601-2616, 2601-2617, 2601-2618, 2601-2619, 2601-2620, 2602-2617, 2602-2618, 2602-2619, 2602-2620, 2602-2621, 2603-2618, 2603-2619, 2603-2620, 2603-2621, 2603-2622, 2604-2619, 2604-2620, 2604-2621, 2604-2622, 2604-2623, 2605-2620, 2605-2621, 2605-2622, 2605-2623, 2605-2624, 2606-2621, 2606-2622, 2606-2623, 2606-2624, 2606-2625, 2607-2622, 2607-2623, 2607-2624, 2607-2625, 2607-2626, 2608-2623, 2608-2624, 2608-2625, 2608-2626, 2608-2627, 2609-2624, 2609-2625, 2609-2626, 2609-2627, 2609-2628, 2610-2625, 2610-2626, 2610-2627, 2610-2628, 2610-2629, 2611-2626, 2611-2627, 2611-2628, 2611-2629, 2611-2630, 2612-2627, 2612-2628, 2612-2629, 2612-2630, 2612-2631, 2613-2628, 2613-2629, 2613-2630, 2613-2631, 2614-2629, 2614-2630, 2614-2631, 2615-2630, 2615-2631, or 2616-2631 of SEQ ID NO:1, wherein the nucleobase sequence of the modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to SEQ ID NO: 1.

[0116] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides complementary within nucleobases 1608-1627, 1685-1704, 1686-1705, 1751-1770, 1769-1784, 1871-1890, 1872-1891, 1873-1892, 1875-1890, 1875-1894, 1877-1892, 1877-1896, 1878-1897, 1879-1894, 1879-1898, 2288-2307, 2808-2827, 2846-2865, 2852-2871, 2946-2965, 3773-3792, 3819-3838, 3825-3844, 3831-3850, 3834-3853, 3837-3856, 3843-3862, 4151-4166, 4151-4170, 4153-4172, 4159-4178, 4184-4203, 4211-4230, 4609-4628, 4612-4631, 4615-4634, 4621-4640, 4642-4661, 4648-4667, 4686-4705, 4689-4708, 4692-4711, 4698-4717, 4714-4733, 5270-5289, 5295-5314, 5296-5315, 5830-5849, 5890-5909, 5904-5923, 6406-6425, 6662-6681, 6674-6693, 6954-6973, 6960-6979, 6977-6996, 6979-6998, 6981-7000, 6983-6998, 6983-7002, 6984-7003, 6985-7000, 6985-7004, 6990-7009, 7122-7141, 7125-7144, 7151-7170, 7353-7372, 7362-7381, 7683-7702, 7688-7707, 7690-7709, 7692-7707, 7692-7711, 7694-7709, 7694-7713, 7696-7711, 7696-7715, 7767-7786, 7785-7804, 7786-7801, 7787-7803, 7787-7805, 7787-7806, 7788-7803, 7788-7805, 7788-7806, 7788-7807, 7789-7806, 7789-7807, 7789-7808, 7790-7805, 7790-7807, 7790-7809, 7791-7808, 7791-7809, 7791-7810, 7792-7808, 7792-7809, 7792-7810, 7792-7811, 7793-7810, 7793-7811, 7793-7812, 7794-7811, 7794-7812, 7794-7813, 7795-7812, 7795-7813, 7795-7814, 7796-7811, 7796-7813, 7796-7814, 7796-7815, 7797-7812, 7797-7814, 7797-7816, 7798-7813, 7798-7815, 7798-7817, 7799-7816, 7799-7818, 7800-7819, 7801-7818, 7801-7820, 7802-7817, 7802-7819, 7802-7821, 7803-7818, 7803-7820, 7803-7822, 7804-7821, 7804-7823, 7805-7820, 7805-7822, 7805-7824, 7806-7821, 7806-7823, 7806-7825, 7807-7824, 7807-7825, 7807-7826, 7808-7825, 7808-7827, 7809-7825, 7809-7826, 7809-7828, 7810-7825, 7810-7826, 7810-7827, 7810-7829, 7811-7828, 7811-7830, 7812-7829, 7812-7830, 7812-7831, 7813-7829, 7813-7831, 7813-7832, 7814-7833, 7815-7831, 7815-7832, 7815-7833, 7815-7834, 7816-7832, 7816-7833, 7816-7834, 7816-7835, 7817-7833, 7817-7834, 7817-7835, 7817-7836, 7818-7834, 7818-7835, 7818-7836, 7818-7837, 7819-7835, 7819-7836, 7819-7837, 7819-7838, 7820-7836, 7820-7838, 7820-7839, 7821-7836, 7821-7837, 7821-7839, 7821-7840, 7822-7837, 7822-7838, 7822-7840, 7822-7841, 7823-7838, 7823-7839, 7823-7839, 7823-7840, 7823-7841, 7823-7842, 7824-7839, 7824-7840, 7824-7840, 7824-7841, 7824-7842, 7824-7843, 7825-7840, 7825-7841, 7825-7842, 7825-7843, 7825-7844, 7826-7842, 7826-7843, 7826-7844, 7826-7845, 7827-7842, 7827-7843, 7827-7844, 7827-7845, 7827-7846, 7828-7843, 7828-7844, 7828-7845, 7828-7847, 7829-7844, 7829-7845, 7829-7846, 7829-7847, 7829-7848, 7830-7845, 7830-7846, 7830-7847, 7830-7848, 7830-7849, 7831-7846, 7831-7847, 7831-7848, 7831-7849, 7831-7850, 7832-7847, 7832-7848, 7832-7849, 7832-7850, 7832-7851, 7833-7848, 7833-7849, 7833-7850, 7833-7851, 7833-7852, 7834-7849, 7834-7850, 7834-7851, 7834-7852, 7834-7853, 7835-7850, 7835-7851, 7835-7852, 7835-7853, 7835-7854, 7836-7851, 7836-7852, 7836-7853, 7836-7854, 7836-7855, 7837-7852, 7837-7853, 7837-7854, 7837-7855, 7837-7856, 7838-7853, 7838-7854, 7838-7855, 7838-7856, 7838-7857, 7839-7854, 7839-7855, 7839-7856, 7839-7857, 7839-7858, 7840-7855, 7840-7856, 7840-7857, 7840-7858, 7840-7859, 7841-7856, 7841-7857, 7841-7858, 7841-7859, 7841-7860, 7842-7857, 7842-7858, 7842-7859, 7842-7860, 7842-7861, 7843-7858, 7843-7859, 7843-7860, 7843-7861, 7843-7862, 7844-7859, 7844-7860, 7844-7861, 7844-7862, 7845-7860, 7845-7861, 7845-7862, 7846-7861, or 7846-7862 of SEQ ID NO: 2, wherein said modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to SEQ ID NO: 2.

[0117] Certain embodiments provide a compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising a portion of at least 8 contiguous nucleobases complementary to an equal length portion of nucleobases 1608-1627, 1685-1704, 1686-1705, 1751-1770, 1769-1784, 1871-1890, 1872-1891, 1873-1892, 1875-1890, 1875-1894, 1877-1892, 1877-1896, 1878-1897, 1879-1894, 1879-1898, 2288-2307, 2808-2827, 2846-2865, 2852-2871, 2946-2965, 3773-3792, 3819-3838, 3825-3844, 3831-3850, 3834-3853, 3837-3856, 3843-3862, 4151-4166, 4151-4170, 4153-4172, 4159-4178, 4184-4203, 4211-4230, 4609-4628, 4612-4631, 4615-4634, 4621-4640, 4642-4661, 4648-4667, 4686-4705, 4689-4708, 4692-4711, 4698-4717, 4714-4733, 5270-5289, 5295-5314, 5296-5315, 5830-5849, 5890-5909, 5904-5923, 6406-6425, 6662-6681, 6674-6693, 6954-6973, 6960-6979, 6977-6996, 6979-6998, 6981-7000, 6983-6998, 6983-7002, 6984-7003, 6985-7000, 6985-7004, 6990-7009, 7122-7141, 7125-7144, 7151-7170, 7353-7372, 7362-7381, 7683-7702, 7688-7707, 7690-7709, 7692-7707, 7692-7711, 7694-7709, 7694-7713, 7696-7711, 7696-7715, 7767-7786, 7785-7804, 7786-7801, 7787-7803, 7787-7805, 7787-7806, 7788-7803, 7788-7805, 7788-7806, 7788-7807, 7789-7806, 7789-7807, 7789-7808, 7790-7805, 7790-7807, 7790-7809, 7791-7808, 7791-7809, 7791-7810, 7792-7808, 7792-7809, 7792-7810, 7792-7811, 7793-7810, 7793-7811, 7793-7812, 7794-7811, 7794-7812, 7794-7813, 7795-7812, 7795-7813, 7795-7814, 7796-7811, 7796-7813, 7796-7814, 7796-7815, 7797-7812, 7797-7814, 7797-7816, 7798-7813, 7798-7815, 7798-7817, 7799-7816, 7799-7818, 7800-7819, 7801-7818, 7801-7820, 7802-7817, 7802-

7819, 7802-7821, 7803-7818, 7803-7820, 7803-7822, 7804-7821, 7804-7823, 7805-7820, 7805-7822, 7805-7824, 7806-7821, 7806-7823, 7806-7825, 7807-7824, 7807-7825, 7807-7826, 7808-7825, 7808-7827, 7809-7825, 7809-7826, 7809-7828, 7810-7825, 7810-7826, 7810-7827, 7810-7829, 7811-7828, 7811-7830, 7812-7829, 7812-7830, 7812-7831, 7813-7829, 7813-7831, 7813-7832, 7814-7833, 7815-7831, 7815-7832, 7815-7833, 7815-7834, 7816-7832, 7816-7833, 7816-7834, 7816-7835, 7817-7833, 7817-7834, 7817-7835, 7817-7836, 7818-7834, 7818-7835, 7818-7836, 7818-7837, 7819-7835, 7819-7836, 7819-7837, 7819-7838, 7820-7836, 7820-7838, 7820-7839, 7821-7836, 7821-7837, 7821-7839, 7821-7840, 7822-7837, 7822-7838, 7822-7840, 7822-7841, 7823-7838, 7823-7839, 7823-7839, 7823-7840, 7823-7841, 7823-7842, 7824-7839, 7824-7840, 7824-7840, 7824-7841, 7824-7842, 7824-7843, 7825-7840, 7825-7841, 7825-7842, 7825-7843, 7825-7844, 7826-7842, 7826-7843, 7826-7844, 7826-7845, 7827-7842, 7827-7843, 7827-7844, 7827-7845, 7827-7846, 7828-7843, 7828-7844, 7828-7845, 7828-7847, 7829-7844, 7829-7845, 7829-7846, 7829-7847, 7829-7848, 7830-7845, 7830-7846, 7830-7847, 7830-7848, 7830-7849, 7831-7846, 7831-7847, 7831-7848, 7831-7849, 7831-7850, 7832-7847, 7832-7848, 7832-7849, 7832-7850, 7832-7851, 7833-7848, 7833-7849, 7833-7850, 7833-7851, 7833-7852, 7834-7849, 7834-7850, 7834-7851, 7834-7852, 7834-7853, 7835-7850, 7835-7851, 7835-7852, 7835-7853, 7835-7854, 7836-7851, 7836-7852, 7836-7853, 7836-7854, 7836-7855, 7837-7852, 7837-7853, 7837-7854, 7837-7855, 7837-7856, 7838-7853, 7838-7854, 7838-7855, 7838-7856, 7838-7857, 7839-7854, 7839-7855, 7839-7856, 7839-7857, 7839-7858, 7840-7855, 7840-7856, 7840-7857, 7840-7858, 7840-7859, 7841-7856, 7841-7857, 7841-7858, 7841-7859, 7841-7860, 7842-7857, 7842-7858, 7842-7859, 7842-7860, 7842-7861, 7843-7858, 7843-7859, 7843-7860, 7843-7861, 7843-7862, 7844-7859, 7844-7860, 7844-7861, 7844-7862, 7845-7860, 7845-7861, 7845-7862, 7846-7861, and 7846-7862 of SEQ ID NO: 2, wherein the nucleobase sequence of the modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to SEQ ID NO: 2.

[0118] In certain embodiments, antisense compounds or oligonucleotides target a region of a CFB nucleic acid. In certain embodiments, such compounds or oligonucleotides targeted to a region of a CFB nucleic acid have a contiguous nucleobase portion that is complementary to an equal length nucleobase portion of the region. For example, the portion can be at least an 8, 9, 10, 11, 12, 13, 14, 15, or 16 contiguous nucleobase portion complementary to an equal length portion of a region recited herein. In certain embodiments, such compounds or oligonucleotide target the following nucleotide regions of SEQ ID NO: 1: 30-49, 48-63, 150-169, 151-170, 152-171, 154-169, 154-173, 156-171, 156-175, 157-176, 158-173, 158-177, 480-499, 600-619, 638-657, 644-663, 738-757, 1089-1108, 1135-1154, 1141-1160, 1147-1166, 1150-1169, 1153-1172, 1159-1178, 1162-1181, 1165-1184, 1171-1186, 1171-1190, 1173-1188, 1173-1192, 1175-1190, 1175-1194, 1177-1196, 1183-1202, 1208-1227, 1235-1254, 1298-1317, 1304-1323, 1310-1329, 1316-1335, 1319-1338, 1322-1341, 1328-1347, 1349-1368, 1355-1374, 1393-1412, 1396-1415, 1399-1418, 1405-1424, 1421-1440, 1621-1640, 1646-1665, 1646-1665, 1647-1666, 1689-1708, 1749-1768, 1763-1782, 1912-1931, 2073-2092, 2085-2104, 2166-2185, 2172-2191, 2189-2208, 2191-2210, 2193-2212, 2195-2210, 2195-2214, 2196-2215, 2197-2212, 2197-2216, 2202-2221, 2223-2238, 2223-2242, 2225-2240, 2226-2245, 2227-2242, 2227-2246, 2238-2257, 2241-2260, 2267-2286, 2361-2380, 2388-2407, 2397-2416, 2448-2467, 2453-2472, 2455-2474, 2457-2472, 2457-2476, 2459-2474, 2459-2478, 2461-2476, 2461-2480, 2532-2551, 2550-2569, 2551-2566, 2551-2570, 2552-2568, 2552-2570, 2552-2571, 2553-2568, 2553-2570, 2553-2571, 2553-2572, 2554-2571, 2554-2572, 2554-2573, 2555-2570, 2555-2572, 2555-2574, 2556-2573, 2556-2574, 2556-2575, 2557-2573, 2557-2574, 2557-2575, 2557-2576, 2558-2575, 2558-2576, 2558-2577, 2559-2576, 2559-2577, 2559-2578, 2560-2577, 2560-2578, 2560-2579, 2561-2576, 2561-2578, 2561-2579, 2561-2580, 2562-2577, 2562-2579, 2562-2581, 2563-2578, 2563-2580, 2563-2582, 2564-2581, 2564-2583, 2565-2584, 2566-2583, 2566-2585, 2567-2582, 2567-2584, 2567-2586, 2568-2583, 2568-2585, 2568-2587, 2569-2586, 2569-2588, 2570-2585, 2570-2587, 2570-2589, 2571-2586, 2571-2588, 2571-2590, 2572-2589, 2572-2590, 2572-2591, 2573-2590, 2573-2592, 2574-2590, 2574-2591, 2574-2593, 2575-2590, 2575-2591, 2575-2592, 2575-2594, 2576-2593, 2576-2595, 2577-2594, 2577-2595, 2577-2596, 2578-2594, 2578-2596, 2578-2597, 2579-2598, 2580-2596, 2580-2597, 2580-2598, 2580-2599, 2581-2597, 2581-2598, 2581-2599, 2581-2600, 2582-2598, 2582-2599, 2582-2600, 2582-2601, 2583-2599, 2583-2600, 2583-2601, 2583-2602, 2584-2600, 2584-2601, 2584-2602, 2584-2603, 2585-2601, 2585-2603, 2585-2604, 2586-2601, 2586-2602, 2586-2604, 2586-2605, 2587-2602, 2587-2603, 2587-2605, 2587-2606, 2588-2603, 2588-2604, 2588-2605, 2588-2606, 2588-2607, 2589-2604, 2589-2605, 2589-2606, 2589-2607, 2589-2608, 2590-2605, 2590-2606, 2590-2607, 2590-2608, 2590-2609, 2590-2609, 2591-2607, 2591-2608, 2591-2609, 2591-2610, 2592-2607, 2592-2608, 2592-2609, 2592-2610, 2592-2611, 2593-2608, 2593-2609, 2593-2610, 2593-2612, 2594-2609, 2594-2610, 2594-2611, 2594-2612, 2594-2613, 2595-2610, 2595-2611, 2595-2612, 2595-2613, 2595-2614, 2596-2611, 2596-2612, 2596-2613, 2596-2614, 2596-2615, 2597-2612, 2597-2612, 2597-2613, 2597-2614, 2597-2615, 2597-2616, 2598-2613, 2598-2614, 2598-2615, 2598-2616, 2598-2617, 2599-2614, 2599-2615, 2599-2616, 2599-2617, 2599-2618, 2600-2615, 2600-2616, 2600-2617, 2600-2618, 2600-2619, 2601-2616, 2601-2617, 2601-2618, 2601-2619, 2601-2620, 2602-2617, 2602-2618, 2602-2619, 2602-2620, 2602-2621, 2603-2618, 2603-2619, 2603-2620, 2603-2621, 2603-2622, 2604-2619, 2604-2620, 2604-2621, 2604-2622, 2604-2623, 2605-2620, 2605-2621, 2605-2622, 2605-2623, 2605-2624, 2606-2621, 2606-2622, 2606-2623, 2606-2624, 2606-2625, 2607-2622, 2607-2623, 2607-2624, 2607-2625, 2607-2626, 2608-2623, 2608-2624, 2608-2625, 2608-2626, 2608-2627, 2609-2624, 2609-2625, 2609-2626, 2609-2627, 2609-2628, 2610-2625, 2610-2626, 2610-2627, 2610-2628, 2610-2629, 2611-2626, 2611-2627, 2611-2628, 2611-2629, 2611-2630, 2612-2627, 2612-2628, 2612-2629, 2612-2630, 2612-2631, 2613-2628, 2613-2629, 2613-2630, 2613-2631, 2614-2629, 2614-2630, 2614-2631, 2615-2630, 2615-2631, and 2616-2631.

[0119] In certain embodiments, antisense compounds or oligonucleotides target a region of a CFB nucleic acid. In certain embodiments, such compounds or oligonucleotides targeted to a region of a CFB nucleic acid have a contiguous nucleobase portion that is complementary to an equal length nucleobase portion of the region. For example, the portion can be at least an 8, 9, 10, 11, 12, 13, 14, 15, or 16 contiguous nucleobase portion complementary to an equal length portion of a region recited herein. In certain embodiments, such compounds or oligonucleotide target the following nucleotide

regions of SEQ ID NO: 2: 1608-1627, 1685-1704, 1686-1705, 1751-1770, 1769-1784, 1871-1890, 1872-1891, 1873-1892, 1875-1890, 1875-1894, 1877-1892, 1877-1896, 1878-1897, 1879-1894, 1879-1898, 2288-2307, 2808-2827, 2846-2865, 2852-2871, 2946-2965, 3773-3792, 3819-3838, 3825-3844, 3831-3850, 3834-3853, 3837-3856, 3843-3862, 4151-4166, 4151-4170, 4153-4172, 4159-4178, 4184-4203, 4211-4230, 4609-4628, 4612-4631, 4615-4634, 4621-4640, 4642-4661, 4648-4667, 4686-4705, 4689-4708, 4692-4711, 4698-4717, 4714-4733, 5270-5289, 5295-5314, 5296-5315, 5830-5849, 5890-5909, 5904-5923, 6406-6425, 6662-6681, 6674-6693, 6954-6973, 6960-6979, 6977-6996, 6979-6998, 6981-7000, 6983-6998, 6983-7002, 6984-7003, 6985-7000, 6985-7004, 6990-7009, 7122-7141, 7125-7144, 7151-7170, 7353-7372, 7362-7381, 7683-7702, 7688-7707, 7690-7709, 7692-7707, 7692-7711, 7694-7709, 7694-7713, 7696-7711, 7696-7715, 7767-7786, 7785-7804, 7786-7801, 7787-7803, 7787-7805, 7787-7806, 7788-7803, 7788-7805, 7788-7806, 7788-7807, 7789-7806, 7789-7807, 7789-7808, 7790-7805, 7790-7807, 7790-7809, 7791-7808, 7791-7809, 7791-7810, 7792-7808, 7792-7809, 7792-7810, 7792-7811, 7793-7810, 7793-7811, 7793-7812, 7794-7811, 7794-7812, 7794-7813, 7795-7812, 7795-7813, 7795-7814, 7796-7811, 7796-7813, 7796-7814, 7796-7815, 7797-7812, 7797-7814, 7797-7816, 7798-7813, 7798-7815, 7798-7817, 7799-7816, 7799-7818, 7800-7819, 7801-7818, 7801-7820, 7802-7817, 7802-7819, 7802-7821, 7803-7818, 7803-7820, 7803-7822, 7804-7821, 7804-7823, 7805-7820, 7805-7822, 7805-7824, 7806-7821, 7806-7823, 7806-7825, 7807-7824, 7807-7825, 7807-7826, 7808-7825, 7808-7827, 7809-7825, 7809-7826, 7809-7828, 7810-7825, 7810-7826, 7810-7827, 7810-7829, 7811-7828, 7811-7830, 7812-7829, 7812-7830, 7812-7831, 7813-7829, 7813-7831, 7813-7832, 7814-7833, 7815-7831, 7815-7832, 7815-7833, 7815-7834, 7816-7832, 7816-7833, 7816-7834, 7816-7835, 7817-7833, 7817-7834, 7817-7835, 7817-7836, 7818-7834, 7818-7835, 7818-7836, 7818-7837, 7819-7835, 7819-7836, 7819-7837, 7819-7838, 7820-7836, 7820-7838, 7820-7839, 7821-7836, 7821-7837, 7821-7839, 7821-7840, 7822-7837, 7822-7838, 7822-7840, 7822-7841, 7823-7838, 7823-7839, 7823-7839, 7823-7840, 7823-7841, 7823-7842, 7824-7839, 7824-7840, 7824-7840, 7824-7841, 7824-7842, 7824-7843, 7825-7840, 7825-7841, 7825-7842, 7825-7843, 7825-7844, 7826-7842, 7826-7843, 7826-7844, 7826-7845, 7827-7842, 7827-7843, 7827-7844, 7827-7845, 7827-7846, 7828-7843, 7828-7844, 7828-7845, 7828-7847, 7829-7844, 7829-7845, 7829-7846, 7829-7847, 7829-7848, 7830-7845, 7830-7846, 7830-7847, 7830-7848, 7830-7849, 7831-7846, 7831-7847, 7831-7848, 7831-7849, 7831-7850, 7832-7847, 7832-7848, 7832-7849, 7832-7850, 7832-7851, 7833-7848, 7833-7849, 7833-7850, 7833-7851, 7833-7852, 7834-7849, 7834-7850, 7834-7851, 7834-7852, 7834-7853, 7835-7850, 7835-7851, 7835-7852, 7835-7853, 7835-7854, 7836-7851, 7836-7852, 7836-7853, 7836-7854, 7836-7855, 7837-7852, 7837-7853, 7837-7854, 7837-7855, 7837-7856, 7838-7853, 7838-7854, 7838-7855, 7838-7856, 7838-7857, 7839-7854, 7839-7855, 7839-7856, 7839-7857, 7839-7858, 7840-7855, 7840-7856, 7840-7857, 7840-7858, 7840-7859, 7841-7856, 7841-7857, 7841-7858, 7841-7859, 7841-7860, 7842-7857, 7842-7858, 7842-7859, 7842-7860, 7842-7861, 7843-7858, 7843-7859, 7843-7860, 7843-7861, 7843-7862, 7844-7859, 7844-7860, 7844-7861, 7844-7862, 7845-7860, 7845-7861, 7845-7862, 7846-7861, and 7846-7862.

[0120] In certain embodiments, antisense compounds or oligonucleotides target the 3'UTR of a CFB nucleic acid. In certain embodiments, antisense compounds or oligonucleotides target within nucleotides 2574-2626 of a CFB nucleic acid having the nucleobase sequence of SEQ ID NO: 1. In certain embodiments, antisense compounds or oligonucleotides have at least an 8, 9, 10, 11, 12, 13, 14, 15, or 16 contiguous nucleobase portion complementary to an equal length portion within nucleotides 2574-2626 of a CFB nucleic acid having the nucleobase sequence of SEQ ID NO: 1.

[0121] In certain embodiments, antisense compounds or oligonucleotides target a region of a CFB nucleic acid having the nucleobase sequence of SEQ ID NO: 1 within nucleobases 2457-2631, 2457-2472, 2457-2474, 2457-2476, 2457-2566, 2457-2570, 2457-2571, 2457-2572, 2457-2573, 2457-2574, 2457-2575, 2457-2576, 2457-2577, 2457-2578, 2457-2579, 2457-2580, 2457-2581, 2457-2582, 2457-2583, 2457-2584, 2457-2585, 2457-2586, 2457-2587, 2457-2588, 2457-2589, 2457-2590, 2457-2591, 2457-2592, 2457-2593, 2457-2594, 2457-2595, 2457-2596, 2457-2597, 2457-2598, 2457-2599, 2457-2600, 2457-2601, 2457-2602, 2457-2603, 2457-2604, 2457-2605, 2457-2606, 2457-2607, 2457-2608, 2457-2609, 2457-2610, 2457-2611, 2457-2612, 2457-2613, 2457-2614, 2457-2615, 2457-2616, 2457-2617, 2457-2618, 2457-2619, 2457-2620, 2457-2621, 2457-2622, 2457-2623, 2457-2624, 2457-2625, 2457-2626, 2457-2627, 2457-2628, 2457-2629, 2457-2630, 2457-2631, 2459-2474, 2459-2476, 2459-2566, 2459-2570, 2459-2571, 2459-2572, 2459-2573, 2459-2574, 2459-2575, 2459-2576, 2459-2577, 2459-2578, 2459-2579, 2459-2580, 2459-2581, 2459-2582, 2459-2583, 2459-2584, 2459-2585, 2459-2586, 2459-2587, 2459-2588, 2459-2589, 2459-2590, 2459-2591, 2459-2592, 2459-2593, 2459-2594, 2459-2595, 2459-2596, 2459-2597, 2459-2598, 2459-2599, 2459-2600, 2459-2601, 2459-2602, 2459-2603, 2459-2604, 2459-2605, 2459-2606, 2459-2607, 2459-2608, 2459-2609, 2459-2610, 2459-2611, 2459-2612, 2459-2613, 2459-2614, 2459-2615, 2459-2616, 2459-2617, 2459-2618, 2459-2619, 2459-2620, 2459-2621, 2459-2622, 2459-2623, 2459-2624, 2459-2625, 2459-2626, 2459-2627, 2459-2628, 2459-2629, 2459-2630, 2459-2631, 2461-2476, 2461-2566, 2461-2570, 2461-2571, 2461-2572, 2461-2573, 2461-2574, 2461-2575, 2461-2576, 2461-2577, 2461-2578, 2461-2579, 2461-2580, 2461-2581, 2461-2582, 2461-2583, 2461-2584, 2461-2585, 2461-2586, 2461-2587, 2461-2588, 2461-2589, 2461-2590, 2461-2591, 2461-2592, 2461-2593, 2461-2594, 2461-2595, 2461-2596, 2461-2597, 2461-2598, 2461-2599, 2461-2600, 2461-2601, 2461-2602, 2461-2603, 2461-2604, 2461-2605, 2461-2606, 2461-2607, 2461-2608, 2461-2609, 2461-2610, 2461-2611, 2461-2612, 2461-2613, 2461-2614, 2461-2615, 2461-2616, 2461-2617, 2461-2618, 2461-2619, 2461-2620, 2461-2621, 2461-2622, 2461-2623, 2461-2624, 2461-2625, 2461-2626, 2461-2627, 2461-2628, 2461-2629, 2461-2630, 2461-2631, 2551-2566, 2551-2570, 2551-2571, 2551-2572, 2551-2573, 2551-2574, 2551-2575, 2551-2576, 2551-2577, 2551-2578, 2551-2579, 2551-2580, 2551-2581, 2551-2582, 2551-2583, 2551-2584, 2551-2585, 2551-2586, 2551-2587, 2551-2588, 2551-2589, 2551-2590, 2551-2591, 2551-2592, 2551-2593, 2551-2594, 2551-2595, 2551-2596, 2551-2597, 2551-2598, 2551-2599, 2551-2600, 2551-2601, 2551-2602, 2551-2603, 2551-2604, 2551-2605, 2551-2606, 2551-2607, 2551-2608, 2551-2609, 2551-2610, 2551-2611, 2551-2612, 2551-2613, 2551-2614, 2551-2615, 2551-2616, 2551-2617, 2551-2618, 2551-2619, 2551-2620, 2551-2621, 2551-2622, 2551-2623, 2551-2624, 2551-2625, 2551-2626, 2551-2627, 2551-2628, 2551-2629, 2551-2630, 2551-2631, 2553-

2570, 2553-2571, 2553-2572, 2553-2573, 2553-2574, 2553-2575, 2553-2576, 2553-2577, 2553-2578, 2553-2579, 2553-2580, 2553-2581, 2553-2582, 2553-2583, 2553-2584, 2553-2585, 2553-2586, 2553-2587, 2553-2588, 2553-2589, 2553-2590, 2553-2591, 2553-2592, 2553-2593, 2553-2594, 2553-2595, 2553-2596, 2553-2597, 2553-2598, 2553-2599, 2553-2600, 2553-2601, 2553-2602, 2553-2603, 2553-2604, 2553-2605, 2553-2606, 2553-2607, 2553-2608, 2553-2609, 2553-2610, 2553-2611, 2553-2612, 2553-2613, 2553-2614, 2553-2615, 2553-2616, 2553-2617, 2553-2618, 2553-2619, 2553-2620, 2553-2621, 2553-2622, 2553-2623, 2553-2624, 2553-2625, 2553-2626, 2553-2627, 2553-2628, 2553-2629, 2553-2630, 2553-2631, 2554-2573, 2554-2574, 2554-2575, 2554-2576, 2554-2577, 2554-2578, 2554-2579, 2554-2580, 2554-2581, 2554-2582, 2554-2583, 2554-2584, 2554-2585, 2554-2586, 2554-2587, 2554-2588, 2554-2589, 2554-2590, 2554-2591, 2554-2592, 2554-2593, 2554-2594, 2554-2595, 2554-2596, 2554-2597, 2554-2598, 2554-2599, 2554-2600, 2554-2601, 2554-2602, 2554-2603, 2554-2604, 2554-2605, 2554-2606, 2554-2607, 2554-2608, 2554-2609, 2554-2610, 2554-2611, 2554-2612, 2554-2613, 2554-2614, 2554-2615, 2554-2616, 2554-2617, 2554-2618, 2554-2619, 2554-2620, 2554-2621, 2554-2622, 2554-2623, 2554-2624, 2554-2625, 2554-2626, 2554-2627, 2554-2628, 2554-2629, 2554-2630, 2554-2631, 2555-2572, 2555-2573, 2555-2574, 2555-2575, 2555-2576, 2555-2577, 2555-2578, 2555-2579, 2555-2580, 2555-2581, 2555-2582, 2555-2583, 2555-2584, 2555-2585, 2555-2586, 2555-2587, 2555-2588, 2555-2589, 2555-2590, 2555-2591, 2555-2592, 2555-2593, 2555-2594, 2555-2595, 2555-2596, 2555-2597, 2555-2598, 2555-2599, 2555-2600, 2555-2601, 2555-2602, 2555-2603, 2555-2604, 2555-2605, 2555-2606, 2555-2607, 2555-2608, 2555-2609, 2555-2610, 2555-2611, 2555-2612, 2555-2613, 2555-2614, 2555-2615, 2555-2616, 2555-2617, 2555-2618, 2555-2619, 2555-2620, 2555-2621, 2555-2622, 2555-2623, 2555-2624, 2555-2625, 2555-2626, 2555-2627, 2555-2628, 2555-2629, 2555-2630, 2555-2631, 2556-2573, 2556-2574, 2556-2575, 2556-2576, 2556-2577, 2556-2578, 2556-2579, 2556-2580, 2556-2581, 2556-2582, 2556-2583, 2556-2584, 2556-2585, 2556-2586, 2556-2587, 2556-2588, 2556-2589, 2556-2590, 2556-2591, 2556-2592, 2556-2593, 2556-2594, 2556-2595, 2556-2596, 2556-2597, 2556-2598, 2556-2599, 2556-2600, 2556-2601, 2556-2602, 2556-2603, 2556-2604, 2556-2605, 2556-2606, 2556-2607, 2556-2608, 2556-2609, 2556-2610, 2556-2611, 2556-2612, 2556-2613, 2556-2614, 2556-2615, 2556-2616, 2556-2617, 2556-2618, 2556-2619, 2556-2620, 2556-2621, 2556-2622, 2556-2623, 2556-2624, 2556-2625, 2556-2626, 2556-2627, 2556-2628, 2556-2629, 2556-2630, 2556-2631, 2557-2574, 2557-2575, 2557-2576, 2557-2577, 2557-2578, 2557-2579, 2557-2580, 2557-2581, 2557-2582, 2557-2583, 2557-2584, 2557-2585, 2557-2586, 2557-2587, 2557-2588, 2557-2589, 2557-2590, 2557-2591, 2557-2592, 2557-2593, 2557-2594, 2557-2595, 2557-2596, 2557-2597, 2557-2598, 2557-2599, 2557-2600, 2557-2601, 2557-2602, 2557-2603, 2557-2604, 2557-2605, 2557-2606, 2557-2607, 2557-2608, 2557-2609, 2557-2610, 2557-2611, 2557-2612, 2557-2613, 2557-2614, 2557-2615, 2557-2616, 2557-2617, 2557-2618, 2557-2619, 2557-2620, 2557-2621, 2557-2622, 2557-2623, 2557-2624, 2557-2625, 2557-2626, 2557-2627, 2557-2628, 2557-2629, 2557-2630, 2557-2631, 2558-2575, 2558-2576, 2558-2577, 2558-2578, 2558-2579, 2558-2580, 2558-2581, 2558-2582, 2558-2583, 2558-2584, 2558-2585, 2558-2586, 2558-2587, 2558-2588, 2558-2589, 2558-2590, 2558-2591, 2558-2592, 2558-2593, 2558-2594, 2558-2595, 2558-2596, 2558-2597, 2558-2598, 2558-2599, 2558-2600, 2558-2601, 2558-2602, 2558-2603, 2558-2604, 2558-2605, 2558-2606, 2558-2607, 2558-2608, 2558-2609, 2558-2610, 2558-2611, 2558-2612, 2558-2613, 2558-2614, 2558-2615, 2558-2616, 2558-2617, 2558-2618, 2558-2619, 2558-2620, 2558-2621, 2558-2622, 2558-2623, 2558-2624, 2558-2625, 2558-2626, 2558-2627, 2558-2628, 2558-2629, 2558-2630, 2558-2631, 2559-2576, 2559-2577, 2559-2578, 2559-2579, 2559-2580, 2559-2581, 2559-2582, 2559-2583, 2559-2584, 2559-2585, 2559-2586, 2559-2587, 2559-2588, 2559-2589, 2559-2590, 2559-2591, 2559-2592, 2559-2593, 2559-2594, 2559-2595, 2559-2596, 2559-2597, 2559-2598, 2559-2599, 2559-2600, 2559-2601, 2559-2602, 2559-2603, 2559-2604, 2559-2605, 2559-2606, 2559-2607, 2559-2608, 2559-2609, 2559-2610, 2559-2611, 2559-2612, 2559-2613, 2559-2614, 2559-2615, 2559-2616, 2559-2617, 2559-2618, 2559-2619, 2559-2620, 2559-2621, 2559-2622, 2559-2623, 2559-2624, 2559-2625, 2559-2626, 2559-2627, 2559-2628, 2559-2629, 2559-2630, 2559-2631, 2560-2577, 2560-2578, 2560-2579, 2560-2580, 2560-2581, 2560-2582, 2560-2583, 2560-2584, 2560-2585, 2560-2586, 2560-2587, 2560-2588, 2560-2589, 2560-2590, 2560-2591, 2560-2592, 2560-2593, 2560-2594, 2560-2595, 2560-2596, 2560-2597, 2560-2598, 2560-2599, 2560-2600, 2560-2601, 2560-2602, 2560-2603, 2560-2604, 2560-2605, 2560-2606, 2560-2607, 2560-2608, 2560-2609, 2560-2610, 2560-2611, 2560-2612, 2560-2613, 2560-2614, 2560-2615, 2560-2616, 2560-2617, 2560-2618, 2560-2619, 2560-2620, 2560-2621, 2560-2622, 2560-2623, 2560-2624, 2560-2625, 2560-2626, 2560-2627, 2560-2628, 2560-2629, 2560-2630, 2560-2631, 2561-2578, 2561-2579, 2561-2580, 2561-2581, 2561-2582, 2561-2583, 2561-2584, 2561-2585, 2561-2586, 2561-2587, 2561-2588, 2561-2589, 2561-2590, 2561-2591, 2561-2592, 2561-2593, 2561-2594, 2561-2595, 2561-2596, 2561-2597, 2561-2598, 2561-2599, 2561-2600, 2561-2601, 2561-2602, 2561-2603, 2561-2604, 2561-2605, 2561-2606, 2561-2607, 2561-2608, 2561-2609, 2561-2610, 2561-2611, 2561-2612, 2561-2613, 2561-2614, 2561-2615, 2561-2616, 2561-2617, 2561-2618, 2561-2619, 2561-2620, 2561-2621, 2561-2622, 2561-2623, 2561-2624, 2561-2625, 2561-2626, 2561-2627, 2561-2628, 2561-2629, 2561-2630, 2561-2631, 2562-2577, 2562-2578, 2562-2579, 2562-2580, 2562-2581, 2562-2582, 2562-2583, 2562-2584, 2562-2585, 2562-2586, 2562-2587, 2562-2588, 2562-2589, 2562-2590, 2562-2591, 2562-2592, 2562-2593, 2562-2594, 2562-2595, 2562-2596, 2562-2597, 2562-2598, 2562-2599, 2562-2600, 2562-2601, 2562-2602, 2562-2603, 2562-2604, 2562-2605, 2562-2606, 2562-2607, 2562-2608, 2562-2609, 2562-2610, 2562-2611, 2562-2612, 2562-2613, 2562-2614, 2562-2615, 2562-2616, 2562-2617, 2562-2618, 2562-2619, 2562-2620, 2562-2621, 2562-2622, 2562-2623, 2562-2624, 2562-2625, 2562-2626, 2562-2627, 2562-2628, 2562-2629, 2562-2630, 2562-2631, 2563-2580, 2563-2581, 2563-2582, 2563-2583, 2563-2584, 2563-2585, 2563-2586, 2563-2587, 2563-2588, 2563-2589, 2563-2590, 2563-2591, 2563-2592, 2563-2593, 2563-2594, 2563-2595, 2563-2596, 2563-2597, 2563-2598, 2563-2599, 2563-2600, 2563-2601, 2563-2602, 2563-2603, 2563-2604, 2563-2605, 2563-2606, 2563-2607, 2563-2608, 2563-2609, 2563-2610, 2563-2611, 2563-2612, 2563-2613, 2563-2614, 2563-2615, 2563-2616, 2563-2617, 2563-2618, 2563-2619, 2563-2620, 2563-2621, 2563-2622, 2563-2623, 2563-2624, 2563-2625, 2563-2626, 2563-2627, 2563-2628, 2563-2629, 2563-2630, 2563-2631, 2564-2581, 2564-2582, 2564-2583, 2564-2584, 2564-2585, 2564-2586, 2564-2587, 2564-2588, 2564-2589, 2564-2590, 2564-2591, 2564-2592, 2564-2593, 2564-

2594, 2564-2595, 2564-2596, 2564-2597, 2564-2598, 2564-2599, 2564-2600, 2564-2601, 2564-2602, 2564-2603, 2564-2604, 2564-2605, 2564-2606, 2564-2607, 2564-2608, 2564-2609, 2564-2610, 2564-2611, 2564-2612, 2564-2613, 2564-2614, 2564-2615, 2564-2616, 2564-2617, 2564-2618, 2564-2619, 2564-2620, 2564-2621, 2564-2622, 2564-2623, 2564-2624, 2564-2625, 2564-2626, 2564-2627, 2564-2628, 2564-2629, 2564-2630, 2564-2631, 2565-2584, 2565-2585, 2565-2586, 2565-2587, 2565-2588, 2565-2589, 2565-2590, 2565-2591, 2565-2592, 2565-2593, 2565-2594, 2565-2595, 2565-2596, 2565-2597, 2565-2598, 2565-2599, 2565-2600, 2565-2601, 2565-2602, 2565-2603, 2565-2604, 2565-2605, 2565-2606, 2565-2607, 2565-2608, 2565-2609, 2565-2610, 2565-2611, 2565-2612, 2565-2613, 2565-2614, 2565-2615, 2565-2616, 2565-2617, 2565-2618, 2565-2619, 2565-2620, 2565-2621, 2565-2622, 2565-2623, 2565-2624, 2565-2625, 2565-2626, 2565-2627, 2565-2628, 2565-2629, 2565-2630, 2565-2631, 2566-2583, 2566-2584, 2566-2585, 2566-2586, 2566-2587, 2566-2588, 2566-2589, 2566-2590, 2566-2591, 2566-2592, 2566-2593, 2566-2594, 2566-2595, 2566-2596, 2566-2597, 2566-2598, 2566-2599, 2566-2600, 2566-2601, 2566-2602, 2566-2603, 2566-2604, 2566-2605, 2566-2606, 2566-2607, 2566-2608, 2566-2609, 2566-2610, 2566-2611, 2566-2612, 2566-2613, 2566-2614, 2566-2615, 2566-2616, 2566-2617, 2566-2618, 2566-2619, 2566-2620, 2566-2621, 2566-2622, 2566-2623, 2566-2624, 2566-2625, 2566-2626, 2566-2627, 2566-2628, 2566-2629, 2566-2630, 2566-2631, 2567-2584, 2567-2585, 2567-2586, 2567-2587, 2567-2588, 2567-2589, 2567-2590, 2567-2591, 2567-2592, 2567-2593, 2567-2594, 2567-2595, 2567-2596, 2567-2597, 2567-2598, 2567-2599, 2567-2600, 2567-2601, 2567-2602, 2567-2603, 2567-2604, 2567-2605, 2567-2606, 2567-2607, 2567-2608, 2567-2609, 2567-2610, 2567-2611, 2567-2612, 2567-2613, 2567-2614, 2567-2615, 2567-2616, 2567-2617, 2567-2618, 2567-2619, 2567-2620, 2567-2621, 2567-2622, 2567-2623, 2567-2624, 2567-2625, 2567-2626, 2567-2627, 2567-2628, 2567-2629, 2567-2630, 2567-2631, 2568-2585, 2568-2586, 2568-2587, 2568-2588, 2568-2589, 2568-2590, 2568-2591, 2568-2592, 2568-2593, 2568-2594, 2568-2595, 2568-2596, 2568-2597, 2568-2598, 2568-2599, 2568-2600, 2568-2601, 2568-2602, 2568-2603, 2568-2604, 2568-2605, 2568-2606, 2568-2607, 2568-2608, 2568-2609, 2568-2610, 2568-2611, 2568-2612, 2568-2613, 2568-2614, 2568-2615, 2568-2616, 2568-2617, 2568-2618, 2568-2619, 2568-2620, 2568-2621, 2568-2622, 2568-2623, 2568-2624, 2568-2625, 2568-2626, 2568-2627, 2568-2628, 2568-2629, 2568-2630, 2568-2631, 2569-2586, 2569-2587, 2569-2588, 2569-2589, 2569-2590, 2569-2591, 2569-2592, 2569-2593, 2569-2594, 2569-2595, 2569-2596, 2569-2597, 2569-2598, 2569-2599, 2569-2600, 2569-2601, 2569-2602, 2569-2603, 2569-2604, 2569-2605, 2569-2606, 2569-2607, 2569-2608, 2569-2609, 2569-2610, 2569-2611, 2569-2612, 2569-2613, 2569-2614, 2569-2615, 2569-2616, 2569-2617, 2569-2618, 2569-2619, 2569-2620, 2569-2621, 2569-2622, 2569-2623, 2569-2624, 2569-2625, 2569-2626, 2569-2627, 2569-2628, 2569-2629, 2569-2630, 2569-2631, 2571-2588, 2571-2589, 2571-2590, 2571-2591, 2571-2592, 2571-2593, 2571-2594, 2571-2595, 2571-2596, 2571-2597, 2571-2598, 2571-2599, 2571-2600, 2571-2601, 2571-2602, 2571-2603, 2571-2604, 2571-2605, 2571-2606, 2571-2607, 2571-2608, 2571-2609, 2571-2610, 2571-2611, 2571-2612, 2571-2613, 2571-2614, 2571-2615, 2571-2616, 2571-2617, 2571-2618, 2571-2619, 2571-2620, 2571-2621, 2571-2622, 2571-2623, 2571-2624, 2571-2625, 2571-2626, 2571-2627, 2571-2628, 2571-2629, 2571-2630, 2571-2631, 2572-2589, 2572-2590, 2572-2591, 2572-2592, 2572-2593, 2572-2594, 2572-2595, 2572-2596, 2572-2597, 2572-2598, 2572-2599, 2572-2600, 2572-2601, 2572-2602, 2572-2603, 2572-2604, 2572-2605, 2572-2606, 2572-2607, 2572-2608, 2572-2609, 2572-2610, 2572-2611, 2572-2612, 2572-2613, 2572-2614, 2572-2615, 2572-2616, 2572-2617, 2572-2618, 2572-2619, 2572-2620, 2572-2621, 2572-2622, 2572-2623, 2572-2624, 2572-2625, 2572-2626, 2572-2627, 2572-2628, 2572-2629, 2572-2630, 2572-2631, 2573-2590, 2573-2591, 2573-2592, 2573-2593, 2573-2594, 2573-2595, 2573-2596, 2573-2597, 2573-2598, 2573-2599, 2573-2600, 2573-2601, 2573-2602, 2573-2603, 2573-2604, 2573-2605, 2573-2606, 2573-2607, 2573-2608, 2573-2609, 2573-2610, 2573-2611, 2573-2612, 2573-2613, 2573-2614, 2573-2615, 2573-2616, 2573-2617, 2573-2618, 2573-2619, 2573-2620, 2573-2621, 2573-2622, 2573-2623, 2573-2624, 2573-2625, 2573-2626, 2573-2627, 2573-2628, 2573-2629, 2573-2630, 2573-2631, 2574-2591, 2574-2592, 2574-2593, 2574-2594, 2574-2595, 2574-2596, 2574-2597, 2574-2598, 2574-2599, 2574-2600, 2574-2601, 2574-2602, 2574-2603, 2574-2604, 2574-2605, 2574-2606, 2574-2607, 2574-2608, 2574-2609, 2574-2610, 2574-2611, 2574-2612, 2574-2613, 2574-2614, 2574-2615, 2574-2616, 2574-2617, 2574-2618, 2574-2619, 2574-2620, 2574-2621, 2574-2622, 2574-2623, 2574-2624, 2574-2625, 2574-2626, 2574-2627, 2574-2628, 2574-2629, 2574-2630, 2574-2631, 2575-2592, 2575-2593, 2575-2594, 2575-2595, 2575-2596, 2575-2597, 2575-2598, 2575-2599, 2575-2600, 2575-2601, 2575-2602, 2575-2603, 2575-2604, 2575-2605, 2575-2606, 2575-2607, 2575-2608, 2575-2609, 2575-2610, 2575-2611, 2575-2612, 2575-2613, 2575-2614, 2575-2615, 2575-2616, 2575-2617, 2575-2618, 2575-2619, 2575-2620, 2575-2621, 2575-2622, 2575-2623, 2575-2624, 2575-2625, 2575-2626, 2575-2627, 2575-2628, 2575-2629, 2575-2630, 2575-2631, 2576-2593, 2576-2594, 2576-2595, 2576-2596, 2576-2597, 2576-2598, 2576-2599, 2576-2600, 2576-2601, 2576-2602, 2576-2603, 2576-2604, 2576-2605, 2576-2606, 2576-2607, 2576-2608, 2576-2609, 2576-2610, 2576-2611, 2576-2612, 2576-2613, 2576-2614, 2576-2615, 2576-2616, 2576-2617, 2576-2618, 2576-2619, 2576-2620, 2576-2621, 2576-2622, 2576-2623, 2576-2624, 2576-2625, 2576-2626, 2576-2627, 2576-2628, 2576-2629, 2576-2630, 2576-2631, 2577-2594, 2577-2595, 2577-2596, 2577-2597, 2577-2598, 2577-2599, 2577-2600, 2577-2601, 2577-2602, 2577-2603, 2577-2604, 2577-2605, 2577-2606, 2577-2607, 2577-2608, 2577-2609, 2577-2610, 2577-2611, 2577-2612, 2577-2613, 2577-2614, 2577-2615, 2577-2616, 2577-2617, 2577-2618, 2577-2619, 2577-2620, 2577-2621, 2577-2622, 2577-2623, 2577-2624, 2577-2625, 2577-2626, 2577-2627, 2577-2628, 2577-2629, 2577-2630, 2577-2631, 2578-2597, 2578-2598, 2578-2599, 2578-2600, 2578-2601, 2578-2602, 2578-2603, 2578-2604, 2578-2605, 2578-2606, 2578-2607, 2578-2608, 2578-2609, 2578-2610, 2578-2611, 2578-2612, 2578-2613, 2578-2614, 2578-2615, 2578-2616, 2578-2617, 2578-2618, 2578-2619, 2578-2620, 2578-2621, 2578-2622, 2578-2623, 2578-2624, 2578-2625, 2578-2626, 2578-2627, 2578-

2628, 2578-2629, 2578-2630, 2578-2631, 2579-2598, 2579-2599, 2579-2600, 2579-2601, 2579-2602, 2579-2603, 2579-2604, 2579-2605, 2579-2606, 2579-2607, 2579-2608, 2579-2609, 2579-2610, 2579-2611, 2579-2612, 2579-2613, 2579-2614, 2579-2615, 2579-2616, 2579-2617, 2579-2618, 2579-2619, 2579-2620, 2579-2621, 2579-2622, 2579-2623, 2579-2624, 2579-2625, 2579-2626, 2579-2627, 2579-2628, 2579-2629, 2579-2630, 2579-2631, 2580-2598, 2580-2599, 2580-2600, 2580-2601, 2580-2602, 2580-2603, 2580-2604, 2580-2605, 2580-2606, 2580-2607, 2580-2608, 2580-2609, 2580-2610, 2580-2611, 2580-2612, 2580-2613, 2580-2614, 2580-2615, 2580-2616, 2580-2617, 2580-2618, 2580-2619, 2580-2620, 2580-2621, 2580-2622, 2580-2623, 2580-2624, 2580-2625, 2580-2626, 2580-2627, 2580-2628, 2580-2629, 2580-2630, 2580-2631, 2581-2597, 2581-2598, 2581-2599, 2581-2600, 2581-2601, 2581-2602, 2581-2603, 2581-2604, 2581-2605, 2581-2606, 2581-2607, 2581-2608, 2581-2609, 2581-2610, 2581-2611, 2581-2612, 2581-2613, 2581-2614, 2581-2615, 2581-2616, 2581-2617, 2581-2618, 2581-2619, 2581-2620, 2581-2621, 2581-2622, 2581-2623, 2581-2624, 2581-2625, 2581-2626, 2581-2627, 2581-2628, 2581-2629, 2581-2630, 2581-2631, 2582-2600, 2582-2601, 2582-2602, 2582-2603, 2582-2604, 2582-2605, 2582-2606, 2582-2607, 2582-2608, 2582-2609, 2582-2610, 2582-2611, 2582-2612, 2582-2613, 2582-2614, 2582-2615, 2582-2616, 2582-2617, 2582-2618, 2582-2619, 2582-2620, 2582-2621, 2582-2622, 2582-2623, 2582-2624, 2582-2625, 2582-2626, 2582-2627, 2582-2628, 2582-2629, 2582-2630, 2582-2631, 2583-2601, 2583-2602, 2583-2603, 2583-2604, 2583-2605, 2583-2606, 2583-2607, 2583-2608, 2583-2609, 2583-2610, 2583-2611, 2583-2612, 2583-2613, 2583-2614, 2583-2615, 2583-2616, 2583-2617, 2583-2618, 2583-2619, 2583-2620, 2583-2621, 2583-2622, 2583-2623, 2583-2624, 2583-2625, 2583-2626, 2583-2627, 2583-2628, 2583-2629, 2583-2630, 2583-2631, 2585-2603, 2585-2604, 2585-2605, 2585-2606, 2585-2607, 2585-2608, 2585-2609, 2585-2610, 2585-2611, 2585-2612, 2585-2613, 2585-2614, 2585-2615, 2585-2616, 2585-2617, 2585-2618, 2585-2619, 2585-2620, 2585-2621, 2585-2622, 2585-2623, 2585-2624, 2585-2625, 2585-2626, 2585-2627, 2585-2628, 2585-2629, 2585-2630, 2585-2631, 2586-2604, 2586-2605, 2586-2606, 2586-2607, 2586-2608, 2586-2609, 2586-2610, 2586-2611, 2586-2612, 2586-2613, 2586-2614, 2586-2615, 2586-2616, 2586-2617, 2586-2618, 2586-2619, 2586-2620, 2586-2621, 2586-2622, 2586-2623, 2586-2624, 2586-2625, 2586-2626, 2586-2627, 2586-2628, 2586-2629, 2586-2630, 2586-2631, 2587-2605, 2587-2606, 2587-2607, 2587-2608, 2587-2609, 2587-2610, 2587-2611, 2587-2612, 2587-2613, 2587-2614, 2587-2615, 2587-2616, 2587-2617, 2587-2618, 2587-2619, 2587-2620, 2587-2621, 2587-2622, 2587-2623, 2587-2624, 2587-2625, 2587-2626, 2587-2627, 2587-2628, 2587-2629, 2587-2630, 2587-2631, 2588-2606, 2588-2607, 2588-2608, 2588-2609, 2588-2610, 2588-2611, 2588-2612, 2588-2613, 2588-2614, 2588-2615, 2588-2616, 2588-2617, 2588-2618, 2588-2619, 2588-2620, 2588-2621, 2588-2622, 2588-2623, 2588-2624, 2588-2625, 2588-2626, 2588-2627, 2588-2628, 2588-2629, 2588-2630, 2588-2631, 2589-2607, 2589-2608, 2589-2609, 2589-2610, 2589-2611, 2589-2612, 2589-2613, 2589-2614, 2589-2615, 2589-2616, 2589-2617, 2589-2618, 2589-2619, 2589-2620, 2589-2621, 2589-2622, 2589-2623, 2589-2624, 2589-2625, 2589-2626, 2589-2627, 2589-2628, 2589-2629, 2589-2630, 2589-2631, 2590-2606, 2590-2607, 2590-2608, 2590-2609, 2590-2610, 2590-2611, 2590-2612, 2590-2613, 2590-2614, 2590-2615, 2590-2616, 2590-2617, 2590-2618, 2590-2619, 2590-2620, 2590-2621, 2590-2622, 2590-2623, 2590-2624, 2590-2625, 2590-2626, 2590-2627, 2590-2628, 2590-2629, 2590-2630, 2590-2631, 2591-2610, 2591-2611, 2591-2612, 2591-2613, 2591-2614, 2591-2615, 2591-2616, 2591-2617, 2591-2618, 2591-2619, 2591-2620, 2591-2621, 2591-2622, 2591-2623, 2591-2624, 2591-2625, 2591-2626, 2591-2627, 2591-2628, 2591-2629, 2591-2630, 2591-2631, 2592-2611, 2592-2612, 2592-2613, 2592-2614, 2592-2615, 2592-2616, 2592-2617, 2592-2618, 2592-2619, 2592-2620, 2592-2621, 2592-2622, 2592-2623, 2592-2624, 2592-2625, 2592-2626, 2592-2627, 2592-2628, 2592-2629, 2592-2630, 2592-2631, 2593-2608, 2593-2612, 2593-2613, 2593-2614, 2593-2615, 2593-2616, 2593-2617, 2593-2618, 2593-2619, 2593-2620, 2593-2621, 2593-2622, 2593-2623, 2593-2624, 2593-2625, 2593-2626, 2593-2627, 2593-2628, 2593-2629, 2593-2630, 2593-2631, 2594-2612, 2594-2613, 2594-2614, 2594-2615, 2594-2616, 2594-2617, 2594-2618, 2594-2619, 2594-2620, 2594-2621, 2594-2622, 2594-2623, 2594-2624, 2594-2625, 2594-2626, 2594-2627, 2594-2628, 2594-2629, 2594-2630, 2594-2631, 2595-2611, 2595-2612, 2595-2613, 2595-2614, 2595-2615, 2595-2616, 2595-2617, 2595-2618, 2595-2619, 2595-2620, 2595-2621, 2595-2622, 2595-2623, 2595-2624, 2595-2625, 2595-2626, 2595-2627, 2595-2628, 2595-2629, 2595-2630, 2595-2631, 2596-2614, 2596-2615, 2596-2616, 2596-2617, 2596-2618, 2596-2619, 2596-2620, 2596-2621, 2596-2622, 2596-2623, 2596-2624, 2596-2625, 2596-2626, 2596-2627, 2596-2628, 2596-2629, 2596-2630, 2596-2631, 2597-2612, 2597-2613, 2597-2614, 2597-2615, 2597-2616, 2597-2617, 2597-2618, 2597-2619, 2597-2620, 2597-2621, 2597-2622, 2597-2623, 2597-2624, 2597-2625, 2597-2626, 2597-2627, 2597-2628, 2597-2629, 2597-2630, 2597-2631, 2598-2613, 2598-2614, 2598-2615, 2598-2616, 2598-2617, 2598-2618, 2598-2619, 2598-2620, 2598-2621, 2598-2622, 2598-2623, 2598-2624, 2598-2625, 2598-2626, 2598-2627, 2598-2628, 2598-2629, 2598-2630, 2598-2631, 2599-2614, 2599-2615, 2599-2616, 2599-2617, 2599-2618, 2599-2619, 2599-2620, 2599-2621, 2599-2622, 2599-2623, 2599-2624, 2599-2625, 2599-2626, 2599-2627, 2599-2628, 2599-2629, 2599-2630, 2599-2631, 2600-2615, 2600-2616, 2600-2617, 2600-2618, 2600-2619, 2600-2620, 2600-2621, 2600-2622, 2600-2623, 2600-2624, 2600-2625, 2600-2626, 2600-2627, 2600-2628, 2600-2629, 2600-2630, 2600-2631, 2601-2616, 2601-2617, 2601-2618, 2601-2619, 2601-2620, 2601-2621, 2601-2622, 2601-2623, 2601-2624, 2601-2625, 2601-2626, 2601-2627, 2601-2628, 2601-2629, 2601-2630, 2601-2631, 2602-2618, 2602-2619, 2602-2620, 2602-2621, 2602-2622, 2602-2623, 2602-2624, 2602-2625, 2602-2626, 2602-2627, 2602-2628, 2602-2629, 2602-2630, 2602-2631, 2603-2620, 2603-2621, 2603-2622, 2603-2623, 2603-2624, 2603-2625, 2603-2626, 2603-2627, 2603-2628, 2603-2629, 2603-2630, 2603-2631, 2604-2619, 2604-2620, 2604-2621, 2604-2622, 2604-2623, 2604-2624, 2604-2625, 2604-2626, 2604-2627, 2604-2628, 2604-2629, 2604-2630, 2604-2631, 2605-2620, 2605-2621, 2605-2622, 2605-2623, 2605-2624, 2605-2625, 2605-2626, 2605-2627, 2605-2628, 2605-2629, 2605-2630, 2605-2631, 2606-2621, 2606-2622, 2606-2623, 2606-2624, 2606-2625, 2606-2626, 2606-2627, 2606-2628, 2606-2629, 2606-2630, 2606-2631, 2607-2622, 2607-2623, 2607-2624, 2607-2625, 2607-2626, 2607-2627, 2607-2628, 2607-2629, 2607-2630, 2607-2631, 2608-2623, 2608-2624, 2608-2625, 2608-2626, 2608-2627, 2608-2628, 2608-2629, 2608-2630, 2608-2631, 2609-2624, 2609-2625, 2609-2626, 2609-2627, 2609-2628, 2609-2629, 2609-2630, 2609-2631, 2610-2625, 2610-2626, 2610-2627, 2610-2628, 2610-2629, 2610-2630, 2610-2631, 2611-

2626, 2611-2627, 2611-2628, 2611-2629, 2611-2630, 2611-2631, 2612-2627, 2612-2628, 2612-2629, 2612-2630, 2612-2631, 2613-2628, 2613-2629, 2613-2630, 2613-2631, 2614-2629, 2614-2630, 2614-2631, 2615-2630, 2615-2631, or 2616-2631. In certain embodiments, antisense compounds or oligonucleotides target at least an 8, 9, 10, 11, 12, 13, 14, 15, or 16 contiguous nucleobases within the aforementioned nucleobase regions.

[0122] In certain embodiments, the following nucleotide regions of SEQ ID NO: 1, when targeted by antisense compounds or oligonucleotides, display at least 50% inhibition: 30-49, 48-63, 150-169, 151-170, 152-171, 154-169, 154-173, 156-171, 156-175, 157-176, 158-173, 158-177, 480-499, 600-619, 638-657, 644-663, 738-757, 1089-1108, 1135-1154, 1141-1160, 1147-1166, 1150-1169, 1153-1172, 1159-1178, 1162-1181, 1165-1184, 1171-1186, 1171-1190, 1173-1188, 1173-1192, 1175-1190, 1175-1194, 1177-1196, 1183-1202, 1208-1227, 1235-1254, 1298-1317, 1304-1323, 1310-1329, 1316-1335, 1319-1338, 1322-1341, 1328-1347, 1349-1368, 1355-1374, 1393-1412, 1396-1415, 1399-1418, 1405-1424, 1421-1440, 1621-1640, 1646-1665, 1646-1665, 1647-1666, 1689-1708, 1749-1768, 1763-1782, 1912-1931, 2073-2092, 2085-2104, 2166-2185, 2172-2191, 2189-2208, 2191-2210, 2193-2212, 2195-2210, 2195-2214, 2196-2215, 2197-2212, 2197-2216, 2202-2221, 2223-2238, 2223-2242, 2225-2240, 2226-2245, 2227-2242, 2227-2246, 2238-2257, 2241-2260, 2267-2286, 2361-2380, 2388-2407, 2397-2416, 2448-2467, 2453-2472, 2455-2474, 2457-2472, 2457-2476, 2459-2474, 2459-2478, 2461-2476, 2461-2480, 2532-2551, 2550-2569, 2551-2566, 2551-2570, 2552-2568, 2552-2570, 2552-2571, 2553-2568, 2553-2570, 2553-2571, 2553-2572, 2554-2571, 2554-2572, 2554-2573, 2555-2570, 2555-2572, 2555-2574, 2556-2573, 2556-2574, 2556-2575, 2557-2573, 2557-2574, 2557-2575, 2557-2576, 2558-2575, 2558-2576, 2558-2577, 2559-2576, 2559-2577, 2559-2578, 2560-2577, 2560-2578, 2560-2579, 2561-2576, 2561-2578, 2561-2579, 2561-2580, 2562-2577, 2562-2579, 2562-2581, 2563-2578, 2563-2580, 2563-2582, 2564-2581, 2564-2583, 2565-2584, 2566-2583, 2566-2585, 2567-2582, 2567-2584, 2567-2586, 2568-2583, 2568-2585, 2568-2587, 2569-2586, 2569-2588, 2570-2585, 2570-2587, 2570-2589, 2571-2586, 2571-2588, 2571-2590, 2572-2589, 2572-2590, 2572-2591, 2573-2590, 2573-2592, 2574-2590, 2574-2591, 2574-2593, 2575-2590, 2575-2591, 2575-2592, 2575-2594, 2576-2593, 2576-2595, 2577-2594, 2577-2595, 2577-2596, 2578-2594, 2578-2596, 2578-2597, 2579-2598, 2580-2596, 2580-2597, 2580-2598, 2580-2599, 2581-2597, 2581-2598, 2581-2599, 2581-2600, 2582-2598, 2582-2599, 2582-2600, 2582-2601, 2583-2599, 2583-2600, 2583-2601, 2583-2602, 2584-2600, 2584-2601, 2584-2602, 2584-2603, 2585-2601, 2585-2603, 2585-2604, 2586-2601, 2586-2602, 2586-2604, 2586-2605, 2587-2602, 2587-2603, 2587-2605, 2587-2606, 2588-2603, 2588-2604, 2588-2605, 2588-2606, 2588-2607, 2589-2604, 2589-2605, 2589-2606, 2589-2607, 2589-2608, 2590-2605, 2590-2606, 2590-2607, 2590-2608, 2590-2609, 2590-2609, 2591-2607, 2591-2608, 2591-2609, 2591-2610, 2592-2607, 2592-2608, 2592-2609, 2592-2610, 2592-2611, 2593-2608, 2593-2609, 2593-2610, 2593-2612, 2594-2609, 2594-2610, 2594-2611, 2594-2612, 2594-2613, 2595-2610, 2595-2611, 2595-2612, 2595-2613, 2595-2614, 2596-2611, 2596-2612, 2596-2613, 2596-2614, 2596-2615, 2597-2612, 2597-2612, 2597-2613, 2597-2614, 2597-2615, 2597-2616, 2598-2613, 2598-2614, 2598-2615, 2598-2616, 2598-2617, 2599-2614, 2599-2615, 2599-2616, 2599-2617, 2599-2618, 2600-2615, 2600-2616, 2600-2617, 2600-2618, 2600-2619, 2601-2616, 2601-2617, 2601-2618, 2601-2619, 2601-2620, 2602-2617, 2602-2618, 2602-2619, 2602-2620, 2602-2621, 2603-2618, 2603-2619, 2603-2620, 2603-2621, 2603-2622, 2604-2619, 2604-2620, 2604-2621, 2604-2622, 2604-2623, 2605-2620, 2605-2621, 2605-2622, 2605-2623, 2605-2624, 2606-2621, 2606-2622, 2606-2623, 2606-2624, 2606-2625, 2607-2622, 2607-2623, 2607-2624, 2607-2625, 2607-2626, 2608-2623, 2608-2624, 2608-2625, 2608-2626, 2608-2627, 2609-2624, 2609-2625, 2609-2626, 2609-2627, 2609-2628, 2610-2625, 2610-2626, 2610-2627, 2610-2628, 2610-2629, 2611-2626, 2611-2627, 2611-2628, 2611-2629, 2611-2630, 2612-2627, 2612-2628, 2612-2629, 2612-2630, 2612-2631, 2613-2628, 2613-2629, 2613-2630, 2613-2631, 2614-2629, 2614-2630, 2614-2631, 2615-2630, 2615-2631, and 2616-2631.

[0123] In certain embodiments, the following nucleotide regions of SEQ ID NO: 2, when targeted by antisense compounds or oligonucleotides, display at least 50% inhibition: 1608-1627, 1685-1704, 1686-1705, 1751-1770, 1769-1784, 1871-1890, 1872-1891, 1873-1892, 1875-1890, 1875-1894, 1877-1892, 1877-1896, 1878-1897, 1879-1894, 1879-1898, 2288-2307, 2808-2827, 2846-2865, 2852-2871, 2946-2965, 3773-3792, 3819-3838, 3825-3844, 3831-3850, 3834-3853, 3837-3856, 3843-3862, 4151-4166, 4151-4170, 4153-4172, 4159-4178, 4184-4203, 4211-4230, 4609-4628, 4612-4631, 4615-4634, 4621-4640, 4642-4661, 4648-4667, 4686-4705, 4689-4708, 4692-4711, 4698-4717, 4714-4733, 5270-5289, 5295-5314, 5296-5315, 5830-5849, 5890-5909, 5904-5923, 6406-6425, 6662-6681, 6674-6693, 6954-6973, 6960-6979, 6977-6996, 6979-6998, 6981-7000, 6983-6998, 6983-7002, 6984-7003, 6985-7000, 6985-7004, 6990-7009, 7122-7141, 7125-7144, 7151-7170, 7353-7372, 7362-7381, 7683-7702, 7688-7707, 7690-7709, 7692-7707, 7692-7711, 7694-7709, 7694-7713, 7696-7711, 7696-7715, 7767-7786, 7785-7804, 7786-7801, 7787-7803, 7787-7805, 7787-7806, 7788-7803, 7788-7805, 7788-7806, 7788-7807, 7789-7806, 7789-7807, 7789-7808, 7790-7805, 7790-7807, 7790-7809, 7791-7808, 7791-7809, 7791-7810, 7792-7808, 7792-7809, 7792-7810, 7792-7811, 7793-7810, 7793-7811, 7793-7812, 7794-7811, 7794-7812, 7794-7813, 7795-7812, 7795-7813, 7795-7814, 7796-7811, 7796-7813, 7796-7814, 7796-7815, 7797-7812, 7797-7814, 7797-7816, 7798-7813, 7798-7815, 7798-7817, 7799-7816, 7799-7818, 7800-7819, 7801-7818, 7801-7820, 7802-7817, 7802-7819, 7802-7821, 7803-7818, 7803-7820, 7803-7822, 7804-7821, 7804-7823, 7805-7820, 7805-7822, 7805-7824, 7806-7821, 7806-7823, 7806-7825, 7807-7824, 7807-7825, 7807-7826, 7808-7825, 7808-7827, 7809-7825, 7809-7826, 7809-7828, 7810-7825, 7810-7826, 7810-7827, 7810-7829, 7811-7828, 7811-7830, 7812-7829, 7812-7830, 7812-7831, 7813-7829, 7813-7831, 7813-7832, 7814-7833, 7815-7831, 7815-7832, 7815-7833, 7815-7834, 7816-7832, 7816-7833, 7816-7834, 7816-7835, 7817-7833, 7817-7834, 7817-7835, 7817-7836, 7818-7834, 7818-7835, 7818-7836, 7818-7837, 7819-7835, 7819-7836, 7819-7837, 7819-7838, 7820-7836, 7820-7838, 7820-7839, 7821-7836, 7821-7837, 7821-7839, 7821-7840, 7822-7837, 7822-7838, 7822-7840, 7822-7841, 7823-7838, 7823-7839, 7823-7839, 7823-7840, 7823-7841, 7823-7842, 7824-7839, 7824-7840, 7824-7840, 7824-7841, 7824-7842, 7824-7843, 7825-7840, 7825-7841, 7825-7842, 7825-7843, 7825-7844, 7826-7842, 7826-7843, 7826-7844, 7826-7845, 7827-7842, 7827-7843, 7827-7844, 7827-7845, 7827-7846, 7828-7843, 7828-7844, 7828-7845, 7828-7847, 7829-7844, 7829-7845, 7829-7846, 7829-7847, 7829-7848, 7830-7845, 7830-7846, 7830-7847, 7830-7848,

7830-7849, 7831-7846, 7831-7847, 7831-7848, 7831-7849, 7831-7850, 7832-7847, 7832-7848, 7832-7849, 7832-7850, 7832-7851, 7833-7848, 7833-7849, 7833-7850, 7833-7851, 7833-7852, 7834-7849, 7834-7850, 7834-7851, 7834-7852, 7834-7853, 7835-7850, 7835-7851, 7835-7852, 7835-7853, 7835-7854, 7836-7851, 7836-7852, 7836-7853, 7836-7854, 7836-7855, 7837-7852, 7837-7853, 7837-7854, 7837-7855, 7837-7856, 7838-7853, 7838-7854, 7838-7855, 7838-7856, 7838-7857, 7839-7854, 7839-7855, 7839-7856, 7839-7857, 7839-7858, 7840-7855, 7840-7856, 7840-7857, 7840-7858, 7840-7859, 7841-7856, 7841-7857, 7841-7858, 7841-7859, 7841-7860, 7842-7857, 7842-7858, 7842-7859, 7842-7860, 7842-7861, 7843-7858, 7843-7859, 7843-7860, 7843-7861, 7843-7862, 7844-7859, 7844-7860, 7844-7861, 7844-7862, 7845-7860, 7845-7861, 7845-7862, 7846-7861, and 7846-7862.

[0124] In certain embodiments, the following nucleotide regions of SEQ ID NO: 1, when targeted by antisense compounds or oligonucleotides, display at least 60% inhibition: 48-63, 150-169, 152-171, 154-169, 154-173, 156-171, 156-175, 158-173, 158-177, 600-619, 1135-1154, 1141-1160, 1147-1166, 1153-1172, 1171-1186, 1173-1188, 1175-1190, 1749-1768, 1763-1782, 1763-1782, 1912-1931, 2189-2208, 2191-2210, 2193-2212, 2195-2210, 2195-2214, 2197-2212, 2197-2216, 2223-2238, 2225-2240, 2227-2242, 2238-2257, 2448-2467, 2453-2472, 2455-2474, 2457-2472, 2457-2476, 2459-2474, 2459-2478, 2461-2476, 2461-2480, 2550-2569, 2551-2566, 2552-2571, 2553-2568, 2553-2570, 2553-2571, 2553-2572, 2554-2571, 2554-2572, 2554-2573, 2555-2572, 2555-2574, 2556-2573, 2556-2574, 2556-2575, 2557-2574, 2557-2575, 2557-2576, 2558-2575, 2558-2576, 2558-2577, 2559-2576, 2559-2577, 2559-2578, 2560-2577, 2560-2578, 2560-2579, 2561-2578, 2561-2579, 2561-2580, 2562-2577, 2562-2579, 2562-2581, 2563-2578, 2563-2580, 2563-2582, 2564-2581, 2564-2583, 2565-2584, 2566-2583, 2566-2585, 2567-2582, 2567-2584, 2567-2586, 2568-2583, 2568-2585, 2568-2587, 2569-2586, 2569-2588, 2570-2587, 2570-2589, 2571-2588, 2572-2590, 2572-2591, 2573-2590, 2573-2592, 2574-2591, 2574-2593, 2575-2590, 2575-2592, 2575-2594, 2576-2593, 2576-2595, 2577-2594, 2577-2595, 2577-2596, 2578-2594, 2578-2597, 2579-2598, 2580-2596, 2580-2597, 2580-2598, 2580-2599, 2581-2597, 2581-2598, 2581-2599, 2581-2600, 2582-2598, 2582-2599, 2582-2600, 2582-2601, 2583-2599, 2583-2600, 2583-2601, 2583-2602, 2584-2600, 2584-2602, 2584-2603, 2585-2601, 2585-2603, 2585-2604, 2586-2602, 2586-2604, 2586-2605, 2587-2603, 2587-2605, 2587-2606, 2588-2603, 2588-2604, 2588-2606, 2588-2607, 2589-2605, 2589-2606, 2589-2607, 2589-2608, 2590-2605, 2590-2606, 2590-2607, 2590-2608, 2590-2609, 2591-2607, 2591-2609, 2591-2610, 2592-2608, 2592-2609, 2592-2611, 2593-2608, 2593-2609, 2593-2612, 2594-2609, 2594-2610, 2594-2611, 2594-2612, 2594-2613, 2595-2610, 2595-2611, 2595-2612, 2595-2613, 2595-2614, 2596-2611, 2596-2612, 2596-2613, 2596-2614, 2596-2615, 2597-2612, 2597-2613, 2597-2614, 2597-2615, 2597-2616, 2598-2613, 2598-2614, 2598-2615, 2598-2616, 2598-2617, 2599-2614, 2599-2615, 2599-2616, 2599-2617, 2599-2618, 2600-2615, 2600-2616, 2600-2617, 2600-2618, 2600-2619, 2601-2616, 2601-2617, 2601-2618, 2601-2619, 2601-2620, 2602-2617, 2602-2618, 2602-2619, 2602-2620, 2602-2621, 2603-2618, 2603-2619, 2603-2620, 2603-2621, 2603-2622, 2604-2619, 2604-2620, 2604-2621, 2604-2622, 2604-2623, 2605-2620, 2605-2621, 2605-2622, 2605-2623, 2605-2624, 2606-2621, 2606-2622, 2606-2623, 2606-2624, 2606-2625, 2607-2622, 2607-2623, 2607-2624, 2607-2625, 2607-2626, 2608-2623, 2608-2624, 2608-2625, 2608-2625, 2608-2626, 2608-2627, 2609-2624, 2609-2625, 2609-2626, 2609-2627, 2609-2628, 2610-2625, 2610-2626, 2610-2627, 2610-2628, 2610-2629, 2611-2626, 2611-2626, 2611-2627, 2611-2628, 2611-2629, 2611-2630, 2612-2627, 2612-2628, 2612-2629, 2612-2630, 2612-2631, 2613-2628, 2613-2629, 2613-2630, 2613-2631, 2614-2629, 2614-2630, 2614-2631, 2615-2630, 2615-2630, 2615-2631, 2615-2631, and 2616-2631.

[0125] In certain embodiments, the following nucleotide regions of SEQ ID NO: 2, when targeted by antisense compounds or oligonucleotides, display at least 60% inhibition: 1685-1704, 1686-1705, 1769-1784, 1871-1890, 1873-1892, 1875-1890, 1875-1894, 1877-1892, 1877-1896, 1879-1894, 1879-1898, 2808-2827, 3819-3838, 3825-3844, 3831-3850, 3837-3856, 4151-4166, 5890-5909, 5904-5923, 5904-5923, 6406-6425, 6977-6996, 6979-6998, 6981-7000, 6983-6998, 6983-7002, 6985-7000, 6985-7004, 7122-7141, 7683-7702, 7688-7707, 7690-7709, 7692-7707, 7692-7711, 7694-7709, 7696-7711, 7696-7715, 7786-7801, 7787-7806, 7788-7803, 7788-7805, 7788-7806, 7788-7807, 7789-7806, 7789-7807, 7789-7808, 7790-7807, 7790-7809, 7791-7808, 7791-7809, 7791-7810, 7792-7809, 7792-7810, 7792-7811, 7793-7810, 7793-7811, 7793-7812, 7794-7811, 7794-7812, 7794-7813, 7795-7812, 7795-7813, 7795-7814, 7796-7813, 7796-7814, 7796-7815, 7797-7812, 7797-7814, 7797-7816, 7798-7813, 7798-7815, 7798-7817, 7799-7816, 7799-7818, 7800-7819, 7801-7818, 7801-7820, 7802-7817, 7802-7819, 7802-7821, 7803-7818, 7803-7820, 7803-7822, 7804-7821, 7804-7823, 7805-7822, 7805-7824, 7806-7823, 7806-7825, 7807-7824, 7807-7825, 7807-7826, 7808-7825, 7808-7827, 7809-7826, 7809-7828, 7810-7825, 7810-7827, 7810-7829, 7811-7828, 7811-7830, 7812-7829, 7812-7830, 7812-7831, 7813-7829, 7813-7832, 7814-7833, 7815-7831, 7815-7832, 7815-7833, 7815-7834, 7816-7832, 7816-7833, 7816-7834, 7816-7835, 7817-7833, 7817-7834, 7817-7835, 7817-7836, 7818-7834, 7818-7835, 7818-7836, 7818-7837, 7819-7835, 7819-7837, 7819-7838, 7820-7836, 7820-7838, 7820-7839, 7821-7837, 7821-7839, 7821-7840, 7822-7838, 7822-7840, 7822-7841, 7823-7838, 7823-7839, 7823-7841, 7823-7842, 7824-7840, 7824-7841, 7824-7842, 7824-7843, 7825-7840, 7825-7841, 7825-7842, 7825-7843, 7825-7844, 7826-7842, 7826-7844, 7826-7845, 7827-7843, 7827-7844, 7827-7846, 7828-7843, 7828-7844, 7828-7847, 7829-7844, 7829-7845, 7829-7846, 7829-7847, 7829-7848, 7830-7845, 7830-7846, 7830-7847, 7830-7848, 7830-7849, 7831-7846, 7831-7847, 7831-7848, 7831-7849, 7831-7850, 7832-7847, 7832-7848, 7832-7849, 7832-7850, 7832-7851, 7833-7848, 7833-7849, 7833-7850, 7833-7851, 7833-7852, 7834-7849, 7834-7850, 7834-7851, 7834-7852, 7834-7853, 7835-7850, 7835-7851, 7835-7852, 7835-7853, 7835-7854, 7836-7851, 7836-7852, 7836-7853, 7836-7854, 7836-7855, 7837-7852, 7837-7853, 7837-7854, 7837-7855, 7837-7856, 7838-7853, 7838-7854, 7838-7855, 7838-7856, 7838-7857, 7839-7854, 7839-7855, 7839-7856, 7839-7857, 7839-7858, 7840-7855, 7840-7856, 7840-7857, 7840-7858, 7840-7859, 7841-7856, 7841-7857, 7841-7858, 7841-7859, 7841-7860, 7842-7857, 7842-7858, 7842-7859, 7842-7860, 7842-7861, 7843-7858, 7843-7859, 7843-7860, 7843-7861, 7843-7862, 7844-7859, 7844-7860, 7844-7861, 7844-7862, 7845-7860, 7845-7861, 7845-7862, 7846-7861, 7846-7862, and 7847-7862.

[0126] In certain embodiments, the following nucleotide regions of SEQ ID NO: 1, when targeted by antisense compounds or oligonucleotides, display at least 70% inhibition:

48-63, 150-169, 152-171, 154-169, 154-173, 156-171, 156-175, 158-173, 158-177, 1135-1154, 1141-1160, 1147-1166, 1171-1186, 1173-1188, 1175-1190, 1749-1768, 1763-1782, 1912-1931, 2193-2212, 2195-2210, 2195-2214, 2197-2212, 2197-2216, 2223-2238, 2225-2240, 2227-2242, 2453-2472, 2455-2474, 2457-2472, 2457-2476, 2459-2474, 2461-2476, 2461-2480, 2550-2569, 2551-2566, 2552-2571, 2553-2570, 2553-2571, 2553-2572, 2554-2571, 2554-2572, 2554-2573, 2554-2573, 2555-2572, 2555-2574, 2555-2574, 2556-2573, 2556-2574, 2556-2575, 2557-2574, 2557-2576, 2558-2575, 2558-2576, 2558-2577, 2559-2576, 2559-2577, 2559-2578, 2560-2577, 2560-2578, 2560-2579, 2561-2578, 2561-2579, 2561-2580, 2562-2577, 2562-2579, 2562-2581, 2563-2578, 2563-2580, 2563-2582, 2564-2581, 2564-2583, 2565-2584, 2566-2583, 2566-2585, 2567-2582, 2567-2584, 2567-2586, 2568-2585, 2568-2587, 2569-2586, 2569-2588, 2570-2587, 2570-2589, 2571-2588, 2571-2590, 2572-2589, 2572-2591, 2573-2590, 2573-2592, 2574-2591, 2574-2593, 2575-2592, 2575-2594, 2576-2593, 2576-2595, 2577-2594, 2577-2596, 2578-2597, 2579-2598, 2580-2596, 2580-2598, 2580-2599, 2581-2597, 2581-2600, 2582-2598, 2582-2600, 2582-2601, 2583-2599, 2583-2601, 2583-2602, 2584-2600, 2584-2602, 2584-2603, 2585-2601, 2585-2603, 2585-2604, 2586-2605, 2587-2606, 2588-2604, 2588-2606, 2588-2607, 2589-2605, 2589-2606, 2589-2607, 2589-2608, 2590-2605, 2590-2606, 2590-2607, 2590-2609, 2591-2607, 2591-2610, 2592-2611, 2593-2608, 2593-2612, 2594-2609, 2594-2610, 2594-2612, 2594-2613, 2595-2610, 2595-2611, 2595-2612, 2595-2613, 2595-2614, 2596-2611, 2596-2614, 2596-2615, 2597-2612, 2597-2613, 2597-2614, 2597-2615, 2597-2616, 2598-2613, 2598-2614, 2598-2615, 2598-2616, 2598-2617, 2599-2614, 2599-2615, 2599-2616, 2599-2617, 2599-2618, 2600-2615, 2600-2616, 2600-2617, 2600-2618, 2600-2619, 2601-2616, 2601-2617, 2601-2618, 2601-2619, 2601-2620, 2602-2617, 2602-2618, 2602-2619, 2602-2620, 2602-2621, 2603-2619, 2603-2620, 2603-2621, 2603-2622, 2604-2619, 2604-2620, 2604-2621, 2604-2622, 2604-2623, 2605-2620, 2605-2621, 2605-2622, 2605-2623, 2605-2624, 2606-2621, 2606-2622, 2606-2623, 2606-2624, 2606-2625, 2607-2622, 2607-2623, 2607-2624, 2607-2625, 2607-2626, 2608-2623, 2608-2624, 2608-2625, 2608-2626, 2608-2627, 2609-2624, 2609-2625, 2609-2626, 2609-2627, 2609-2628, 2610-2625, 2610-2626, 2610-2627, 2610-2628, 2610-2629, 2611-2626, 2611-2627, 2611-2629, 2611-2630, 2612-2627, 2612-2628, 2612-2629, 2612-2630, 2612-2631, 2613-2628, 2613-2629, 2613-2630, 2613-2631, 2614-2629, 2614-2630, 2614-2631, 2615-2630, 2615-2630, 2615-2631, and 2616-2631.

[0127] In certain embodiments, the following nucleotide regions of SEQ ID NO: 2, when targeted by antisense compounds or oligonucleotides, display at least 70% inhibition: 1685-1704, 1686-1705, 1769-1784, 1871-1890, 1873-1892, 1875-1890, 1875-1894, 1877-1892, 1877-1896, 1879-1894, 1879-1898, 3819-3838, 3825-3844, 3831-3850, 4151-4166, 5890-5909, 5904-5923, 5904-5923, 6406-6425, 6983-6998, 6983-7002, 6985-7000, 6985-7004, 7688-7707, 7690-7709, 7692-7707, 7692-7711, 7694-7709, 7696-7711, 7696-7715, 7786-7801, 7787-7806, 7788-7805, 7788-7806, 7788-7807, 7789-7806, 7789-7807, 7789-7808, 7790-7807, 7790-7809, 7791-7808, 7791-7809, 7791-7810, 7792-7809, 7792-7811, 7793-7810, 7793-7811, 7793-7812, 7794-7811, 7794-7812, 7794-7813, 7795-7812, 7795-7813, 7795-7814, 7796-7813, 7796-7814, 7796-7815, 7797-7812, 7797-7814, 7797-7816, 7798-7813, 7798-7815, 7798-7817, 7799-7816, 7799-7818, 7800-7819, 7801-7818, 7801-7820, 7802-7817, 7802-7819, 7802-7821, 7803-7820, 7803-7822, 7804-7821, 7804-7823, 7805-7822, 7805-7824, 7806-7823, 7806-7825, 7807-7824, 7807-7826, 7808-7825, 7808-7827, 7809-7826, 7809-7828, 7810-7827, 7811-7828, 7811-7830, 7812-7829, 7812-7831, 7813-7832, 7814-7833, 7815-7831, 7815-7833, 7815-7834, 7816-7832, 7816-7835, 7817-7833, 7817-7835, 7817-7836, 7818-7834, 7818-7836, 7818-7837, 7819-7835, 7819-7837, 7819-7838, 7820-7836, 7820-7838, 7820-7839, 7821-7840, 7822-7841, 7823-7839, 7823-7841, 7823-7842, 7824-7840, 7824-7841, 7824-7842, 7824-7843, 7825-7840, 7825-7841, 7825-7842, 7825-7844, 7826-7842, 7826-7845, 7827-7846, 7828-7843, 7828-7847, 7829-7844, 7829-7845, 7829-7847, 7829-7848, 7830-7845, 7830-7846, 7830-7847, 7830-7848, 7830-7849, 7831-7846, 7831-7849, 7831-7850, 7832-7847, 7832-7848, 7832-7849, 7832-7850, 7832-7851, 7833-7848, 7833-7849, 7833-7850, 7833-7851, 7833-7852, 7834-7849, 7834-7850, 7834-7851, 7834-7852, 7834-7853, 7835-7850, 7835-7851, 7835-7852, 7835-7853, 7835-7854, 7836-7851, 7836-7852, 7836-7853, 7836-7854, 7836-7855, 7837-7852, 7837-7853, 7837-7854, 7837-7855, 7837-7856, 7838-7854, 7838-7855, 7838-7856, 7838-7857, 7839-7854, 7839-7855, 7839-7856, 7839-7857, 7839-7858, 7840-7855, 7840-7856, 7840-7857, 7840-7858, 7840-7859, 7841-7856, 7841-7857, 7841-7858, 7841-7859, 7841-7860, 7842-7857, 7842-7858, 7842-7859, 7842-7860, 7842-7861, 7843-7858, 7843-7859, 7843-7860, 7843-7861, 7843-7862, 7844-7859, 7844-7860, 7844-7861, 7844-7862, 7845-7860, 7845-7861, 7845-7862, 7846-7861, 7846-7862, and 7847-7862.

[0128] In certain embodiments, the following nucleotide regions of SEQ ID NO: 1, when targeted by antisense compounds or oligonucleotides, display at least 80% inhibition: 152-171, 154-169, 156-171, 158-173, 1135-1154, 1171-1186, 1173-1188, 1175-1190, 1763-1782, 1912-1931, 2197-2212, 2223-2238, 2225-2240, 2227-2242, 2457-2472, 2459-2474, 2461-2476, 2551-2566, 2553-2570, 2553-2571, 2553-2572, 2554-2573, 2555-2572, 2555-2574, 2556-2573, 2556-2574, 2556-2575, 2557-2574, 2557-2576, 2558-2575, 2558-2576, 2559-2577, 2559-2578, 2560-2577, 2560-2578, 2560-2579, 2561-2578, 2561-2579, 2561-2580, 2562-2577, 2562-2579, 2562-2581, 2563-2580, 2563-2582, 2564-2581, 2564-2583, 2565-2584, 2566-2583, 2567-2584, 2567-2586, 2568-2585, 2568-2587, 2569-2586, 2569-2588, 2570-2587, 2571-2588, 2571-2590, 2572-2589, 2572-2591, 2573-2590, 2573-2592, 2574-2591, 2574-2593, 2575-2592, 2576-2593, 2576-2595, 2577-2594, 2577-2596, 2578-2597, 2580-2598, 2580-2599, 2581-2597, 2581-2600, 2582-2601, 2583-2602, 2584-2603, 2585-2604, 2586-2605, 2587-2606, 2588-2607, 2589-2608, 2590-2606, 2590-2607, 2590-2609, 2591-2610, 2592-2611, 2593-2608, 2593-2612, 2594-2613, 2595-2611, 2595-2614, 2596-2615, 2597-2612, 2597-2613, 2597-2614, 2597-2615, 2597-2616, 2598-2613, 2598-2613, 2598-2614, 2598-2615, 2598-2616, 2598-2617, 2599-2614, 2599-2617, 2599-2618, 2600-2615, 2600-2617, 2600-2618, 2600-2619, 2601-2616, 2601-2617, 2601-2619, 2601-2620, 2602-2618, 2602-2621, 2603-2620, 2603-2621, 2603-2622, 2604-2619, 2604-2620, 2604-2621, 2604-2622, 2604-2623, 2605-2620, 2605-2621, 2605-2622, 2605-2623, 2605-2624, 2606-2621, 2606-2622, 2606-2623, 2606-2624, 2606-2625, 2607-2622, 2607-2623, 2607-2624, 2607-2625, 2607-2626, 2608-2623, 2608-2624, 2608-2625, 2608-2627, 2609-2624, 2609-2626, 2609-2627, 2609-2628, 2610-2625, 2610-2626, 2610-2628, 2610-2629, 2611-2626, 2611-2627, 2611-2629, 2611-2630, 2612-

2627, 2612-2628, 2612-2630, 2612-2631, 2613-2628, 2613-2629, 2613-2631, 2614-2629, 2614-2630, 2614-2631, 2615-2630, and 2616-2631.

[0129] In certain embodiments, the following nucleotide regions of SEQ ID NO: 2, when targeted by antisense compounds or oligonucleotides, display at least 80% inhibition: 1685-1704, 1686-1705, 1873-1892, 1875-1890, 1877-1892, 1879-1894, 3819-3838, 4151-4166, 5904-5923, 6406-6425, 6985-7000, 7692-7707, 7694-7709, 7696-7711, 7786-7801, 7788-7805, 7788-7806, 7788-7807, 7789-7808, 7790-7807, 7790-7809, 7791-7808, 7791-7809, 7791-7810, 7792-7809, 7792-7811, 7793-7810, 7793-7811, 7794-7812, 7794-7813, 7795-7812, 7795-7813, 7795-7814, 7796-7813, 7796-7814, 7796-7815, 7797-7812, 7797-7814, 7797-7816, 7798-7815, 7798-7817, 7799-7816, 7799-7818, 7800-7819, 7801-7818, 7802-7819, 7802-7821, 7803-7820, 7803-7822, 7804-7821, 7804-7823, 7805-7822, 7806-7823, 7806-7825, 7807-7824, 7807-7826, 7808-7825, 7808-7827, 7809-7826, 7809-7828, 7810-7827, 7811-7828, 7812-7829, 7812-7831, 7813-7832, 7814-7833, 7815-7834, 7816-7832, 7816-7835, 7817-7836, 7818-7837, 7819-7838, 7820-7839, 7821-7840, 7822-7841, 7823-7842, 7824-7843, 7825-7841, 7825-7842, 7825-7844, 7826-7845, 7827-7846, 7828-7843, 7828-7847, 7829-7848, 7830-7846, 7830-7849, 7831-7850, 7832-7847, 7832-7848, 7832-7849, 7832-7850, 7832-7851, 7833-7848, 7833-7849, 7833-7850, 7833-7851, 7833-7852, 7834-7849, 7834-7852, 7834-7853, 7835-7850, 7835-7852, 7835-7853, 7835-7854, 7836-7851, 7836-7852, 7836-7854, 7836-7855, 7837-7853, 7837-7856, 7838-7855, 7838-7856, 7838-7857, 7839-7854, 7839-7855, 7839-7856, 7839-7857, 7839-7858, 7840-7855, 7840-7856, 7840-7857, 7840-7858, 7840-7859, 7841-7856, 7841-7857, 7841-7858, 7841-7859, 7841-7860, 7842-7857, 7842-7858, 7842-7859, 7842-7860, 7842-7861, 7843-7858, 7843-7859, 7843-7860, 7843-7862, 7844-7859, 7844-7861, 7844-7862, 7845-7860, 7845-7861, 7846-7862, and 7847-7862.

[0130] In certain embodiments, the following nucleotide regions of SEQ ID NO: 1, when targeted by antisense compounds or oligonucleotides, display at least 90% inhibition: 154-169, 156-171, 158-173, 1135-1154, 1171-1186, 1173-1188, 1763-1782, 1912-1931, 2223-2238, 2227-2242, 2459-2474, 2461-2476, 2554-2573, 2555-2574, 2560-2577, 2561-2578, 2561-2579, 2562-2581, 2563-2580, 2563-2582, 2564-2581, 2566-2583, 2567-2584, 2568-2585, 2568-2587, 2569-2586, 2570-2587, 2576-2593, 2577-2594, 2577-2596, 2578-2597, 2580-2599, 2581-2600, 2582-2601, 2583-2602, 2584-2603, 2586-2605, 2587-2605, 2587-2606, 2588-2607, 2589-2608, 2590-2607, 2590-2609, 2592-2611, 2595-2614, 2596-2615, 2597-2612, 2597-2613, 2597-2615, 2597-2616, 2598-2613, 2598-2613, 2598-2617, 2599-2614, 2599-2618, 2600-2615, 2600-2619, 2601-2617, 2601-2620, 2602-2621, 2603-2622, 2604-2623, 2605-2621, 2605-2622, 2605-2624, 2606-2625, 2607-2626, 2608-2623, 2608-2625, 2609-2628, 2611-2627, 2611-2630, 2612-2628, 2612-2631, 2613-2629, 2614-2629, 2615-2630, and 2616-2631.

[0131] In certain embodiments, the following nucleotide regions of SEQ ID NO: 2, when targeted by antisense compounds or oligonucleotides, display at least 90% inhibition: 1685-1704, 1686-1705, 1875-1890, 1877-1892, 1879-1894, 3819-3838, 5904-5923, 6406-6425, 7694-7709, 7696-7711, 7789-7808, 7790-7809, 7795-7812, 7795-7813, 7796-7813, 7796-7814, 7797-7814, 7797-7816, 7798-7815, 7798-7817, 7799-7816, 7801-7818, 7802-7819, 7803-7820, 7803-7822, 7804-7821, 7805-7822, 7811-7828, 7812-7829, 7812-7831, 7813-7832, 7815-7834, 7818-7837, 7819-7838, 7821-7840, 7822-7840, 7822-7841, 7825-7842, 7832-7847, 7832-7848, 7832-7850, 7833-7848, 7833-7852, 7834-7849, 7834-7853, 7835-7850, 7836-7852, 7836-7855, 7837-7856, 7838-7856, 7839-7857, 7839-7858, 7840-7856, 7840-7857, 7840-7859, 7843-7858, 7843-7860, and 7846-7862.

[0132] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least a 50% inhibition of a CFB mRNA, ISIS NOs: 516350, 532614, 532632, 532635, 532638, 532639, 532686, 532687, 532688, 532689, 532690, 532691, 532692, 532692, 532693, 532694, 532695, 532696, 532697, 532698, 532699, 532700, 532701, 532702, 532703, 532704, 532705, 532706, 532707, 532770, 532775, 532778, 532780, 532791, 532800, 532809, 532810, 532811, 532917, 532952, 588509, 588510, 588511, 588512, 588513, 588514, 588515, 588516, 588517, 588518, 588519, 588520, 588522, 588523, 588524, 588525, 588527, 588528, 588529, 588530, 588531, 588532, 588533, 588534, 588535, 588536, 588537, 588538, 588539, 588540, 588541, 588542, 588543, 588544, 588545, 588546, 588547, 588548, 588549, 588550, 588551, 588552, 588553, 588554, 588555, 588556, 588557, 588558, 588559, 588560, 588561, 588562, 588563, 588564, 588565, 588566, 588567, 588568, 588569, 588570, 588571, 588572, 588573, 588574, 588575, 588576, 588577, 588580, 588581, 588585, 588586, 588589, 588590, 588599, 588603, 588606, 588608, 588610, 588614, 588616, 588628, 588631, 588632, 588634, 588636, 588638, 588640, 588645, 588646, 588654, 588656, 588658, 588660, 588662, 588664, 588670, 588672, 588676, 588682, 588688, 588696, 588698, 588807, 588808, 588809, 588813, 588814, 588815, 588819, 588820, 588822, 588823, 588838, 588839, 588840, 588841, 588842, 588846, 588847, 588848, 588849, 588850, 588851, 588852, 588853, 588854, 588855, 588856, 588857, 588858, 588859, 588860, 588861, 588862, 588863, 588864, 588865, 588866, 588867, 588868, 588870, 588871, 588872, 588873, 588874, 588875, 588876, 588877, 588878, 588879, 588880, 588881, 588882, 588883, 588884, 598999, 599000, 599001, 599002, 599003, 599004, 599005, 599006, 599007, 599008, 599009, 599010, 599011, 599012, 599013, 599014, 599015, 599018, 599019, 599023, 599024, 599025, 599026, 599027, 599028, 599029, 599030, 599031, 599032, 599033, 599034, 599035, 599058, 599062, 599063, 599064, 599065, 599070, 599071, 599072, 599073, 599074, 599076, 599077, 599078, 599079, 599080, 599081, 599082, 599083, 599084, 599085, 599086, 599087, 599088, 599089, 599090, 599091, 599092, 599093, 599094, 599095, 599096, 599097, 599098, 599102, 599119, 599123, 599124, 599125, 599126, 599127, 599128, 599132, 599133, 599134, 599135, 599136, 599137, 599138, 599139, 599140, 599141, 599142, 599143, 599144, 599145, 599147, 599148, 599149, 599150, 599151, 599152, 599153, 599154, 599155, 599156, 599157, 599158, 599159, 599178, 599179, 599180, 599181, 599182, 599186, 599187, 599188, 599189, 599190, 599191, 599192, 599193, 599194, 599195, 599196, 599197, 599198, 599199, 599200, 599201, 599202, 599203, 599204, 599205, 599206, 599207, 599208, 599209, 599210, 599211, 599212, 599213, 599214, 599215, 599216, 599217, 599218, 599219, 599220, 599221, 599221, 599222, 599223, 599224, 599225, 599226, 599227, 599228, 599229, 599230, 599231, 599232, 599233, 599234, 599235, 599236, 599241, 599247, 599248, 599249, 599255, 599256, 599257, 599258, 599260, 599261, 599262, 599263, 599264, 599265, 599266, 599267, 599268, 599269, 599270, 599271, 599272, 599273, 599274, 599275, 599276, 599277, 599278, 599279, 599280, 599297,

599299, 599306, 599307, 599308, 599309, 599311, 599312, 599313, 599314, 599315, 599316, 599317, 599318, 599319, 599320, 599321, 599322, 599323, 599324, 599325, 599326, 599327, 599328, 599329, 599330, 599338, 599349, 599353, 599354, 599355, 599356, 599357, 599358, 599359, 599360, 599361, 599362, 599363, 599364, 599369, 599371, 599372, 599373, 599376, 599378, 599379, 599382, 599383, 599384, 599385, 599386, 599387, 599388, 599389, 599390, 599391, 599392, 599393, 599394, 599395, 599396, 599397, 599398, 599399, 599400, 599401, 599402, 599403, 599404, 599405, 599406, 599407, 599408, 599409, 599410, 599412, 599413, 599414, 599415, 599416, 599417, 599418, 599419, 599420, 599421, 599422, 599423, 599424, 599425, 599426, 599433, 599434, 599435, 599436, 599437, 599438, 599439, 599440, 599441, 599442, 599443, 599444, 599445, 599446, 599447, 599448, 599450, 599454, 599455, 599456, 599467, 599468, 599469, 599471, 599472, 599473, 599474, 599475, 599476, 599477, 599478, 599479, 599480, 599481, 599482, 599483, 599484, 599485, 599486, 599487, 599488, 599489, 599490, 599491, 599492, 599493, 599494, 599495, 599496, 599497, 599498, 599499, 599500, 599501, 599502, 599503, 599504, 599505, 599506, 599507, 599508, 599509, 599512, 599515, 599518, 599531, 599541, 599541, 599546, 599547, 599548, 599549, 599550, 599552, 599553, 599554, 599555, 599557, 599558, 599561, 599562, 599563, 599564, 599565, 599566, 599567, 599568, 599569, 599570, 599577, 599578, 599579, 599580, 599581, 599581, 599582, 599584, 599585, 599586, 599587, 599588, 599589, 599590, 599591, 599592, 599593, 599594, 599595, 601321, 601322, 601323, 601325, 601327, 601328, 601329, 601330, 601332, 601333, 601334, 601335, 601336, 601337, 601338, 601339, 601341, 601342, 601343, 601344, 601345, 601346, 601347, 601348, 601349, 601362, 601367, 601368, 601369, 601371, 601372, 601373, 601374, 601375, 601377, 601378, 601380, 601381, 601382, 601383, 601384, 601385, 601386, 601387, and 601388.

[0133] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least a 50% inhibition of a CFB mRNA, SEQ ID NOs: 12, 30, 33, 36, 37, 84, 85, 86, 87, 88, 89, 90, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 198, 203, 206, 208, 219, 228, 237, 238, 239, 317, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 468, 472, 473, 475, 478, 479, 488, 492, 494, 495, 498, 499, 500, 502, 503, 509, 510, 511, 512, 513, 514, 515, 517, 518, 522, 523, 524, 525, 529, 530, 531, 534, 535, 537, 540, 541, 542, 543, 544, 545, 546, 547, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 563, 564, 565, 569, 570, 572, 573, 577, 588, 589, 590, 591, 592, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 623, 640, 641, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 700, 704, 705, 706, 707, 708, 709, 711, 712, 713, 714, 715, 716, 717, 718, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 758, 759, 760, 761, 762, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 813, 833, 834, 841, 846, 849, 850, 867, and 873.

[0134] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least a 60% inhibition of a CFB mRNA, ISIS NOs: 516350, 532614, 532635, 532686, 532687, 532688, 532689, 532770, 532800, 532809, 532810, 532811, 532917, 532952, 588512, 588513, 588514, 588515, 588516, 588517, 588518, 588519, 588522, 588523, 588524, 588525, 588527, 588528, 588529, 588530, 588531, 588532, 588533, 588534, 588535, 588536, 588537, 588538, 588539, 588540, 588541, 588542, 588543, 588544, 588545, 588546, 588547, 588548, 588549, 588550, 588551, 588552, 588553, 588554, 588555, 588556, 588557, 588558, 588559, 588560, 588561, 588562, 588563, 588564, 588565, 588566, 588567, 588568, 588569, 588570, 588571, 588572, 588573, 588574, 588575, 588576, 588577, 588636, 588638, 588640, 588664, 588676, 588696, 588698, 588807, 588808, 588814, 588815, 588819, 588820, 588840, 588842, 588846, 588847, 588848, 588849, 588850, 588851, 588852, 588853, 588854, 588855, 588856, 588857, 588858, 588859, 588860, 588861, 588862, 588863, 588864, 588866, 588867, 588868, 588870, 588871, 588872, 588873, 588874, 588875, 588876, 588877, 588878, 588879, 588880, 588881, 588882, 588883, 588884, 598999, 599000, 599001, 599002, 599003, 599004, 599005, 599006, 599007, 599008, 599009, 599010, 599011, 599012, 599013, 599014, 599015, 599019, 599024, 599025, 599026, 599027, 599028, 599029, 599030, 599031, 599032, 599033, 599034, 599035, 599064, 599065, 599071, 599072, 599077, 599078, 599079, 599080, 599083, 599084, 599085, 599086, 599087, 599088, 599089, 599090, 599091, 599092, 599093, 599094, 599095, 599096, 599097, 599125, 599126, 599127, 599133, 599134, 599135, 599136, 599138, 599139, 599140, 599141, 599142, 599148, 599149, 599150, 599151, 599152, 599154, 599155, 599156, 599157, 599158, 599159, 599178, 599179, 599180, 599181, 599187, 599188, 599190, 599192, 599193, 599194, 599195, 599196, 599197, 599198, 599199, 599200, 599201, 599202, 599203, 599204, 599205, 599206, 599207, 599208, 599209, 599210, 599211, 599212, 599213, 599214, 599215, 599216, 599217, 599218, 599219, 599220, 599221, 599222, 599223, 599224, 599225, 599226, 599227, 599228, 599229, 599230, 599231, 599232, 599233, 599234, 599235, 599236, 599247, 599255, 599256, 599257, 599263, 599264, 599265, 599266, 599270, 599271, 599272, 599273, 599274, 599275, 599276, 599277, 599278, 599279, 599280, 599306, 599307, 599308, 599311, 599312, 599313, 599314, 599315, 599316, 599317, 599318, 599319, 599320, 599321, 599322, 599323, 599324, 599325, 599327, 599328, 599329, 599330, 599349, 599353, 599355, 599356, 599357, 599358, 599359, 599360, 599361, 599362, 599363, 599364, 599369, 599371, 599372, 599373, 599376, 599378, 599379, 599382, 599384, 599386, 599387, 599388, 599389, 599390, 599391, 599392, 599393, 599394, 599395, 599396, 599397, 599398, 599399, 599400, 599401, 599402, 599403, 599404, 599405, 599406, 599407, 599408, 599409, 599410, 599412, 599413, 599414, 599415, 599416, 599417, 599418, 599419, 599420, 599421, 599422, 599423, 599424, 599425, 599433, 599434, 599435, 599436, 599437, 599438, 599439, 599440, 599441, 599442, 599443, 599444, 599445, 599446, 599447, 599448, 599456, 599467, 599468, 599471, 599472, 599473, 599474, 599475, 599476, 599477, 599478, 599479, 599480, 599481, 599482, 599483, 599484, 599485, 599486, 599487, 599488, 599489,

599490, 599491, 599492, 599493, 599494, 599495, 599496, 599497, 599498, 599499, 599500, 599501, 599502, 599503, 599504, 599505, 599506, 599507, 599508, 599512, 599531, 599547, 599548, 599549, 599552, 599553, 599554, 599555, 599557, 599558, 599562, 599563, 599564, 599565, 599566, 599567, 599568, 599569, 599570, 599577, 599578, 599579, 599580, 599581, 599582, 599584, 599585, 599586, 599587, 599588, 599589, 599590, 599591, 599592, 599593, 599594, 599595, 601323, 601327, 601329, 601332, 601333, 601333, 601334, 601335, 601336, 601338, 601339, 601341, 601342, 601343, 601344, 601345, 601346, 601347, 601348, 601349, 601368, 601369, 601371, 601372, 601374, 601375, 601377, 601378, 601380, 601381, 601382, 601383, 601384, 601385, 601386, 601387, and 601388.

[0135] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least a 60% inhibition of a CFB mRNA, SEQ ID NOs: 12, 33, 84, 85, 86, 87, 198, 228, 237, 238, 239, 317, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 472, 473, 513, 514, 515, 531, 537, 541, 542, 543, 544, 545, 546, 547, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 564, 565, 569, 570, 577, 590, 592, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 682, 683, 684, 685, 686, 687, 688, 689, 700, 704, 706, 707, 708, 709, 711, 712, 713, 714, 715, 716, 717, 720, 721, 722, 723, 724, 725, 726, 727, 727, 728, 729, 730, 731, 732, 733, 734, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 758, 759, 760, 761, 767, 768, 770, 772, 773, 774, 775, 775, 776, 776, 777, 777, 778, 779, 780, 781, 782, 783, 783, 784, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 813, 833, 834, 841, 846, 849, and 850.

[0136] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least a 70% inhibition of a CFB mRNA, ISIS NOs: 516350, 532614, 532686, 532687, 532688, 532770, 532800, 532809, 532810, 532811, 532917, 532952, 588512, 588513, 588514, 588515, 588516, 588517, 588518, 588524, 588529, 588530, 588531, 588532, 588533, 588534, 588535, 588536, 588537, 588538, 588539, 588540, 588541, 588542, 588543, 588544, 588545, 588546, 588547, 588548, 588549, 588550, 588551, 588552, 588553, 588554, 588555, 588556, 588557, 588558, 588559, 588560, 588561, 588562, 588563, 588564, 588565, 588568, 588569, 588570, 588571, 588572, 588573, 588574, 588575, 588577, 588636, 588638, 588640, 588696, 588698, 588807, 588814, 588815, 588819, 588842, 588847, 588848, 588849, 588850, 588851, 588852, 588853, 588856, 588857, 588858, 588859, 588860, 588861, 588862, 588863, 588866, 588867, 588870, 588871, 588872, 588873, 588874, 588875, 588876, 588877, 588878, 588879, 588880, 588881, 588882, 588883, 588884, 599000, 599001, 599003, 599004, 599005, 599008, 599009, 599010, 599011, 599014, 599015, 599024, 599025, 599027, 599028, 599029, 599030, 599031, 599032, 599033, 599034, 599072, 599077, 599080, 599085, 599086, 599087, 599088, 599089, 599090, 599091, 599093, 599094, 599095, 599096, 599097, 599125, 599126, 599134, 599138, 599139, 599148, 599149, 599150, 599151, 599152, 599154, 599155, 599156, 599157, 599158, 599187, 599188, 599193, 599195, 599196, 599197, 599198, 599199, 599200, 599201, 599202, 599203, 599204, 599205, 599206, 599207, 599208, 599210, 599211, 599212, 599213, 599214, 599215, 599216, 599217, 599218, 599219, 599220, 599221, 599222, 599223, 599224, 599225, 599226, 599227, 599228, 599229, 599230, 599231, 599232, 599233, 599234, 599235, 599236, 599266, 599272, 599272, 599273, 599274, 599275, 599277, 599278, 599279, 599280, 599280, 599306, 599311, 599312, 599313, 599314, 599315, 599316, 599317, 599318, 599319, 599320, 599321, 599322, 599323, 599325, 599327, 599328, 599329, 599330, 599355, 599357, 599358, 599359, 599360, 599361, 599362, 599363, 599364, 599369, 599371, 599372, 599373, 599378, 599379, 599382, 599384, 599386, 599387, 599388, 599389, 599390, 599391, 599392, 599393, 599394, 599395, 599396, 599397, 599398, 599399, 599400, 599401, 599402, 599403, 599404, 599405, 599406, 599407, 599408, 599409, 599410, 599413, 599414, 599415, 599416, 599417, 599418, 599419, 599420, 599421, 599422, 599423, 599424, 599433, 599434, 599435, 599436, 599437, 599438, 599439, 599440, 599441, 599442, 599443, 599445, 599446, 599447, 599448, 599472, 599473, 599474, 599475, 599476, 599477, 599478, 599479, 599480, 599481, 599482, 599483, 599484, 599485, 599486, 599487, 599488, 599489, 599490, 599491, 599492, 599493, 599494, 599495, 599496, 599497, 599498, 599499, 599500, 599501, 599502, 599503, 599504, 599505, 599506, 599507, 599508, 599512, 599547, 599548, 599552, 599553, 599554, 599555, 599558, 599562, 599563, 599564, 599566, 599567, 599568, 599569, 599570, 599577, 599578, 599579, 599580, 599581, 599582, 599585, 599586, 599587, 599588, 599589, 599590, 599591, 599592, 599593, 599594, 599595, 601332, 601335, 601341, 601343, 601344, 601345, 601346, 601347, 601348, 601349, 601371, 601372, 601380, 601382, 601383, 601384, 601385, 601386, and 601387.

[0137] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least a 70% inhibition of a CFB mRNA, SEQ ID NOs: 12, 84, 85, 86, 198, 228, 237, 238, 239, 317, 395, 396, 397, 398, 399, 402, 403, 404, 405, 407, 408, 410, 411, 412, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 464, 465, 472, 473, 513, 514, 515, 541, 542, 543, 544, 545, 546, 547, 549, 550, 551, 552, 553, 554, 555, 556, 557, 564, 565, 569, 592, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 645, 646, 647, 648, 649, 650, 653, 654, 655, 656, 659, 660, 662, 663, 664, 665, 666, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 677, 678, 679, 680, 682, 683, 684, 686, 687, 688, 689, 706, 708, 709, 711, 712, 713, 714, 715, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 767, 768, 773, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 793, 794, 795, 797, 798, 799, 813, 833, 834, 841, 846, 849, 867, and 873.

[0138] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least an 80% inhibition of a CFB

mRNA, ISIS NOs: 532686, 532809, 532810, 532811, 532917, 532952, 588512, 588517, 588518, 588533, 588534, 588535, 588536, 588537, 588538, 588539, 588540, 588542, 588543, 588544, 588545, 588546, 588547, 588548, 588549, 588550, 588551, 588552, 588553, 588554, 588555, 588556, 588557, 588558, 588559, 588560, 588561, 588562, 588563, 588564, 588565, 588571, 588638, 588640, 588696, 588698, 588807, 588814, 588849, 588850, 588851, 588853, 588857, 588858, 588859, 588860, 588861, 588862, 588863, 588866, 588867, 588871, 588872, 588873, 588874, 588875, 588876, 588877, 588878, 588879, 588880, 588881, 588882, 588883, 599001, 599024, 599025, 599033, 599086, 599087, 599088, 599089, 599093, 599094, 599095, 599096, 599134, 599139, 599148, 599149, 599151, 599154, 599155, 599156, 599158, 599188, 599195, 599196, 599198, 599201, 599202, 599203, 599204, 599205, 599206, 599207, 599212, 599213, 599215, 599216, 599217, 599218, 599219, 599220, 599221, 599222, 599223, 599224, 599225, 599226, 599227, 599228, 599229, 599230, 599231, 599232, 599233, 599234, 599235, 599236, 599272, 599273, 599275, 599277, 599278, 599279, 599280, 599311, 599313, 599314, 599316, 599317, 599318, 599320, 599321, 599322, 599323, 599327, 599328, 599329, 599330, 599355, 599357, 599358, 599359, 599360, 599361, 599362, 599363, 599364, 599371, 599372, 599373, 599378, 599379, 599382, 599384, 599386, 599387, 599388, 599389, 599390, 599391, 599392, 599393, 599397, 599398, 599399, 599400, 599401, 599403, 599404, 599405, 599407, 599408, 599409, 599410, 599413, 599414, 599415, 599416, 599417, 599418, 599419, 599420, 599421, 599422, 599423, 599424, 599433, 599434, 599435, 599436, 599437, 599438, 599439, 599440, 599441, 599445, 599446, 599447, 599448, 599474, 599476, 599477, 599479, 599481, 599482, 599483, 599485, 599486, 599487, 599488, 599489, 599490, 599491, 599492, 599494, 599495, 599496, 599497, 599498, 599499, 599500, 599502, 599503, 599504, 599505, 599506, 599507, 599508, 599547, 599552, 599553, 599554, 599558, 599563, 599567, 599568, 599569, 599570, 599577, 599578, 599581, 599582, 599585, 599587, 599588, 599590, 599591, 599592, 599593, 599594, 601332, 601344, 601345, 601382, 601383, and 601385.

[0139] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least a 80% inhibition of a CFB mRNA, SEQ ID NOs: 84, 237, 238, 239, 317, 395, 397, 411, 412, 413, 414, 415, 417, 418, 419, 420, 421, 422, 423, 425, 426, 427, 429, 430, 431, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 472, 473, 514, 515, 542, 543, 544, 545, 546, 547, 550, 551, 552, 553, 554, 555, 556, 557, 564, 595, 599, 600, 601, 602, 603, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 646, 655, 660, 662, 663, 666, 669, 670, 671, 672, 673, 675, 676, 677, 678, 679, 682, 684, 686, 687, 688, 689, 706, 708, 709, 711, 712, 713, 714, 715, 720, 722, 723, 724, 725, 726, 727, 729, 730, 731, 732, 733, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 768, 775, 776, 778, 781, 782, 783, 784, 785, 787, 788, 789, 790, 791, 792, 793, 794, 799, 813, 833, 834, 841, 849, 867, and 873.

[0140] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least a 90% inhibition of a CFB mRNA, ISIS NOs: 532686, 532811, 532917, 588536, 588537, 588538, 588539, 588544, 588545, 588546, 588548, 588551, 588552, 588553, 588554, 588555, 588556, 588557, 588558, 588559, 588560, 588561, 588562, 588564, 588638, 588640, 588696, 588698, 588849, 588850, 588851, 588860, 588866, 588867, 588872, 588873, 588874, 588876, 588877, 588878, 588879, 588881, 588883, 599149, 599188, 599203, 599206, 599220, 599221, 599222, 599223, 599224, 599225, 599226, 599227, 599228, 599229, 599235, 599236, 599279, 599280, 599314, 599321, 599362, 599378, 599390, 599391, 599398, 599399, 599404, 599413, 599414, 599416, 599419, 599420, 599422, 599435, 599437, 599438, 599441, 599483, 599494, 599508, 599552, 599553, 599554, 599568, 599570, 599577, 599581, 599591, 599592, and 599593.

[0141] In certain embodiments, the following antisense compounds or oligonucleotides target a region of a CFB nucleic acid and effect at least a 90% inhibition of a CFB mRNA, SEQ ID NOs: 84, 238, 239, 317, 412, 413, 420, 421, 426, 434, 436, 437, 438, 439, 440, 442, 443, 444, 445, 446, 448, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 464, 465, 472, 473, 514, 515, 542, 543, 544, 545, 546, 551, 553, 555, 556, 599, 600, 601, 602, 610, 616, 617, 618, 662, 666, 670, 676, 677, 678, 688, 689, 713, 723, 729, 730, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 755, 756, 768, 783, 793, 833, and 867.

[0142] In certain embodiments, a compound comprises a modified oligonucleotide consisting of 10 to 30 linked nucleosides complementary within nucleotides 2193-2212, 2195-2210, 2457-2476, 2571-2590, 2584-2603, 2588-2607, 2592-2611, 2594-2613, 2597-2616, 2600-2619, or 2596-2611 of SEQ ID NO: 1.

[0143] In certain embodiments, a compound comprises a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598.

[0144] In certain embodiments, a compound comprises a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598.

[0145] In certain embodiments, any of the foregoing compounds or oligonucleotides comprises at least one modified internucleoside linkage, at least one modified sugar, and/or at least one modified nucleobase.

[0146] In certain embodiments, any of the foregoing compounds or oligonucleotides comprises at least one modified sugar. In certain embodiments, at least one modified sugar comprises a 2'-O-methoxyethyl group.

[0147] In certain embodiments, at least one modified sugar is a bicyclic sugar, such as a 4'-$CH(CH_3)$—O-2' group, a 4'-CH_2—O-2' group, or a 4'-$(CH_2)_2$—O-2' group.

[0148] In certain embodiments, the modified oligonucleotide comprises at least one modified internucleoside linkage, such as a phosphorothioate internucleoside linkage.

[0149] In certain embodiments, any of the foregoing compounds or oligonucleotides comprises at least one modified nucleobase, such as 5-methylcytosine.

[0150] In certain embodiments, any of the foregoing compounds or oligonucleotides comprises:

[0151] a gap segment consisting of linked deoxynucleosides;

[0152] a 5' wing segment consisting of linked nucleosides; and

[0153] a 3' wing segment consisting of linked nucleosides;

[0154] wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar. In certain embodiments, the oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, or 598.

[0155] In certain embodiments, the modified oligonucleotide has a nucleobase sequence comprising the sequence recited in SEQ ID NO: 198, 228, 237, 440, 444, 448, 450, 453, or 455, wherein the modified oligonucleotide comprises

[0156] a gap segment consisting of ten linked deoxynucleosides;

[0157] a 5' wing segment consisting of five linked nucleosides; and

[0158] a 3' wing segment consisting of five linked nucleosides;

[0159] wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment, wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; wherein each internucleoside linkage is a phosphorothioate linkage and wherein each cytosine is a 5-methylcytosine.

[0160] In certain embodiments, a compound comprises or consists of a single-stranded modified oligonucleotide consisting of 20 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 198, 228, 237, 440, 444, 448, 450, 453, or 455, wherein the oligonucleotide comprises:

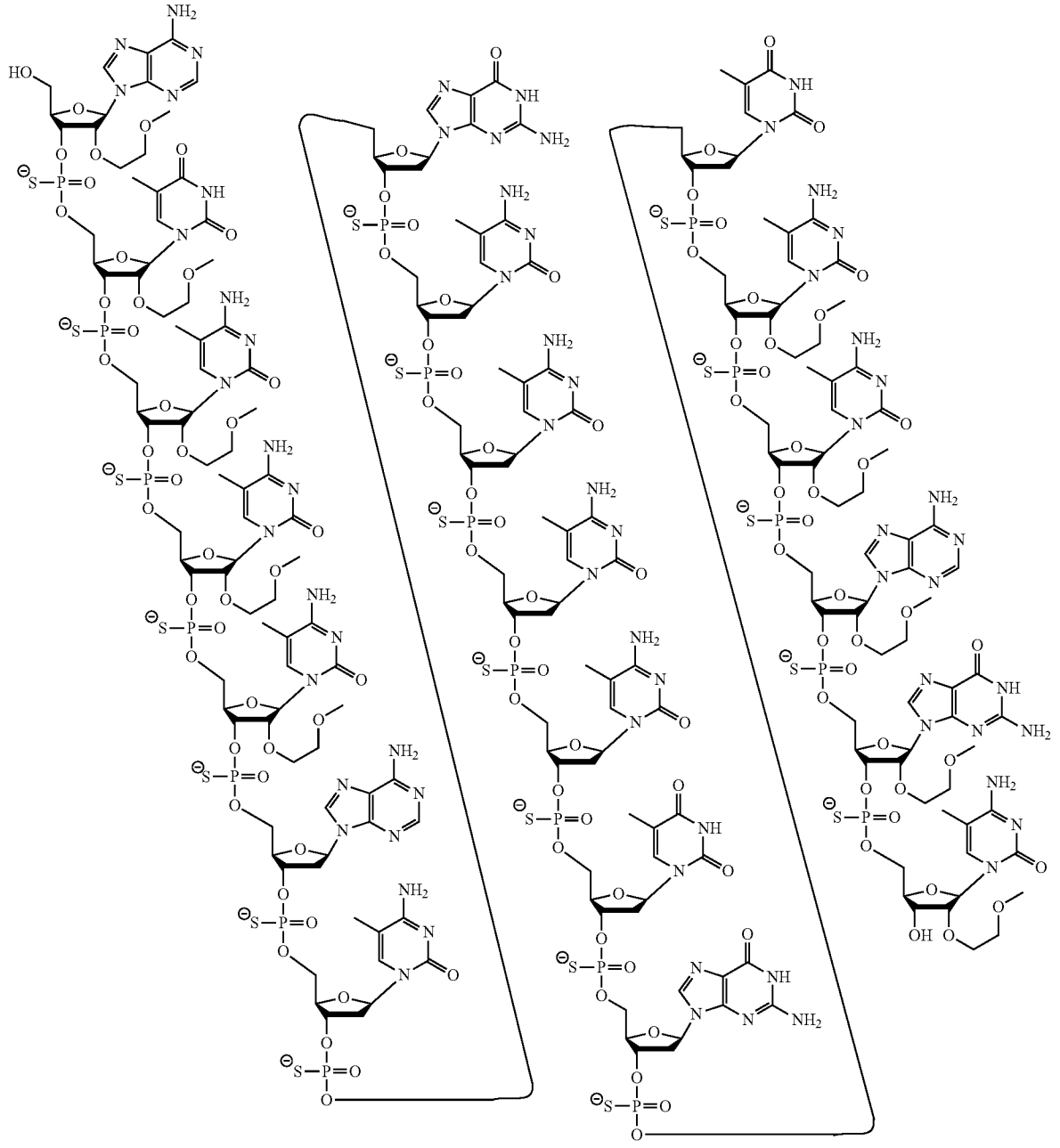
[0161] a gap segment consisting of ten linked deoxynucleosides;

[0162] a 5' wing segment consisting of five linked nucleosides; and

[0163] a 3' wing segment consisting of five linked nucleosides;

[0164] wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment, wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

[0165] In certain embodiments, a compound comprises ISIS 588540. In certain embodiments, a compound consists of ISIS 588540. In certain embodiments, ISIS 588540 has the following chemical structure:



[0166] In certain embodiments, a compound comprises or consists of a single-stranded modified oligonucleotide consisting of 16 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 549, wherein the modified oligonucleotide comprises

[0167] a gap segment consisting of ten linked deoxynucleosides;

[0168] a 5' wing segment consisting of three linked nucleosides; and

[0169] a 3' wing segment consisting of three linked nucleosides;

[0170] wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein each nucleoside of each wing segment comprises a cEt sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

[0171] In certain embodiments, a compound comprises or consists of a single-stranded modified oligonucleotide consisting of 16 linked nucleosides having a nucleobase sequence comprising the sequence recited in SEQ ID NO: 598, wherein the modified oligonucleotide comprises

[0172] a gap segment consisting of ten linked deoxynucleosides;

[0173] a 5' wing segment consisting of three linked nucleosides; and

[0174] a 3' wing segment consisting of three linked nucleosides;

[0175] wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment; wherein the 5' wing segment comprises a 2'-O-methoxyethyl sugar, 2'-O-methoxyethyl sugar, and cEt sugar in the 5' to 3' direction; wherein the 3' wing segment comprises a cEt sugar, cEt sugar, and 2'-O-methoxyethyl sugar in the 5' to 3' direction; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

[0176] In any of the foregoing embodiments, the compound or oligonucleotide can be at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% complementary to a nucleic acid encoding CFB.

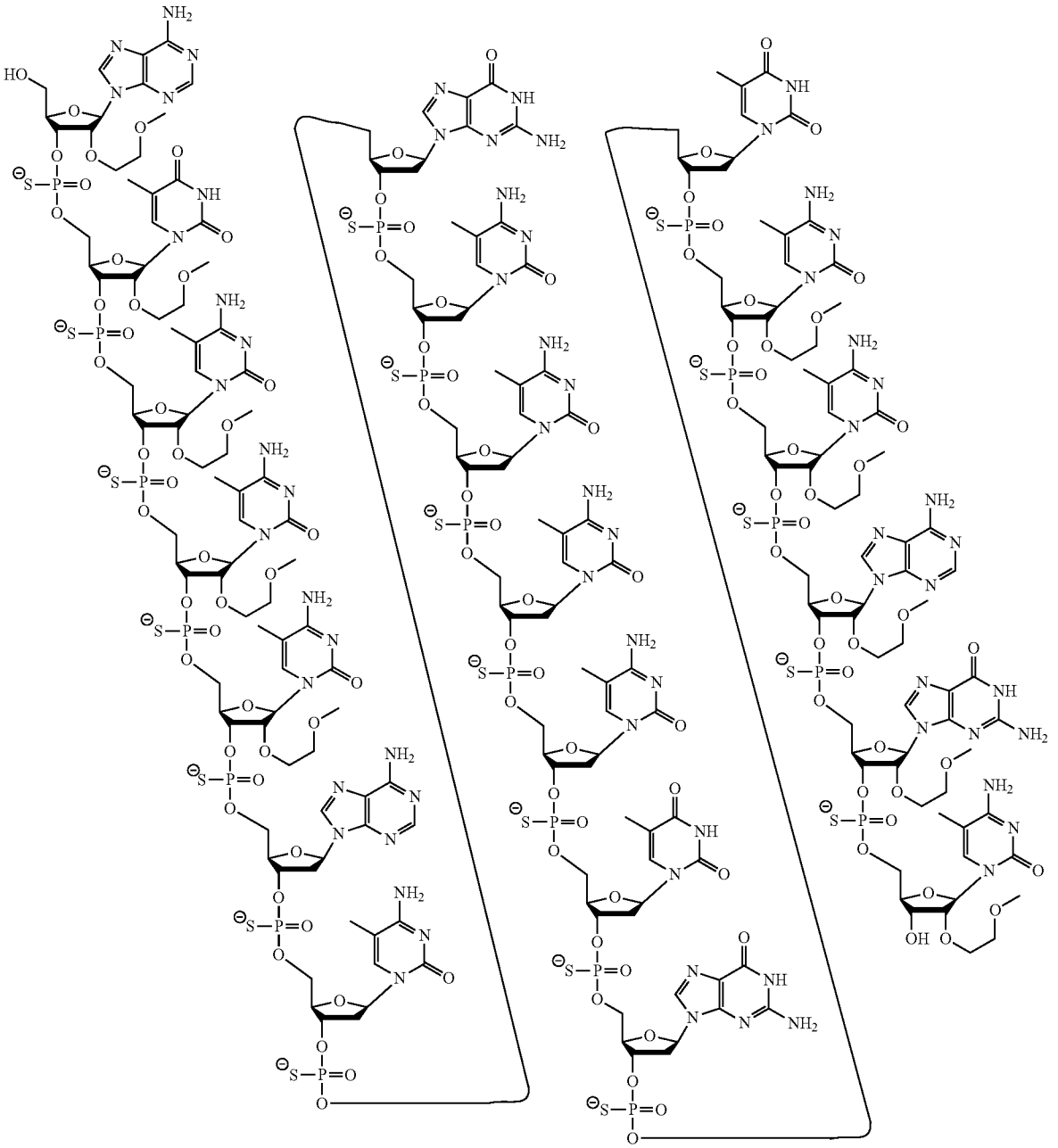
[0177] In any of the foregoing embodiments, the compound or oligonucleotide can be single-stranded.

[0178] In certain embodiments, the compounds or compositions as described herein are efficacious by virtue of having at least one of an in vitro IC_{50} of less than 250 nM, less than 200 nM, less than 150 nM, less than 100 nM, less than 90 nM, less than 80 nM, less than 70 nM, less than 65 nM, less than 60 nM, less than 55 nM, less than 50 nM, less than 45 nM, less than 40 nM, less than 35 nM, less than 30 nM, less than 25 nM, or less than 20 nM.

[0179] In certain embodiments, the compounds or compositions as described herein are highly tolerable as demonstrated by having at least one of an increase an ALT or AST value of no more than 4 fold, 3 fold, or 2 fold over saline treated animals or an increase in liver, spleen, or kidney weight of no more than 30%, 20%, 15%, 12%, 10%, 5%, or 2%. In certain embodiments, the compounds or compositions as described herein are highly tolerable as demonstrated by having no increase of ALT or AST over saline treated animals. In certain embodiments, the compounds or compositions as described herein are highly tolerable as demonstrated by having no increase in liver, spleen, or kidney weight over saline treated animals.

[0180] Certain embodiments provide a composition comprising the compound of any of the aforementioned embodiments or salt thereof and at least one of a pharmaceutically acceptable carrier or diluent. In certain embodiments, the composition has a viscosity less than about 40 centipoise (cP), less than about 30 centipose (cP), less than about 20 centipose (cP), less than about 15 centipose (cP), or less than about 10 centipose (cP). In certain embodiments, the composition having any of the aforementioned viscosities comprises a compound provided herein at a concentration of about 100 mg/mL, about 125 mg/mL, about 150 mg/mL, about 175 mg/mL, about 200 mg/mL, about 225 mg/mL, about 250 mg/mL, about 275 mg/mL, or about 300 mg/mL. In certain embodiments, the composition having any of the aforementioned viscosities and/or compound concentrations has a temperature of room temperature or about 20° C., about 21° C., about 22° C., about 23° C., about 24° C., about 25° C., about 26° C., about 27° C., about 28° C., about 29° C., or about 30° C.

[0181] In certain embodiments, a method of treating, preventing, or ameliorating a disease associated with dysregulation of the complement alternative pathway in a subject comprises administering to the subject a specific inhibitor of Complement Factor B (CFB), thereby treating, preventing, or ameliorating the disease. In certain embodiments, the complement alternative pathway is activated greater than normal. In certain embodiments, the CFB specific inhibitor is an antisense compound targeted to CFB, such as an antisense oligonucleotide targeted to CFB. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of ISIS 532770, 532800, 532809, 588540, 588544, 588548, 588550, 588553, 588555, 588848, or 594430. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of ISIS 588540, which has the following chemical structure:



In certain embodiments, the disease is macular degeneration, such as age related macular degeneration (AMD), which can be wet AMD or dry AMD. In certain embodiments, dry AMD can be Geographic Atrophy. In certain embodiments, the disease is a kidney disease such as lupus nephritis, systemic lupus erythematosus (SLE), dense deposit disease (DDD), C3 glomerulonephritis (C3GN), CFHR5 nephropathy, or atypical hemolytic uremic syndrome (aHUS), or any combination thereof.

[0182] In certain embodiments, a method of treating, preventing, or ameliorating macular degeneration, such as age-related macular degeneration (AMD) in a subject comprises administering to the subject a CFB specific inhibitor, thereby treating, preventing, or ameliorating AMD, such as wet AMD and dry AMD. In certain embodiments, dry AMD can be Geographic Atrophy. Geographic Atrophy is considered an advanced form of dry AMD involving degeneration of the retina. In certain embodiments, the subject has a complement alternative pathway that is activated greater than normal. In certain embodiments, administering the antisense compound reduces or inhibits accumulation of ocular C3 levels, such as C3 protein levels. In certain embodiments, administering the antisense compound reduces the level of ocular C3 deposits or inhibits accumulation of ocular C3 deposits. In certain embodiments, the CFB specific inhibitor is an antisense compound targeted to CFB, such as an antisense oligonucleotide

targeted to CFB. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of ISIS 532770, 532800, 532809, 588540, 588544, 588548, 588550, 588553, 588555, 588848, or 594430. In certain embodiments, the compound is administered to the subject parenterally.

[0183] In certain embodiments, a method of treating, preventing, or ameliorating a kidney disease associated with dysregulation of the complement alternative pathway in a subject comprises administering to the subject a specific inhibitor of Complement Factor B (CFB), thereby treating, preventing, or ameliorating the kidney disease. In certain embodiments, the complement alternative pathway is activated greater than normal. In certain embodiments, the CFB specific inhibitor is an antisense compound targeted to CFB, such as an antisense oligonucleotide targeted to CFB. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of ISIS 532770, 532800, 532809, 588540, 588544, 588548, 588550, 588553, 588555, 588848, or 594430. In certain embodiments, the compound is administered to the subject parenterally. In certain embodiments, the kidney disease is lupus nephritis, systemic lupus erythematosus (SLE), dense deposit disease (DDD), C3 glomerulonephritis (C3GN), CFHR5 nephropathy, or atypical hemolytic uremic syndrome (aHUS), or any combination thereof. In certain embodiments, the kidney disease is associated with C3 deposits, such as C3 deposits in the glomerulus. In certain embodiments, the kidney disease is associated with lower than normal circulating C3 levels, such as serum or plasma C3 levels. In certain embodiments, administering the compound reduces or inhibits accumulation of C3 levels in the kidney, such as C3 protein levels. In certain embodiments, administering the compound reduces the level of kidney C3 deposits or inhibits accumulation of kidney C3 deposits, such as C3 levels in the glomerulus. In certain embodiments, the subject is identified as having or at risk of having a disease associated with dysregulation of the complement alternative pathway, for example by detecting complement levels or membrane-attack complex levels in the subject's blood and/or performing a genetic test for gene mutations of complement factors associated with the disease.

[0184] In certain embodiments, a method of inhibiting expression of Complement Factor B (CFB) in a subject having, or at risk of having, a disease associated with dysregulation of the complement alternative pathway comprises administering a Complement Factor B (CFB) specific inhibitor to the subject, thereby inhibiting expression of CFB in the subject. In certain embodiments, administering the inhibitor inhibits expression of CFB in the eye. In certain embodiments, the subject has, or is at risk of having, age related macular degeneration (AMD), such as wet AMD and dry AMD. In certain embodiments, dry AMD can be Geographic Atrophy. In certain embodiments, administering the inhibitor inhibits expression of CFB in the kidney, such as in the glomerulus. In certain embodiments, the subject has, or is at risk of having, lupus nephritis, systemic lupus erythematosus (SLE), dense deposit disease (DDD), C3 glomerulonephritis (C3GN), CFHR5 nephropathy, or atypical hemolytic uremic syndrome (aHUS), or any combination thereof. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of ISIS 532770, 532800, 532809, 588540, 588544, 588548, 588550, 588553, 588555, 588848, or 594430. In certain embodiments, the compound is administered to the subject parenterally.

[0185] In certain embodiments, a method of reducing or inhibiting accumulation of C3 deposits in the eye of a subject having, or at risk of having, a disease associated with dysregulation of the complement alternative pathway comprises administering a Complement Factor B (CFB) specific inhibitor to the subject, thereby reducing or inhibiting accumulation

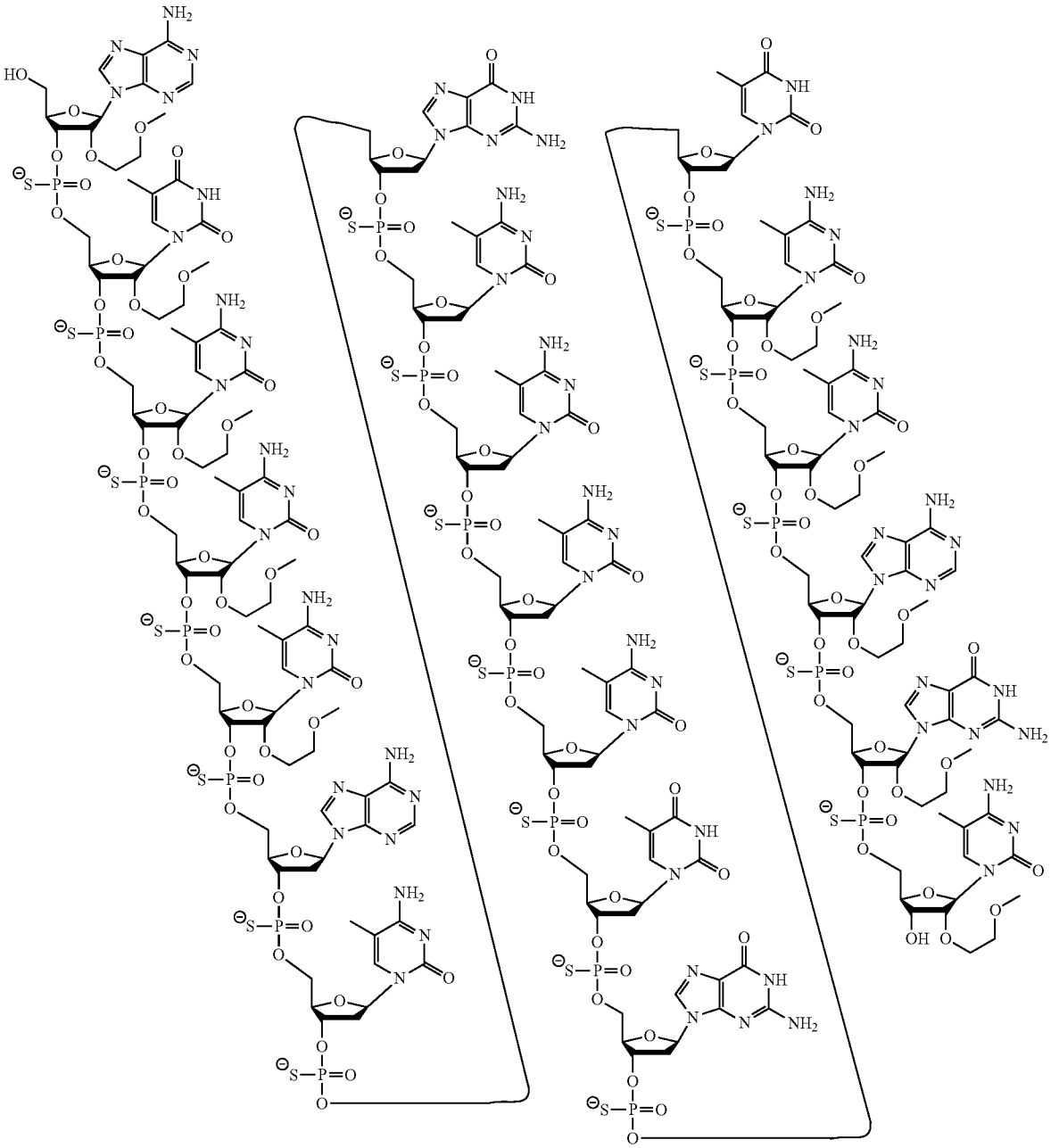
of C3 deposits in the eye of the subject. In certain embodiments, the subject has, or is at risk of having, age related macular degeneration (AMD), such as wet AMD and dry AMD. In certain embodiments, dry AMD can be Geographic Atrophy. In certain embodiments, the inhibitor is an antisense compound targeted to CFB. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of ISIS 532770, 532800, 532809, 588540, 588544, 588548, 588550, 588553, 588555, 588848, or 594430. In certain embodiments, the compound is administered to the subject parenterally.

[0186] In certain embodiments, a method of reducing or inhibiting accumulation of C3 deposits in the kidney of a subject having, or at risk of having, a disease associated with dysregulation of the complement alternative pathway comprises administering a Complement Factor B (CFB) specific inhibitor to the subject, thereby reducing or inhibiting accumulation of C3 deposits in the kidney of the subject. In certain embodiments, the subject has, or is at risk of having, lupus nephritis, systemic lupus erythematosus (SLE), dense deposit disease (DDD), C3 glomerulonephritis (C3GN), CFHR5 nephropathy, or atypical hemolytic uremic syndrome (aHUS), or any combination thereof. In certain embodiments, the inhibitor is an antisense compound targeted to CFB. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 6-808. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598. In certain embodiments, the CFB specific inhibitor is a compound comprising or consisting of ISIS 532770, 532800, 532809, 588540, 588544, 588548, 588550, 588553, 588555, 588848, or 594430. In certain embodiments, the compound is administered to the subject parenterally.

[0187] Certain embodiments are drawn to a compound or composition described herein for use in therapy. Certain embodiments are drawn to a compound comprising or consisting of modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808 for use in therapy. Certain embodiments are drawn to a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 6-808 for use in therapy. Certain embodiments are drawn to a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598, for use in therapy. Certain embodiments are drawn to a compound comprising or consisting of ISIS 532770, 532800, 532809, 588540, 588544, 588548, 588550, 588553, 588555, 588848, or 594430 for use in therapy.

[0188] Certain embodiments are drawn to a compound or composition described herein for use in treating a disease associated with dysregulation of the complement alternative pathway. Certain embodiments are drawn to a compound comprising or consisting of modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808 for use in treating a disease associated with dysregulation of the complement alternative pathway. Certain embodiments are drawn to a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 6-808 for use in treating a disease associated with dysregulation of the complement alternative pathway. Certain embodiments are drawn to a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598, for use in treating a disease associated with dysregulation of the complement alternative pathway. Certain embodiments are drawn to a compound comprising or consisting of ISIS 532770, 532800, 532809, 588540, 588544, 588548, 588550, 588553, 588555, 588848, or 594430 for use in treating a disease associated with dysregulation of the complement alternative pathway. In certain embodiments, the complement alternative pathway is activated greater than normal. In certain embodiments, the disease is macular degeneration, such as age related macular degeneration (AMD), which can be wet AMD or dry AMD. In certain embodiments, dry AMD can be Geographic Atrophy. In certain embodiments, the disease is a kidney disease such as lupus nephritis, systemic lupus erythematosus (SLE), dense deposit disease (DDD), C3 glomerulonephritis (C3GN), CFHR5 nephropathy, or atypical hemolytic uremic syndrome (aHUS), or any combination thereof.

[0189] Certain embodiments are drawn to a compound comprising or consisting of ISIS 588540, which has the following chemical structure:

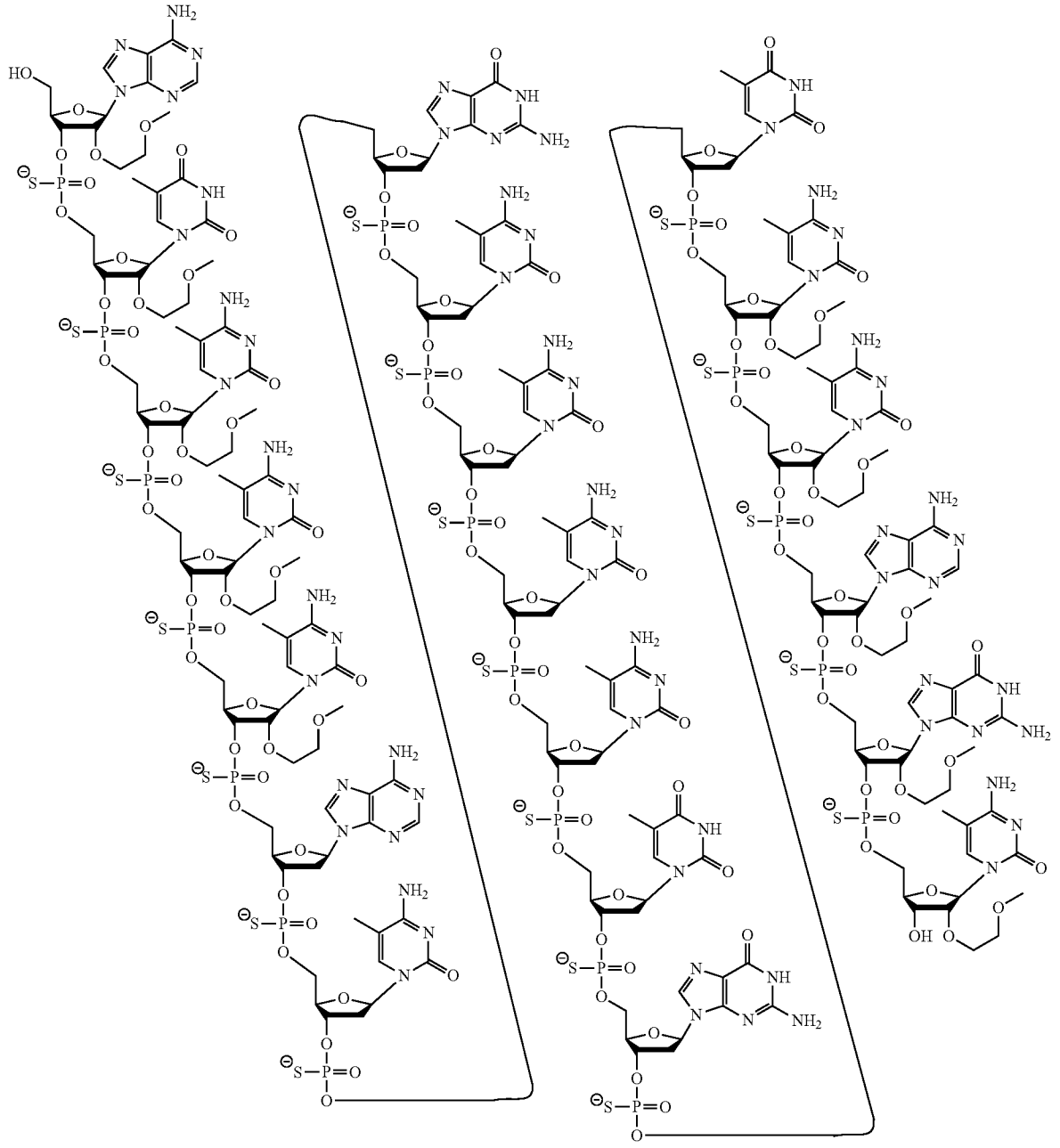


for use in treating a disease associated with dysregulation of the complement alternative pathway. In certain embodiments, the complement alternative pathway is activated greater than normal. In certain embodiments, the disease is macular degeneration, such as age related macular degeneration (AMD), which can be wet AMD or dry AMD. In certain embodiments, dry AMD can be Geographic Atrophy. In certain embodiments, the disease is a kidney disease such as lupus nephritis, systemic lupus erythematosus (SLE), dense deposit disease (DDD), C3 glomerulonephritis (C3GN), CFHR5 nephropathy, or atypical hemolytic uremic syndrome (aHUS), or any combination thereof.

[0190] Certain embodiments are drawn to use of a compound or composition described herein for the manufacture of a medicament for treating a disease associated with dysregulation of the complement alternative pathway. Certain embodiments are drawn to use of a compound comprising or consisting of modified oligonucleotide consisting of 10 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 6-808 for the manufacture of a medicament for treating disease associated with dysregulation of the complement alternative pathway. Certain embodiments are drawn to use of a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked

nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 6-808 for the manufacture of a medicament for treating a disease associated with dysregulation of the complement alternative pathway. Certain embodiments are drawn to use of a compound comprising or consisting of a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising or consisting of any one of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598, for the manufacture of a medicament for treating a disease associated with dysregulation of the complement alternative pathway. Certain embodiments are drawn to use of a compound comprising or consisting of ISIS 532770, 532800, 532809, 588540, 588544, 588548, 588550, 588553, 588555, 588848, or 594430 for the manufacture of a medicament for treating a disease associated with dysregulation of the complement alternative pathway. In certain embodiments, the complement alternative pathway is activated greater than normal. In certain embodiments, the disease is macular degeneration, such as age related macular degeneration (AMD), which can be wet AMD or dry AMD. In certain embodiments, dry AMD can be Geographic Atrophy. In certain embodiments, the disease is a kidney disease such as lupus nephritis, systemic lupus erythematosus (SLE), dense deposit disease (DDD), C3 glomerulonephritis (C3GN), CFHR5 nephropathy, or atypical hemolytic uremic syndrome (aHUS), or any combination thereof.

[0191] Certain embodiments are drawn to use of a compound comprising or consisting of ISIS 588540, which has the following chemical structure:



for the manufacture of a medicament for treating a disease associated with dysregulation of the complement alternative pathway. In certain embodiments, the complement alternative pathway is activated greater than normal. In certain embodiments, the disease is macular degeneration, such as age related macular degeneration (AMD), which can be wet AMD or dry AMD. In certain embodiments, dry AMD can be Geographic Atrophy. In certain embodiments, the disease is a kidney disease such as lupus nephritis, systemic lupus erythematosus (SLE), dense deposit disease (DDD), C3 glomerulonephritis (C3GN), CFHR5 nephropathy, or atypical hemolytic uremic syndrome (aHUS), or any combination thereof.

[0192] In any of the foregoing embodiments, the CFB specific inhibitor can be an antisense compound targeted to CFB. In certain embodiments, the antisense compound comprises an antisense oligonucleotide, for example an antisense oligonucleotide consisting of 8 to 80 linked nucleosides, 12 to 30 linked nucleosides, or 20 linked nucleosides. In certain embodiments, the antisense oligonucleotide is at least 80%, 85%, 90%, 95% or 100% complementary to any of the nucleobase sequences recited in SEQ ID NOs: 1-5. In certain embodiments, the antisense oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar and/or at least one modified nucleobase. In certain embodiments, the modified internucleoside linkage is a phosphorothioate internucleoside linkage, the modified sugar is a bicyclic sugar or a 2'-O-methoxyethyl, and the modified nucleobase is a 5-methylcytosine. In certain embodiments, the modified oligonucleotide comprises a gap segment consisting of linked deoxynucleosides; a 5' wing segment consisting of linked nucleosides; and a 3' wing segment consisting of linked nucleosides, wherein the gap segment is positioned immediately adjacent to and between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar. In certain embodiments, the antisense oligonucleotide is administered parenterally. For example, in certain embodiments the antisense oligonucleotide can be administered through injection or infusion. Parenteral administration includes subcutaneous administration, intravenous administration, intramuscular administration, intraarterial administration, intraperitoneal administration, or intracranial administration, e.g. intrathecal or intracerebroventricular administration.

Antisense Compounds

[0193] Oligomeric compounds include, but are not limited to, oligonucleotides, oligonucleosides, oligonucleotide analogs, oligonucleotide mimetics, antisense compounds, antisense oligonucleotides, and siRNAs. An oligomeric compound may be "antisense" to a target nucleic acid, meaning that is capable of undergoing hybridization to a target nucleic acid through hydrogen bonding.

[0194] In certain embodiments, an antisense compound has a nucleobase sequence that, when written in the 5' to 3' direction, comprises the reverse complement of the target segment of a target nucleic acid to which it is targeted.

[0195] In certain embodiments, an antisense compound is 10 to 30 subunits in length. In certain embodiments, an antisense compound is 12 to 30 subunits in length. In certain embodiments, an antisense compound is 12 to 22 subunits in length. In certain embodiments, an antisense compound is 14 to 30 subunits in length. In certain embodiments, an antisense compound is 14 to 20 subunits in length. In certain embodiments, an antisense compound is 15 to 30 subunits in length. In certain embodiments, an antisense compound is 15 to 20 subunits in length. In certain embodiments, an antisense compound is 16 to 30 subunits in length. In certain embodiments, an antisense compound is 16 to 20 subunits in length. In certain embodiments, an antisense compound is 17 to 30 subunits in length. In certain embodiments, an antisense compound is 17 to 20 subunits in length. In certain embodiments, an antisense compound is 18 to 30 subunits in length. In certain embodiments, an antisense compound is 18 to 21 subunits in length. In certain embodiments, an antisense compound is 18 to 20 subunits in length. In certain embodiments, an antisense compound is 20 to 30 subunits in length. In other words, such antisense compounds are from 12 to 30 linked subunits, 14 to 30 linked subunits, 14 to 20 subunits, 15 to 30 subunits, 15 to 20 subunits, 16 to 30 subunits, 16 to 20 subunits, 17 to 30 subunits, 17 to 20 subunits, 18 to 30 subunits, 18 to 20 subunits, 18 to 21 subunits, 20 to 30 subunits, or 12 to 22 linked subunits, respectively. In certain embodiments, an antisense compound is 14 subunits in length. In certain embodiments, an antisense compound is 16 subunits in length. In certain embodiments, an antisense compound is 17 subunits in length. In certain embodiments, an antisense compound is 18 subunits in length. In certain embodiments, an antisense compound is 19 subunits in length. In certain embodiments, an antisense compound is 20 subunits in length. In other embodiments, the antisense compound is 8 to 80, 12 to 50, 13 to 30, 13 to 50, 14 to 30, 14 to 50, 15 to 30, 15 to 50, 16 to 30, 16 to 50, 17 to 30, 17 to 50, 18 to 22, 18 to 24, 18 to 30, 18 to 50, 19 to 22, 19 to 30, 19 to 50, or 20 to 30 linked subunits. In certain such embodiments, the antisense compounds are 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, or 80 linked subunits in length, or a range defined by any two of the above values. In some embodiments the antisense compound is an antisense oligonucleotide, and the linked subunits are nucleotides.

[0196] In certain embodiments antisense oligonucleotides may be shortened or truncated. For example, a single subunit may be deleted from the 5' end (5' truncation), or alternatively from the 3' end (3' truncation).

[0197] A shortened or truncated antisense compound targeted to an CFB nucleic acid may have two subunits deleted from the 5' end, or alternatively may have two subunits deleted from the 3' end, of the antisense compound. Alternatively, the deleted nucleosides may be dispersed throughout the antisense compound, for example, in an antisense compound having one nucleoside deleted from the 5' end and one nucleoside deleted from the 3' end.

[0198] When a single additional subunit is present in a lengthened antisense compound, the additional subunit may be located at the 5' or 3' end of the antisense compound. When two or more additional subunits are present, the added subunits may be adjacent to each other, for example, in an antisense compound having two subunits added to the 5' end (5' addition), or alternatively to the 3' end (3' addition), of the antisense compound. Alternatively, the added subunits may be dispersed throughout the antisense compound, for example, in an antisense compound having one subunit added to the 5' end and one subunit added to the 3' end.

[0199] It is possible to increase or decrease the length of an antisense compound, such as an antisense oligonucleotide,

and/or introduce mismatch bases without eliminating activity. For example, in Woolf et al. (Proc. Natl. Acad. Sci. USA 89:7305-7309, 1992), a series of antisense oligonucleotides 13-25 nucleobases in length were tested for their ability to induce cleavage of a target RNA in an oocyte injection model. Antisense oligonucleotides 25 nucleobases in length with 8 or 11 mismatch bases near the ends of the antisense oligonucleotides were able to direct specific cleavage of the target mRNA, albeit to a lesser extent than the antisense oligonucleotides that contained no mismatches. Similarly, target specific cleavage was achieved using 13 nucleobase antisense oligonucleotides, including those with 1 or 3 mismatches.

[0200] Gautschi et al. (*J. Natl. Cancer Inst.* 93:463-471, March 2001) demonstrated the ability of an oligonucleotide having 100% complementarity to the bc1-2 mRNA and having 3 mismatches to the bc1-xL mRNA to reduce the expression of both bc1-2 and bc1-xL in vitro and in vivo. Furthermore, this oligonucleotide demonstrated potent anti-tumor activity in vivo.

[0201] Maher and Dolnick (*Nuc. Acid. Res.* 16:3341-3358, 1988) tested a series of tandem 14 nucleobase antisense oligonucleotides, and a 28 and 42 nucleobase antisense oligonucleotides comprised of the sequence of two or three of the tandem antisense oligonucleotides, respectively, for their ability to arrest translation of human DHFR in a rabbit reticulocyte assay. Each of the three 14 nucleobase antisense oligonucleotides alone was able to inhibit translation, albeit at a more modest level than the 28 or 42 nucleobase antisense oligonucleotides.

Certain Antisense Compound Motifs and Mechanisms

[0202] In certain embodiments, antisense compounds have chemically modified subunits arranged in patterns, or motifs, to confer to the antisense compounds properties such as enhanced inhibitory activity, increased binding affinity for a target nucleic acid, or resistance to degradation by in vivo nucleases.

[0203] Chimeric antisense compounds typically contain at least one region modified so as to confer increased resistance to nuclease degradation, increased cellular uptake, increased binding affinity for the target nucleic acid, and/or increased inhibitory activity. A second region of a chimeric antisense compound may confer another desired property e.g., serve as a substrate for the cellular endonuclease RNase H, which cleaves the RNA strand of an RNA:DNA duplex.

[0204] Antisense activity may result from any mechanism involving the hybridization of the antisense compound (e.g., oligonucleotide) with a target nucleic acid, wherein the hybridization ultimately results in a biological effect. In certain embodiments, the amount and/or activity of the target nucleic acid is modulated. In certain embodiments, the amount and/or activity of the target nucleic acid is reduced. In certain embodiments, hybridization of the antisense compound to the target nucleic acid ultimately results in target nucleic acid degradation. In certain embodiments, hybridization of the antisense compound to the target nucleic acid does not result in target nucleic acid degradation. In certain such embodiments, the presence of the antisense compound hybridized with the target nucleic acid (occupancy) results in a modulation of antisense activity. In certain embodiments, antisense compounds having a particular chemical motif or pattern of chemical modifications are particularly suited to exploit one or more mechanisms. In certain embodiments, antisense compounds function through more than one mechanism and/or through mechanisms that have not been elucidated. Accordingly, the antisense compounds described herein are not limited by particular mechanism.

[0205] Antisense mechanisms include, without limitation, RNase H mediated antisense; RNAi mechanisms, which utilize the RISC pathway and include, without limitation, siRNA, ssRNA and microRNA mechanisms; and occupancy based mechanisms. Certain antisense compounds may act through more than one such mechanism and/or through additional mechanisms.

[0206] RNase H-Mediated Antisense

[0207] In certain embodiments, antisense activity results at least in part from degradation of target RNA by RNase H. RNase H is a cellular endonuclease that cleaves the RNA strand of an RNA:DNA duplex. It is known in the art that single-stranded antisense compounds which are "DNA-like" elicit RNase H activity in mammalian cells. Accordingly, antisense compounds comprising at least a portion of DNA or DNA-like nucleosides may activate RNase H, resulting in cleavage of the target nucleic acid. In certain embodiments, antisense compounds that utilize RNase H comprise one or more modified nucleosides. In certain embodiments, such antisense compounds comprise at least one block of 1-8 modified nucleosides. In certain such embodiments, the modified nucleosides do not support RNase H activity. In certain embodiments, such antisense compounds are gapmers, as described herein. In certain such embodiments, the gap of the gapmer comprises DNA nucleosides. In certain such embodiments, the gap of the gapmer comprises DNA-like nucleosides. In certain such embodiments, the gap of the gapmer comprises DNA nucleosides and DNA-like nucleosides.

[0208] Certain antisense compounds having a gapmer motif are considered chimeric antisense compounds. In a gapmer an internal region having a plurality of nucleotides that supports RNaseH cleavage is positioned between external regions having a plurality of nucleotides that are chemically distinct from the nucleosides of the internal region. In the case of an antisense oligonucleotide having a gapmer motif, the gap segment generally serves as the substrate for endonuclease cleavage, while the wing segments comprise modified nucleosides. In certain embodiments, the regions of a gapmer are differentiated by the types of sugar moieties comprising each distinct region. The types of sugar moieties that are used to differentiate the regions of a gapmer may in some embodiments include β-D-ribonucleosides, β-D-deoxyribonucleosides, 2'-modified nucleosides (such 2'-modified nucleosides may include 2'-MOE and 2'-O—CH_3, among others), and bicyclic sugar modified nucleosides (such bicyclic sugar modified nucleosides may include those having a constrained ethyl). In certain embodiments, nucleosides in the wings may include several modified sugar moieties, including, for example 2'-MOE and bicyclic sugar moieties such as constrained ethyl or LNA. In certain embodiments, wings may include several modified and unmodified sugar moieties. In certain embodiments, wings may include various combinations of 2'-MOE nucleosides, bicyclic sugar moieties such as constrained ethyl nucleosides or LNA nucleosides, and 2'-deoxynucleosides.

[0209] Each distinct region may comprise uniform sugar moieties, variant, or alternating sugar moieties. The wing-gap-wing motif is frequently described as "X-Y-Z", where "X" represents the length of the 5'-wing, "Y" represents the length of the gap, and "Z" represents the length of the 3'-wing.

"X" and "Z" may comprise uniform, variant, or alternating sugar moieties. In certain embodiments, "X" and "Y" may include one or more 2'-deoxynucleosides. "Y" may comprise 2'-deoxynucleosides. As used herein, a gapmer described as "X-Y-Z" has a configuration such that the gap is positioned immediately adjacent to each of the 5'-wing and the 3' wing. Thus, no intervening nucleotides exist between the 5'-wing and gap, or the gap and the 3'-wing. Any of the antisense compounds described herein can have a gapmer motif. In certain embodiments, "X" and "Z" are the same; in other embodiments they are different. In certain embodiments, "Y" is between 8 and 15 nucleosides. X, Y, or Z can be any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30 or more nucleosides.

[0210] In certain embodiments, the antisense compound targeted to a CFB nucleic acid has a gapmer motif in which the gap consists of 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 linked nucleosides.

[0211] In certain embodiments, the antisense oligonucleotide has a sugar motif described by Formula A as follows: $(J)_m$-$(B)_n$-$(J)_p$-$(B)_r$-$(A)_t$-$(D)_g$-$(A)_v$-$(B)_w$-$(J)_x$-$(B)_y$-$(J)_z$

[0212] wherein:

[0213] each A is independently a 2'-substituted nucleoside;

[0214] each B is independently a bicyclic nucleoside;

[0215] each J is independently either a 2'-substituted nucleoside or a 2'-deoxynucleoside;

[0216] each D is a 2'-deoxynucleoside;

[0217] m is 0-4; n is 0-2; p is 0-2; r is 0-2; t is 0-2; v is 0-2; w is 0-4; x is 0-2; y is 0-2; z is 0-4; g is 6-14; provided that:

[0218] at least one of m, n, and r is other than 0;

[0219] at least one of w and y is other than 0;

[0220] the sum of m, n, p, r, and t is from 2 to 5; and

[0221] the sum of v, w, x, y, and z is from 2 to 5.

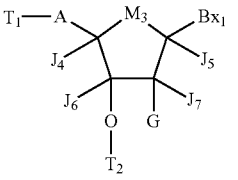
[0222] RNAi Compounds

[0223] In certain embodiments, antisense compounds are interfering RNA compounds (RNAi), which include double-stranded RNA compounds (also referred to as short-interfering RNA or siRNA) and single-stranded RNAi compounds (or ssRNA). Such compounds work at least in part through the RISC pathway to degrade and/or sequester a target nucleic acid (thus, include microRNA/microRNA-mimic compounds). In certain embodiments, antisense compounds comprise modifications that make them particularly suited for such mechanisms.

[0224] i. ssRNA Compounds

[0225] In certain embodiments, antisense compounds including those particularly suited for use as single-stranded RNAi compounds (ssRNA) comprise a modified 5'-terminal end. In certain such embodiments, the 5'-terminal end comprises a modified phosphate moiety. In certain embodiments, such modified phosphate is stabilized (e.g., resistant to degradation/cleavage compared to unmodified 5'-phosphate). In certain embodiments, such 5'-terminal nucleosides stabilize the 5'-phosphorous moiety. Certain modified 5'-terminal nucleosides may be found in the art, for example in WO/2011/139702.

[0226] In certain embodiments, the 5'-nucleoside of an ssRNA compound has Formula IIc:



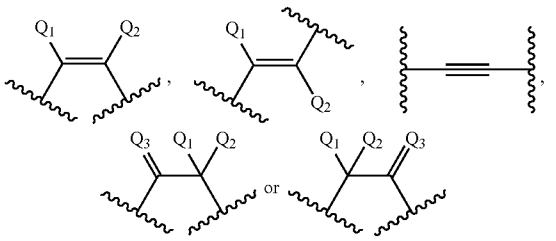
IIc

wherein:

[0227] T_1 is an optionally protected phosphorus moiety;

[0228] T_2 is an internucleoside linking group linking the compound of Formula IIc to the oligomeric compound;

[0229] A has one of the formulas:



[0230] Q_1 and Q_2 are each, independently, H, halogen, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy, substituted C_1-C_6 alkoxy, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl, substituted C_2-C_6 alkynyl or $N(R_3)(R_4)$;

[0231] Q_3 is O, S, $N(R_5)$ or $C(R_6)(R_7)$;

[0232] each R_3, R_4 R_5, R_6 and R_7 is, independently, H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl or C_1-C_6 alkoxy;

[0233] M_3 is O, S, NR_{14}, $C(R_{15})(R_{16})$, $C(R_{15})(R_{16})C(R_{17})(R_{17})$, $C(R_{15})=C(R_{17})$, $OC(R_{15})(R_{16})$ or $OC(R_{15})(Bx_2)$;

[0234] R_{14} is H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy, substituted C_1-C_6 alkoxy, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl or substituted C_2-C_6 alkynyl;

[0235] R_{15}, R_{16}, R_{17} and R_{18} are each, independently, H, halogen, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy, substituted C_1-C_6 alkoxy, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl or substituted C_2-C_6 alkynyl;

[0236] Bx_1 is a heterocyclic base moiety;

[0237] or if Bx_2 is present then Bx_2 is a heterocyclic base moiety and Bx_1 is H, halogen, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy, substituted C_1-C_6 alkoxy, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl or substituted C_2-C_6 alkynyl;

[0238] J_4, J_5, J_6 and J_7 are each, independently, H, halogen, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy, substituted C_1-C_6 alkoxy, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl or substituted C_2-C_6 alkynyl;

[0239] or J_4 forms a bridge with one of J_5 or J_7 wherein said bridge comprises from 1 to 3 linked biradical groups selected from O, S, NR_{19}, $C(R_{20})(R_{21})$, $C(R_{20})=C(R_{21})C[=C(R_{20})(R_{21})]$ and C(=O) and the other two of J_5, J_6 and J_7 are each, independently, H, halogen, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy, substituted C_1-C_6 alkoxy, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl or substituted C_2-C_6 alkynyl;

[0240] each R_{19}, R_{20} and R_{21} is, independently, H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy, substituted

C_1-C_6 alkoxy, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl or substituted C_2-C_6 alkynyl;

[0241] G is H, OH, halogen or O—$[C(R_8)(R_9)]_n$—$[(C{=}O)_m$—$X_1]_j$; —Z;

[0242] each R_8 and R_9 is, independently, H, halogen, C_1-C_6 alkyl or substituted C_1-C_6 alkyl;

[0243] X_1 is O, S or $N(E_1)$;

[0244] Z is H, halogen, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl, substituted C_2-C_6 alkynyl or $N(E_2)(E_3)$;

[0245] E_1, E_2 and E_3 are each, independently, H, C_1-C_6 alkyl or substituted C_1-C_6 alkyl;

[0246] n is from 1 to about 6;

[0247] m is 0 or 1;

[0248] j is 0 or 1;

[0249] each substituted group comprises one or more optionally protected substituent groups independently selected from halogen, OJ_1, $N(J_1)(J_2)$, $=NJ_1$, SJ_1, N_3, CN, $OC(=X_2)J_1$, $OC(=X_2)N(J_1)(J_2)$ and $C(=X_2)N(J_1)(J_2)$;

[0250] X_2 is O, S or NJ_3;

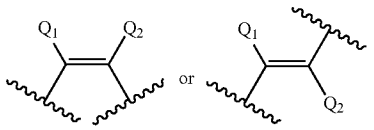
[0251] each J_1, J_2 and J_3 is, independently, H or C_1-C_6 alkyl;

[0252] when j is 1 then Z is other than halogen or $N(E_2)(E_3)$; and

[0253] wherein said oligomeric compound comprises from 8 to 40 monomeric subunits and is hybridizable to at least a portion of a target nucleic acid.

[0254] In certain embodiments, M_3 is O, CH═CH, OCH_2 or $OC(H)(Bx_2)$. In certain embodiments, M_3 is 0. In certain embodiments, J_4, J_5, J_6 and J_7 are each H. In certain embodiments, J_4 forms a bridge with one of J_5 or J_7.

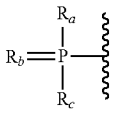
[0255] In certain embodiments, A has one of the formulas:



wherein:

[0256] Q_1 and Q_2 are each, independently, H, halogen, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy or substituted C_1-C_6 alkoxy. In certain embodiments, Q_1 and Q_2 are each H. In certain embodiments, Q_1 and Q_2 are each, independently, H or halogen. In certain embodiments, Q_1 and Q_2 is H and the other of Q_1 and Q_2 is F, CH_3 or OCH_3.

[0257] In certain embodiments, T_1 has the formula:



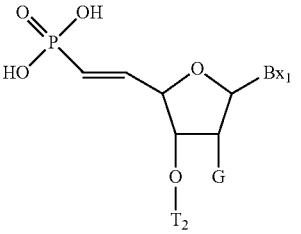
wherein:

[0258] R_a and R_c are each, independently, protected hydroxyl, protected thiol, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy, substituted C_1-C_6 alkoxy, protected amino or substituted amino; and

[0259] R_b is O or S. In certain embodiments, R_b is O and R_a and R_c are each, independently, OCH_3, OCH_2CH_3 or $CH(CH_3)_2$.

[0260] In certain embodiments, G is halogen, OCH_3, OCH_2F, $OCHF_2$, OCF_3, OCH_2CH_3, $O(CH_2)_2F$, OCH_2CHF_2, OCH_2CF_3, OCH_2—CH—CH_2, $O(CH_2)_2$—OCH_3, $O(CH_2)_2$—SCH_3, $O(CH_2)_2$—OCF_3, $O(CH_2)_3$—$N(R_{10})(R_{11})$, $O(CH_2)_2$—$ON(R_{10})(R_{11})$, $O(CH_2)_2$—$O(CH_2)_2$—$N(R_{10})(R_{11})$, $OCH_2C(=O)$—$N(R_{10})(R_{11})$, $OCH_2C(=O)$—$N(R_{12})$—$(CH_2)_2$—$N(R_{10})(R_{11})$ or $O(CH_2)_2$—$N(R_{12})$—$C(=NR_{13})[N(R_{10})(R_{11})]$ wherein R_{10}, R_{11}, R_{12} and R_{13} are each, independently, H or C_1-C_6 alkyl. In certain embodiments, G is halogen, OCH_3, OCF_3, OCH_2CH_3, OCH_2CF_3, OCH_2—CH═CH_2, $O(CH_2)_2$—OCH_3, $O(CH_2)_2$—$O(CH_2)_2$—$N(CH_3)_2$, $OCH_2C(=O)$—$N(H)CH_3$, $OCH_2C(=O)$—$N(H)$—$(CH_2)_2$—$N(CH_3)_2$ or OCH_2—$N(H)$—$C(=NH)NH_2$. In certain embodiments, G is F, OCH_3 or $O(CH_2)_2$—OCH_3. In certain embodiments, G is $O(CH_2)_2$—OCH_3.

[0261] In certain embodiments, the 5'-terminal nucleoside has Formula IIe:



IIe

[0262] In certain embodiments, antisense compounds, including those particularly suitable for ssRNA comprise one or more type of modified sugar moieties and/or naturally occurring sugar moieties arranged along an oligonucleotide or region thereof in a defined pattern or sugar modification motif. Such motifs may include any of the sugar modifications discussed herein and/or other known sugar modifications.

[0263] In certain embodiments, the oligonucleotides comprise or consist of a region having uniform sugar modifications. In certain such embodiments, each nucleoside of the region comprises the same RNA-like sugar modification. In certain embodiments, each nucleoside of the region is a 2'-F nucleoside. In certain embodiments, each nucleoside of the region is a 2'-OMe nucleoside. In certain embodiments, each nucleoside of the region is a 2'-MOE nucleoside. In certain embodiments, each nucleoside of the region is a cEt nucleoside. In certain embodiments, each nucleoside of the region is an LNA nucleoside. In certain embodiments, the uniform region constitutes all or essentially all of the oligonucleotide. In certain embodiments, the region constitutes the entire oligonucleotide except for 1-4 terminal nucleosides.

[0264] In certain embodiments, oligonucleotides comprise one or more regions of alternating sugar modifications, wherein the nucleosides alternate between nucleotides having a sugar modification of a first type and nucleotides having a sugar modification of a second type. In certain embodiments, nucleosides of both types are RNA-like nucleosides. In certain embodiments the alternating nucleosides are selected from: 2'-OMe, 2'-F, 2'-MOE, LNA, and cEt. In certain embodiments, the alternating modifications are 2'-F and 2'-OMe. Such regions may be contiguous or may be interrupted by differently modified nucleosides or conjugated nucleosides.

[0265] In certain embodiments, the alternating region of alternating modifications each consist of a single nucleoside (i.e., the patern is $(AB)_xA_y$, wherein A is a nucleoside having a sugar modification of a first type and B is a nucleoside having a sugar modification of a second type; x is 1-20 and y is 0 or 1). In certain embodiments, one or more alternating regions in an alternating motif includes more than a single nucleoside of a type. For example, oligonucleotides may include one or more regions of any of the following nucleoside motifs:

AABBAA;

ABBABB;

AABAAB;

ABBABAABB;

ABABAA;

AABABAB;

ABABAA;

ABBAABBABABAA;

BABBAABBABABAA; or

ABABBAABBABABAA;

[0266] wherein A is a nucleoside of a first type and B is a nucleoside of a second type. In certain embodiments, A and B are each selected from 2'-F, 2'-OMe, BNA, and MOE.

[0267] In certain embodiments, oligonucleotides having such an alternating motif also comprise a modified 5' terminal nucleoside, such as those of formula IIc or IIe.

[0268] In certain embodiments, oligonucleotides comprise a region having a 2-2-3 motif. Such regions comprises the following motif:

$$-(A)_2-(B)_x-(A)_2-(C)_y-(A)_3-$$

[0269] wherein: A is a first type of modified nucleoside;

[0270] B and C, are nucleosides that are differently modified than A, however, B and C may have the same or different modifications as one another;

[0271] x and y are from 1 to 15.

[0272] In certain embodiments, A is a 2'-OMe modified nucleoside. In certain embodiments, B and C are both 2'-F modified nucleosides. In certain embodiments, A is a 2'-OMe modified nucleoside and B and C are both 2'-F modified nucleosides.

[0273] In certain embodiments, oligonucleosides have the following sugar motif:

$$5'-(Q)-(AB)_xA_y-(D)_z$$

wherein:

[0274] Q is a nucleoside comprising a stabilized phosphate moiety. In certain embodiments, Q is a nucleoside having Formula IIc or IIe;

[0275] A is a first type of modified nucleoside;

[0276] B is a second type of modified nucleoside;

[0277] D is a modified nucleoside comprising a modification different from the nucleoside adjacent to it. Thus, if y is 0, then D must be differently modified than B and if y is 1, then D must be differently modified than A. In certain embodiments, D differs from both A and B.

[0278] X is 5-15;

[0279] Y is 0 or 1;

[0280] Z is 0-4.

[0281] In certain embodiments, oligonucleosides have the following sugar motif:

$$5'-(Q)-(A)_x-(D)_z$$

wherein:

[0282] Q is a nucleoside comprising a stabilized phosphate moiety. In certain embodiments, Q is a nucleoside having Formula IIc or IIe;

[0283] A is a first type of modified nucleoside;

[0284] D is a modified nucleoside comprising a modification different from A.

[0285] X is 11-30;

[0286] Z is 0-4.

[0287] In certain embodiments A, B, C, and D in the above motifs are selected from: 2'-OMe, 2'-F, 2'-MOE, LNA, and cEt. In certain embodiments, D represents terminal nucleosides. In certain embodiments, such terminal nucleosides are not designed to hybridize to the target nucleic acid (though one or more might hybridize by chance). In certain embodiments, the nucleobase of each D nucleoside is adenine, regardless of the identity of the nucleobase at the corresponding position of the target nucleic acid. In certain embodiments the nucleobase of each D nucleoside is thymine.

[0288] In certain embodiments, antisense compounds, including those particularly suited for use as ssRNA comprise modified internucleoside linkages arranged along the oligonucleotide or region thereof in a defined pattern or modified internucleoside linkage motif. In certain embodiments, oligonucleotides comprise a region having an alternating internucleoside linkage motif. In certain embodiments, oligonucleotides comprise a region of uniformly modified internucleoside linkages. In certain such embodiments, the oligonucleotide comprises a region that is uniformly linked by phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide is uniformly linked by phosphorothioate internucleoside linkages. In certain embodiments, each internucleoside linkage of the oligonucleotide is selected from phosphodiester and phosphorothioate. In certain embodiments, each internucleoside linkage of the oligonucleotide is selected from phosphodiester and phosphorothioate and at least one internucleoside linkage is phosphoro-thioate.

[0289] In certain embodiments, the oligonucleotide comprises at least 6 phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least 8 phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least 10 phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least one block of at least 6 consecutive phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least one block of at least 8 consecutive phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least one block of at least 10 consecutive phosphorothioate internucleoside linkages. In certain embodiments, the oligonucleotide comprises at least one block of at least one 12 consecutive phosphorothioate internucleoside linkages. In certain such embodiments, at least one such block is located at the 3' end of the oligonucleotide.

In certain such embodiments, at least one such block is located within 3 nucleosides of the 3' end of the oligonucleotide.

[0290] Oligonucleotides having any of the various sugar motifs described herein, may have any linkage motif. For example, the oligonucleotides, including but not limited to those described above, may have a linkage motif selected from non-limiting the table below:

5' most linkage	Central region	3'-region
PS	Alternating PO/PS	6 PS
PS	Alternating PO/PS	7 PS
PS	Alternating PO/PS	8 PS

[0291] ii. siRNA Compounds

[0292] In certain embodiments, antisense compounds are double-stranded RNAi compounds (siRNA). In such embodiments, one or both strands may comprise any modification motif described above for ssRNA. In certain embodiments, ssRNA compounds may be unmodified RNA. In certain embodiments, siRNA compounds may comprise unmodified RNA nucleosides, but modified internucleoside linkages.

[0293] Several embodiments relate to double-stranded compositions wherein each strand comprises a motif defined by the location of one or more modified or unmodified nucleosides. In certain embodiments, compositions are provided comprising a first and a second oligomeric compound that are fully or at least partially hybridized to form a duplex region and further comprising a region that is complementary to and hybridizes to a nucleic acid target. It is suitable that such a composition comprise a first oligomeric compound that is an antisense strand having full or partial complementarity to a nucleic acid target and a second oligomeric compound that is a sense strand having one or more regions of complementarity to and forming at least one duplex region with the first oligomeric compound.

[0294] The compositions of several embodiments modulate gene expression by hybridizing to a nucleic acid target resulting in loss of its normal function. In certain embodiments, the degradation of the targeted CFB is facilitated by an activated RISC complex that is formed with compositions of the invention.

[0295] Several embodiments are directed to double-stranded compositions wherein one of the strands is useful in, for example, influencing the preferential loading of the opposite strand into the RISC (or cleavage) complex. The compositions are useful for targeting selected nucleic acid molecules and modulating the expression of one or more genes. In some embodiments, the compositions of the present invention hybridize to a portion of a target RNA resulting in loss of normal function of the target RNA.

[0296] Certain embodiments are drawn to double-stranded compositions wherein both the strands comprises a hemimer motif, a fully modified motif, a positionally modified motif or an alternating motif Each strand of the compositions of the present invention can be modified to fulfil a particular role in for example the siRNA pathway. Using a different motif in each strand or the same motif with different chemical modifications in each strand permits targeting the antisense strand for the RISC complex while inhibiting the incorporation of the sense strand. Within this model, each strand can be independently modified such that it is enhanced for its particular role. The antisense strand can be modified at the 5'-end to enhance its role in one region of the RISC while the 3'-end can be modified differentially to enhance its role in a different region of the RISC.

[0297] The double-stranded oligonucleotide molecules can be a double-stranded polynucleotide molecule comprising self-complementary sense and antisense regions, wherein the antisense region comprises nucleotide sequence that is complementary to nucleotide sequence in a target nucleic acid molecule or a portion thereof and the sense region having nucleotide sequence corresponding to the target nucleic acid sequence or a portion thereof. The double-stranded oligonucleotide molecules can be assembled from two separate oligonucleotides, where one strand is the sense strand and the other is the antisense strand, wherein the antisense and sense strands are self-complementary (i.e. each strand comprises nucleotide sequence that is complementary to nucleotide sequence in the other strand; such as where the antisense strand and sense strand form a duplex or double-stranded structure, for example wherein the double-stranded region is about 15 to about 30, e.g., about 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 base pairs; the antisense strand comprises nucleotide sequence that is complementary to nucleotide sequence in a target nucleic acid molecule or a portion thereof and the sense strand comprises nucleotide sequence corresponding to the target nucleic acid sequence or a portion thereof (e.g., about 15 to about 25 or more nucleotides of the double-stranded oligonucleotide molecule are complementary to the target nucleic acid or a portion thereof). Alternatively, the double-stranded oligonucleotide is assembled from a single oligonucleotide, where the self-complementary sense and antisense regions of the siRNA are linked by means of a nucleic acid based or non-nucleic acid-based linker(s).

[0298] The double-stranded oligonucleotide can be a polynucleotide with a duplex, asymmetric duplex, hairpin or asymmetric hairpin secondary structure, having self-complementary sense and antisense regions, wherein the antisense region comprises nucleotide sequence that is complementary to nucleotide sequence in a separate target nucleic acid molecule or a portion thereof and the sense region having nucleotide sequence corresponding to the target nucleic acid sequence or a portion thereof. The double-stranded oligonucleotide can be a circular single-stranded polynucleotide having two or more loop structures and a stem comprising self-complementary sense and antisense regions, wherein the antisense region comprises nucleotide sequence that is complementary to nucleotide sequence in a target nucleic acid molecule or a portion thereof and the sense region having nucleotide sequence corresponding to the target nucleic acid sequence or a portion thereof, and wherein the circular polynucleotide can be processed either in vivo or in vitro to generate an active siRNA molecule capable of mediating RNAi.

[0299] In certain embodiments, the double-stranded oligonucleotide comprises separate sense and antisense sequences or regions, wherein the sense and antisense regions are covalently linked by nucleotide or non-nucleotide linkers molecules as is known in the art, or are alternately non-covalently linked by ionic interactions, hydrogen bonding, van der waals interactions, hydrophobic interactions, and/or stacking interactions. In certain embodiments, the double-stranded oligonucleotide comprises nucleotide sequence that is complementary to nucleotide sequence of a target gene. In another embodiment, the double-stranded oligonucleotide

interacts with nucleotide sequence of a target gene in a manner that causes inhibition of expression of the target gene.

[0300] As used herein, double-stranded oligonucleotides need not be limited to those molecules containing only RNA, but further encompasses chemically modified nucleotides and non-nucleotides. In certain embodiments, the short interfering nucleic acid molecules lack 2'-hydroxy (2'-OH) containing nucleotides. In certain embodiments short interfering nucleic acids optionally do not include any ribonucleotides (e.g., nucleotides having a 2'-OH group). Such double-stranded oligonucleotides that do not require the presence of ribonucleotides within the molecule to support RNAi can however have an attached linker or linkers or other attached or associated groups, moieties, or chains containing one or more nucleotides with 2'-OH groups. Optionally, double-stranded oligonucleotides can comprise ribonucleotides at about 5, 10, 20, 30, 40, or 50% of the nucleotide positions. As used herein, the term siRNA is meant to be equivalent to other terms used to describe nucleic acid molecules that are capable of mediating sequence specific RNAi, for example short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), short hairpin RNA (shRNA), short interfering oligonucleotide, short interfering nucleic acid, short interfering modified oligonucleotide, chemically modified siRNA, post-transcriptional gene silencing RNA (ptgsRNA), and others. In addition, as used herein, the term RNAi is meant to be equivalent to other terms used to describe sequence specific RNA interference, such as post transcriptional gene silencing, translational inhibition, or epigenetics. For example, double-stranded oligonucleotides can be used to epigenetically silence genes at both the post-transcriptional level and the pre-transcriptional level. In a non-limiting example, epigenetic regulation of gene expression by siRNA molecules of the invention can result from siRNA mediated modification of chromatin structure or methylation pattern to alter gene expression (see, for example, Verdel et al., 2004, Science, 303, 672-676; Pal-Bhadra et al., 2004, Science, 303, 669-672; Allshire, 2002, Science, 297, 1818-1819; Volpe et al., 2002, Science, 297, 1833-1837; Jenuwein, 2002, Science, 297, 2215-2218; and Hall et al., 2002, Science, 297, 2232-2237).

[0301] It is contemplated that compounds and compositions of several embodiments provided herein can target CFB by a dsRNA-mediated gene silencing or RNAi mechanism, including, e.g., "hairpin" or stem-loop double-stranded RNA effector molecules in which a single RNA strand with self-complementary sequences is capable of assuming a double-stranded conformation, or duplex dsRNA effector molecules comprising two separate strands of RNA. In various embodiments, the dsRNA consists entirely of ribonucleotides or consists of a mixture of ribonucleotides and deoxynucleotides, such as the RNA/DNA hybrids disclosed, for example, by WO 00/63364, filed Apr. 19, 2000, or U.S. Ser. No. 60/130,377, filed Apr. 21, 1999. The dsRNA or dsRNA effector molecule may be a single molecule with a region of self-complementarity such that nucleotides in one segment of the molecule base pair with nucleotides in another segment of the molecule. In various embodiments, a dsRNA that consists of a single molecule consists entirely of ribonucleotides or includes a region of ribonucleotides that is complementary to a region of deoxyribonucleotides. Alternatively, the dsRNA may include two different strands that have a region of complementarity to each other.

[0302] In various embodiments, both strands consist entirely of ribonucleotides, one strand consists entirely of ribonucleotides and one strand consists entirely of deoxyribonucleotides, or one or both strands contain a mixture of ribonucleotides and deoxyribonucleotides. In certain embodiments, the regions of complementarity are at least 70, 80, 90, 95, 98, or 100% complementary to each other and to a target nucleic acid sequence. In certain embodiments, the region of the dsRNA that is present in a double-stranded conformation includes at least 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 50, 75, 100, 200, 500, 1000, 2000 or 5000 nucleotides or includes all of the nucleotides in a cDNA or other target nucleic acid sequence being represented in the dsRNA. In some embodiments, the dsRNA does not contain any single stranded regions, such as single stranded ends, or the dsRNA is a hairpin. In other embodiments, the dsRNA has one or more single stranded regions or overhangs. In certain embodiments, RNA/DNA hybrids include a DNA strand or region that is an antisense strand or region (e.g, has at least 70, 80, 90, 95, 98, or 100% complementarity to a target nucleic acid) and an RNA strand or region that is a sense strand or region (e.g, has at least 70, 80, 90, 95, 98, or 100% identity to a target nucleic acid), and vice versa.

[0303] In various embodiments, the RNA/DNA hybrid is made in vitro using enzymatic or chemical synthetic methods such as those described herein or those described in WO 00/63364, filed Apr. 19, 2000, or U.S. Ser. No. 60/130,377, filed Apr. 21, 1999. In other embodiments, a DNA strand synthesized in vitro is complexed with an RNA strand made in vivo or in vitro before, after, or concurrent with the transformation of the DNA strand into the cell. In yet other embodiments, the dsRNA is a single circular nucleic acid containing a sense and an antisense region, or the dsRNA includes a circular nucleic acid and either a second circular nucleic acid or a linear nucleic acid (see, for example, WO 00/63364, filed Apr. 19, 2000, or U.S. Ser. No. 60/130,377, filed Apr. 21, 1999.) Exemplary circular nucleic acids include lariat structures in which the free 5' phosphoryl group of a nucleotide becomes linked to the 2' hydroxyl group of another nucleotide in a loop back fashion.

[0304] In other embodiments, the dsRNA includes one or more modified nucleotides in which the 2' position in the sugar contains a halogen (such as fluorine group) or contains an alkoxy group (such as a methoxy group) which increases the half-life of the dsRNA in vitro or in vivo compared to the corresponding dsRNA in which the corresponding 2' position contains a hydrogen or an hydroxyl group. In yet other embodiments, the dsRNA includes one or more linkages between adjacent nucleotides other than a naturally-occurring phosphodiester linkage. Examples of such linkages include phosphoramide, phosphorothioate, and phosphorodithioate linkages. The dsRNAs may also be chemically modified nucleic acid molecules as taught in U.S. Pat. No. 6,673,661. In other embodiments, the dsRNA contains one or two capped strands, as disclosed, for example, by WO 00/63364, filed Apr. 19, 2000, or U.S. Ser. No. 60/130,377, filed Apr. 21, 1999.

[0305] In other embodiments, the dsRNA can be any of the at least partially dsRNA molecules disclosed in WO 00/63364, as well as any of the dsRNA molecules described in U.S. Provisional Application 60/399,998; and U.S. Provisional Application 60/419,532, and PCT/US2003/033466, the teaching of which is hereby incorporated by reference. Any of the dsRNAs may be expressed in vitro or in vivo using the methods described herein or standard methods, such as those described in WO 00/63364.

[0306] Occupancy

[0307] In certain embodiments, antisense compounds are not expected to result in cleavage or the target nucleic acid via RNase H or to result in cleavage or sequestration through the RISC pathway. In certain such embodiments, antisense activity may result from occupancy, wherein the presence of the hybridized antisense compound disrupts the activity of the target nucleic acid. In certain such embodiments, the antisense compound may be uniformly modified or may comprise a mix of modifications and/or modified and unmodified nucleosides.

Target Nucleic Acids, Target Regions and Nucleotide Sequences

[0308] Nucleotide sequences that encode Complement Factor B (CFB) include, without limitation, the following: GENBANK Accession No. NM_001710.5 (incorporated herein as SEQ ID NO: 1), GENBANK Accession No. NT_007592.15 truncated from nucleotides 31852000 to 31861000 (incorporated herein as SEQ ID NO: 2), GENBANK Accession No NW_001116486.1 truncated from nucleotides 536000 to 545000 (incorporated herein as SEQ ID NO: 3), GENBANK Accession No. XM_001113553.2 (incorporated herein as SEQ ID NO: 4), or GENBANK Accession No. NM_008198.2 (incorporated herein as SEQ ID NO: 5).

Hybridization

[0309] In some embodiments, hybridization occurs between an antisense compound disclosed herein and a CFB nucleic acid. The most common mechanism of hybridization involves hydrogen bonding (e.g., Watson-Crick, Hoogsteen or reversed Hoogsteen hydrogen bonding) between complementary nucleobases of the nucleic acid molecules.

[0310] Hybridization can occur under varying conditions. Stringent conditions are sequence-dependent and are determined by the nature and composition of the nucleic acid molecules to be hybridized.

[0311] Methods of determining whether a sequence is specifically hybridizable to a target nucleic acid are well known in the art. In certain embodiments, the antisense compounds provided herein are specifically hybridizable with a CFB nucleic acid.

Complementarity

[0312] An antisense compound and a target nucleic acid are complementary to each other when a sufficient number of nucleobases of the antisense compound can hydrogen bond with the corresponding nucleobases of the target nucleic acid, such that a desired effect will occur (e.g., antisense inhibition of a target nucleic acid, such as a CFB nucleic acid).

[0313] Non-complementary nucleobases between an antisense compound and a CFB nucleic acid may be tolerated provided that the antisense compound remains able to specifically hybridize to a target nucleic acid. Moreover, an antisense compound may hybridize over one or more segments of a CFB nucleic acid such that intervening or adjacent segments are not involved in the hybridization event (e.g., a loop structure, mismatch or hairpin structure).

[0314] In certain embodiments, the antisense compounds provided herein, or a specified portion thereof, are, or are at least, 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% complementary to a CFB nucleic acid, a target region, target segment, or specified portion thereof. Percent complementarity of an antisense compound with a target nucleic acid can be determined using routine methods.

[0315] For example, an antisense compound in which 18 of 20 nucleobases of the antisense compound are complementary to a target region, and would therefore specifically hybridize, would represent 90 percent complementarity. In this example, the remaining noncomplementary nucleobases may be clustered or interspersed with complementary nucleobases and need not be contiguous to each other or to complementary nucleobases. As such, an antisense compound which is 18 nucleobases in length having four noncomplementary nucleobases which are flanked by two regions of complete complementarity with the target nucleic acid would have 77.8% overall complementarity with the target nucleic acid and would thus fall within the scope of the present invention. Percent complementarity of an antisense compound with a region of a target nucleic acid can be determined routinely using BLAST programs (basic local alignment search tools) and PowerBLAST programs known in the art (Altschul et al., *J. Mol. Biol.,* 1990, 215, 403 410; Zhang and Madden, Genome Res., 1997, 7, 649 656). Percent homology, sequence identity or complementarity, can be determined by, for example, the Gap program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, Madison Wis.), using default settings, which uses the algorithm of Smith and Waterman (Adv. Appl. Math., 1981, 2, 482 489).

[0316] In certain embodiments, the antisense compounds provided herein, or specified portions thereof, are fully complementary (i.e. 100% complementary) to a target nucleic acid, or specified portion thereof. For example, an antisense compound may be fully complementary to a CFB nucleic acid, or a target region, or a target segment or target sequence thereof. As used herein, "fully complementary" means each nucleobase of an antisense compound is capable of precise base pairing with the corresponding nucleobases of a target nucleic acid. For example, a 20 nucleobase antisense compound is fully complementary to a target sequence that is 400 nucleobases long, so long as there is a corresponding 20 nucleobase portion of the target nucleic acid that is fully complementary to the antisense compound. Fully complementary can also be used in reference to a specified portion of the first and/or the second nucleic acid. For example, a 20 nucleobase portion of a 30 nucleobase antisense compound can be "fully complementary" to a target sequence that is 400 nucleobases long. The 20 nucleobase portion of the 30 nucleobase oligonucleotide is fully complementary to the target sequence if the target sequence has a corresponding 20 nucleobase portion wherein each nucleobase is complementary to the 20 nucleobase portion of the antisense compound. At the same time, the entire 30 nucleobase antisense compound may or may not be fully complementary to the target sequence, depending on whether the remaining 10 nucleobases of the antisense compound are also complementary to the target sequence.

[0317] The location of a non-complementary nucleobase may be at the 5' end or 3' end of the antisense compound. Alternatively, the non-complementary nucleobase or nucleobases may be at an internal position of the antisense compound. When two or more non-complementary nucleobases are present, they may be contiguous (i.e. linked) or non-

contiguous. In one embodiment, a non-complementary nucleobase is located in the wing segment of a gapmer antisense oligonucleotide.

[0318] In certain embodiments, antisense compounds that are, or are up to 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleobases in length comprise no more than 4, no more than 3, no more than 2, or no more than 1 non-complementary nucleobase(s) relative to a target nucleic acid, such as a CFB nucleic acid, or specified portion thereof

[0319] In certain embodiments, antisense compounds that are, or are up to 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleobases in length comprise no more than 6, no more than 5, no more than 4, no more than 3, no more than 2, or no more than 1 non-complementary nucleobase(s) relative to a target nucleic acid, such as a CFB nucleic acid, or specified portion thereof.

[0320] The antisense compounds provided also include those which are complementary to a portion of a target nucleic acid. As used herein, "portion" refers to a defined number of contiguous (i.e. linked) nucleobases within a region or segment of a target nucleic acid. A "portion" can also refer to a defined number of contiguous nucleobases of an antisense compound. In certain embodiments, the antisense compounds, are complementary to at least an 8 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 9 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 10 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least an 11 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 12 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 13 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 14 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 15 nucleobase portion of a target segment. Also contemplated are antisense compounds that are complementary to at least a 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more nucleobase portion of a target segment, or a range defined by any two of these values.

Identity

[0321] The antisense compounds provided herein may also have a defined percent identity to a particular nucleotide sequence, SEQ ID NO, or compound represented by a specific Isis number, or portion thereof. As used herein, an antisense compound is identical to the sequence disclosed herein if it has the same nucleobase pairing ability. For example, a RNA which contains uracil in place of thymidine in a disclosed DNA sequence would be considered identical to the DNA sequence since both uracil and thymidine pair with adenine. Shortened and lengthened versions of the antisense compounds described herein as well as compounds having non-identical bases relative to the antisense compounds provided herein also are contemplated. The non-identical bases may be adjacent to each other or dispersed throughout the antisense compound. Percent identity of an antisense compound is calculated according to the number of bases that have identical base pairing relative to the sequence to which it is being compared.

[0322] In certain embodiments, the antisense compounds, or portions thereof, are, or are at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to one or more of the antisense compounds or SEQ ID NOs, or a portion thereof, disclosed herein.

[0323] In certain embodiments, a portion of the antisense compound is compared to an equal length portion of the target nucleic acid. In certain embodiments, an 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleobase portion is compared to an equal length portion of the target nucleic acid.

[0324] In certain embodiments, a portion of the antisense oligonucleotide is compared to an equal length portion of the target nucleic acid. In certain embodiments, an 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleobase portion is compared to an equal length portion of the target nucleic acid.

Modifications

[0325] A nucleoside is a base-sugar combination. The nucleobase (also known as base) portion of the nucleoside is normally a heterocyclic base moiety. Nucleotides are nucleosides that further include a phosphate group covalently linked to the sugar portion of the nucleoside. For those nucleosides that include a pentofuranosyl sugar, the phosphate group can be linked to the 2', 3' or 5' hydroxyl moiety of the sugar. Oligonucleotides are formed through the covalent linkage of adjacent nucleosides to one another, to form a linear polymeric oligonucleotide. Within the oligonucleotide structure, the phosphate groups are commonly referred to as forming the internucleoside linkages of the oligonucleotide.

[0326] Modifications to antisense compounds encompass substitutions or changes to internucleoside linkages, sugar moieties, or nucleobases. Modified antisense compounds are often preferred over native forms because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid target, increased stability in the presence of nucleases, or increased inhibitory activity.

[0327] Chemically modified nucleosides may also be employed to increase the binding affinity of a shortened or truncated antisense oligonucleotide for its target nucleic acid. Consequently, comparable results can often be obtained with shorter antisense compounds that have such chemically modified nucleosides.

Modified Internucleoside Linkages

[0328] The naturally occuring internucleoside linkage of RNA and DNA is a 3' to 5' phosphodiester linkage. Antisense compounds having one or more modified, i.e. non-naturally occurring, internucleoside linkages are often selected over antisense compounds having naturally occurring internucleoside linkages because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for target nucleic acids, and increased stability in the presence of nucleases.

[0329] Oligonucleotides having modified internucleoside linkages include internucleoside linkages that retain a phosphorus atom as well as internucleoside linkages that do not have a phosphorus atom. Representative phosphorus containing internucleoside linkages include, but are not limited to, phosphodiesters, phosphotriesters, methylphosphonates, phosphoramidate, and phosphorothioates. Methods of prepa-

ration of phosphorous-containing and non-phosphorous-containing linkages are well known.

[0330] In certain embodiments, antisense compounds targeted to a CFB nucleic acid comprise one or more modified internucleoside linkages. In certain embodiments, the modified internucleoside linkages are phosphorothioate linkages. In certain embodiments, each internucleoside linkage of an antisense compound is a phosphorothioate internucleoside linkage.

Modified Sugar Moieties

[0331] Antisense compounds can optionally contain one or more nucleosides wherein the sugar group has been modified. Such sugar modified nucleosides may impart enhanced nuclease stability, increased binding affinity, or some other beneficial biological property to the antisense compounds. In certain embodiments, nucleosides comprise chemically modified ribofuranose ring moieties. Examples of chemically modified ribofuranose rings include without limitation, addition of substitutent groups (including 5' and 2' substituent groups, bridging of non-geminal ring atoms to form bicyclic nucleic acids (BNA), replacement of the ribosyl ring oxygen atom with S, N(R), or $C(R_1)(R_2)$ (R, R_1 and R_2 are each independently H, C_1-C_{12} alkyl or a protecting group) and combinations thereof. Examples of chemically modified sugars include 2'-F-5'-methyl substituted nucleoside (see PCT International Application WO 2008/101157 Published on Aug. 21, 2008 for other disclosed 5',2'-bis substituted nucleosides) or replacement of the ribosyl ring oxygen atom with S with further substitution at the 2'-position (see published U.S. Patent Application US2005-0130923, published on Jun. 16, 2005) or alternatively 5'-substitution of a BNA (see PCT International Application WO 2007/134181 Published on Nov. 22, 2007 wherein LNA is substituted with for example a 5'-methyl or a 5'-vinyl group).

[0332] Examples of nucleosides having modified sugar moieties include without limitation nucleosides comprising 5'-vinyl, 5'-methyl (R or S), 4'-S, 2'-F, 2'-OCH_3, 2'-OCH_2CH_3, 2'-OCH_2CH_2F and 2'-$O(CH_2)_2OCH_3$ substituent groups. The substituent at the 2' position can also be selected from allyl, amino, azido, thio, 0-allyl, O—C_1-C_{10} alkyl, OCF_3, OCH_2F, $O(CH_2)_2SCH_3$, $O(CH_2)_2$—O—$N(R_m)(R_n)$, O—CH_2—C(═O)—$N(R_m)(R_n)$, and O—CH_2—C(═O)—$N(R_1)$—$(CH_2)_2$—$N(R_m)(R_n)$, where each R_1, R_m and R_n is, independently, H or substituted or unsubstituted C_1-C_{10} alkyl.

[0333] As used herein, "bicyclic nucleosides" refer to modified nucleosides comprising a bicyclic sugar moiety. Examples of bicyclic nucleosides include without limitation nucleosides comprising a bridge between the 4' and the 2' ribosyl ring atoms. In certain embodiments, antisense compounds provided herein include one or more bicyclic nucleosides comprising a 4' to 2' bridge. Examples of such 4' to 2' bridged bicyclic nucleosides, include but are not limited to one of the formulae: 4'-(CH_2)—O-2' (LNA); 4'-(CH_2)—S-2; 4'-$(CH_2)_2$—O-2' (ENA); 4'-$CH(CH_3)$—O-2' (also referred to as constrained ethyl or cEt) and 4'-$CH(CH_2OCH_3)$—O-2' (and analogs thereof see U.S. Pat. No. 7,399,845, issued on Jul. 15, 2008); 4'-$C(CH_3)(CH_3)$—O-2' (and analogs thereof see published International Application WO/2009/006478, published Jan. 8, 2009); 4'-CH_2—$N(OCH_3)$-2' (and analogs thereof see published International Application WO/2008/150729, published Dec. 11, 2008); 4'-CH_2—O—$N(CH_3)$-2' (see published U.S. Patent Application US2004-0171570, published Sep. 2, 2004); 4'-CH_2—N(R)—O-2', wherein R is H, C_1-C_{12} alkyl, or a protecting group (see U.S. Pat. No. 7,427,672, issued on Sep. 23, 2008); 4'-CH_2—$C(H)(CH_3)$-2' (see Chattopadhyaya et al., *J. Org. Chem.,* 2009, 74, 118-134); and 4'-CH_2—$C(═CH_2)$-2' (and analogs thereof see published International Application WO 2008/154401, published on Dec. 8, 2008).

[0334] Further reports related to bicyclic nucleosides can also be found in published literature (see for example: Singh et al., *Chem. Commun.,* 1998, 4, 455-456; Koshkin et al., *Tetrahedron,* 1998, 54, 3607-3630; Wahlestedt et al., *Proc. Natl. Acad. Sci. U.S.A,* 2000, 97, 5633-5638; Kumar et al., *Bioorg. Med. Chem. Lett.,* 1998, 8, 2219-2222; Singh et al., *J. Org. Chem.,* 1998, 63, 10035-10039; Srivastava et al., *J. Am. Chem. Soc.,* 2007, 129(26) 8362-8379; Elayadi et al., *Curr. Opinion Invest. Drugs,* 2001, 2, 558-561; Braasch et al., *Chem. Biol.,* 2001, 8, 1-7; and Orum et al., *Curr. Opinion Mol. Ther.,* 2001, 3, 239-243; U.S. Pat. Nos. 6,268,490; 6,525,191; 6,670,461; 6,770,748; 6,794,499; 7,034,133; 7,053,207; 7,399,845; 7,547,684; and 7,696,345; U.S. Patent Publication No. US2008-0039618; US2009-0012281; U.S. Patent Ser. Nos. 60/989,574; 61/026,995; 61/026,998; 61/056,564; 61/086,231; 61/097,787; and 61/099,844; Published PCT International applications WO 1994/014226; WO 2004/106356; WO 2005/021570; WO 2007/134181; WO 2008/150729; WO 2008/154401; and WO 2009/006478. Each of the foregoing bicyclic nucleosides can be prepared having one or more stereochemical sugar configurations including for example α-L-ribofuranose and β-D-ribofuranose (see PCT international application PCT/DK98/00393, published on Mar. 25, 1999 as WO 99/14226).

[0335] In certain embodiments, bicyclic sugar moieties of BNA nucleosides include, but are not limited to, compounds having at least one bridge between the 4' and the 2' position of the pentofuranosyl sugar moiety wherein such bridges independently comprises 1 or from 2 to 4 linked groups independently selected from —$[C(R_a)(R_b)]_n$—, —$C(R_a)$=$C(R_b)$—, —$C(R_a)$=N—, —C(═O)—, —C(═NR_a)—, —C(═S)—, —O—, —$Si(R_a)_2$—, —S(═O)$_x$—, and —$N(R_a)$—;

[0336] wherein:

[0337] x is 0, 1, or 2;

[0338] n is 1, 2, 3, or 4;

[0339] each R_a and R_b is, independently, H, a protecting group, hydroxyl, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, heterocycle radical, substituted heterocycle radical, heteroaryl, substituted heteroaryl, C_5-C_7 alicyclic radical, substituted C_5-C_7 alicyclic radical, halogen, OJ_1, NJ_1J_2, SJ_1, N_3, $COOJ_1$, acyl (C(═O)—H), substituted acyl, CN, sulfonyl (S(═O)$_2$-J_1), or sulfoxyl (S(═O)-J_1); and

[0340] each J_1 and J_2 is, independently, H, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, acyl (C(═O)—H), substituted acyl, a heterocycle radical, a substituted heterocycle radical, C_1-C_{12} aminoalkyl, substituted C_1-C_{12} aminoalkyl or a protecting group.

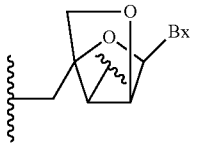
[0341] In certain embodiments, the bridge of a bicyclic sugar moiety is —$[C(R_a)(R_b)]_n$—, —$[C(R_a)(R_b)]_n$—O—, —$C(R_aR_b)$—N(R)—O— or —$C(R_aR_b)$—O—N(R)—. In certain embodiments, the bridge is 4'-CH_2-2', 4'-$(CH_2)_2$-2', 4'-$(CH_2)_3$-2', 4'-CH_2—O-2', 4'-$(CH_2)_2$—O-2', 4'-CH_2—O—

N(R)-2' and 4'-CH_2—N(R)—O-2'- wherein each R is, independently, H, a protecting group or C_1-C_{12} alkyl.

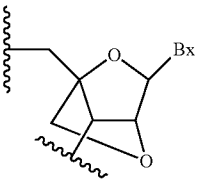
[0342] In certain embodiments, bicyclic nucleosides are further defined by isomeric configuration. For example, a nucleoside comprising a 4'-2' methylene-oxy bridge, may be in the α-L configuration or in the β-D configuration. Previously, α-L-methyleneoxy (4'-CH_2—O-2') BNA's have been incorporated into antisense oligonucleotides that showed antisense activity (Frieden et al., *Nucleic Acids Research,* 2003, 21, 6365-6372).

[0343] In certain embodiments, bicyclic nucleosides include, but are not limited to, (A) α-L-methyleneoxy (4'-CH_2—O-2') BNA, (B) β-D-methyleneoxy (4'-CH_2—O-2') BNA, (C) ethyleneoxy (4'-$(CH_2)_2$—O-2') BNA, (D) aminooxy (4'-CH_2—O—N(R)-2') BNA, (E) oxyamino (4'-CH_2—N(R)—O-2') BNA, and (F) methyl(methyleneoxy) (4'-$CH(CH_3)$—O-2') BNA, (G) methylene-thio (4'-CH_2—S-2') BNA, (H) methylene-amino (4'-CH_2—N(R)-2') BNA, (I) methyl carbocyclic (4'-CH_2—$CH(CH_3)$-2') BNA, (J) propylene carbocyclic (4'-$(CH_2)_3$-2') BNA and (K) vinyl BNA as depicted below:

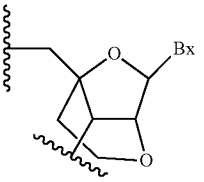
(A)



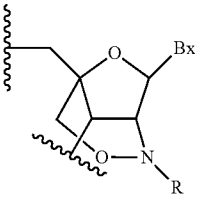
(B)



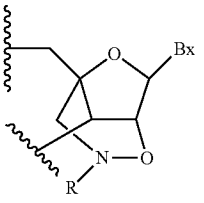
(C)



(D)

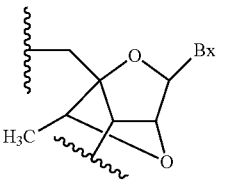


(E)

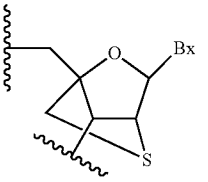


-continued

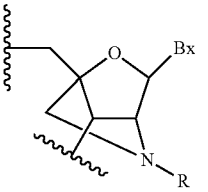
(F)



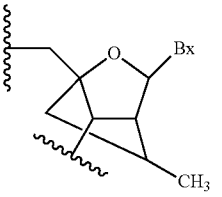
(G)



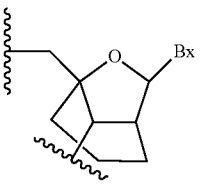
(H)



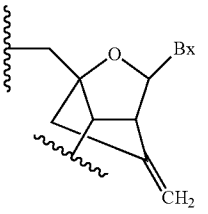
(I)



(J)



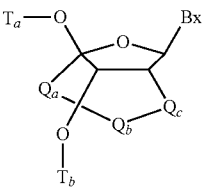
(K)



[0344] wherein Bx is the base moiety and R is independently H, a protecting group, C_1-C_{12} alkyl or C_1-C_{12} alkoxy.

[0345] In certain embodiments, bicyclic nucleosides are provided having Formula I:

I



wherein:

[0346] Bx is a heterocyclic base moiety;

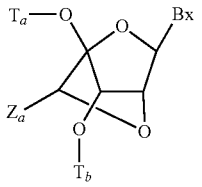
[0347] $-Q_a-Q_b-Q_c-$ is $—CH_2—N(R_c)—CH_2—$, $—C(=O)—N(R_c)—CH_2—$, $—CH_2—O—N(R_c)—$, $—CH_2—N(R_c)—O—$ or $—N(R_c)—O—CH_2$;

[0348] R_e is C_1-C_{12} alkyl or an amino protecting group; and

[0349] T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium.

[0350] In certain embodiments, bicyclic nucleosides are provided having Formula II:

II



wherein:

[0351] Bx is a heterocyclic base moiety;

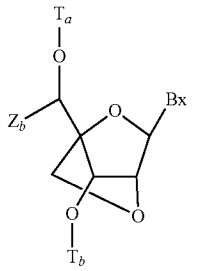
[0352] T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

[0353] Z_a is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, substituted C_1-C_6 alkyl, substituted C_2-C_6 alkenyl, substituted C_2-C_6 alkynyl, acyl, substituted acyl, substituted amide, thiol or substituted thio.

[0354] In one embodiment, each of the substituted groups is, independently, mono or poly substituted with substituent groups independently selected from halogen, oxo, hydroxyl, OJ_c, NJ_cJ_d, SJ_c, N_3, $OC(=X)J_e$, and $NJ_eC(=X)NJ_eJ_d$, wherein each J_e, J_d and J_e is, independently, H, C_1-C_6 alkyl, or substituted C_1-C_6 alkyl and X is O or NJ_e.

[0355] In certain embodiments, bicyclic nucleosides are provided having Formula III:

III



wherein:

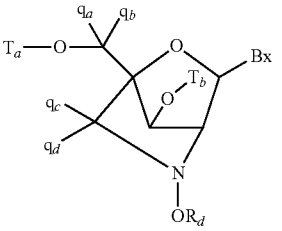
[0356] Bx is a heterocyclic base moiety;

[0357] T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

[0358] Z_b is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, substituted C_1-C_6 alkyl, substituted C_2-C_6 alkenyl, substituted C_2-C_6 alkynyl or substituted acyl (C(=O)—).

[0359] In certain embodiments, bicyclic nucleosides are provided having Formula IV:

IV



wherein:

[0360] Bx is a heterocyclic base moiety;

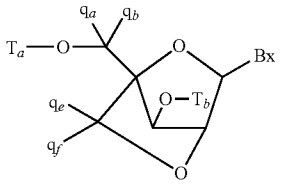
[0361] T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

[0362] R_d is C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl or substituted C_2-C_6 alkynyl;

[0363] each q_a, q_b, q_c and q_d is, independently, H, halogen, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl or substituted C_2-C_6 alkynyl, C_1-C_6 alkoxyl, substituted C_1-C_6 alkoxyl, acyl, substituted acyl, C_1-C_6 aminoalkyl or substituted C_1-C_6 aminoalkyl;

[0364] In certain embodiments, bicyclic nucleosides are provided having Formula V:

V



wherein:

[0365] Bx is a heterocyclic base moiety;

[0366] T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

[0367] q_a, q_b, q_e and q_f are each, independently, hydrogen, halogen, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, alkoxy, substituted C_1-C_{12} alkoxy, OJ_j, SJ_j, SOJ_j, SO_2J_j, NJ_jJ_k, N_3, CN, $C(=O)OJ_j$, $C(=O)NJ_jJ_k$, $C(=O)J_j$, $O—C(=O)NJ_jJ_k$, $N(H)C(=NH)NJ_jJ_k$, $N(H)C(=O)NJ_jJ_k$ or $N(H)C(=S)NJ_jJ_k$;

[0368] or q_e and q_f together are $=C(q_g)(q_h)$;

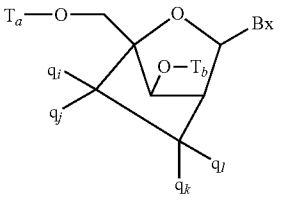
[0369] q_g and q_h are each, independently, H, halogen, C_1-C_{12} alkyl or substituted C_1-C_{12} alkyl.

[0370] The synthesis and preparation of the methyleneoxy (4'-CH_2—O-2') BNA monomers adenine, cytosine, guanine, 5-methyl-cytosine, thymine and uracil, along with their oligomerization, and nucleic acid recognition properties have been described (Koshkin et al., *Tetrahedron,* 1998, 54, 3607-

3630). BNAs and preparation thereof are also described in WO 98/39352 and WO 99/14226.

[0371] Analogs of methyleneoxy (4'-CH_2—O-2') BNA and 2'-thio-BNAs, have also been prepared (Kumar et al., *Bioorg. Med. Chem. Lett.,* 1998, 8, 2219-2222). Preparation of locked nucleoside analogs comprising oligodeoxyribonucleotide duplexes as substrates for nucleic acid polymerases has also been described (Wengel et al., WO 99/14226). Furthermore, synthesis of 2'-amino-BNA, a novel comformationally restricted high-affinity oligonucleotide analog has been described in the art (Singh et al., *J. Org. Chem.,* 1998, 63, 10035-10039). In addition, 2'-amino- and 2'-methylamino-BNA's have been prepared and the thermal stability of their duplexes with complementary RNA and DNA strands has been previously reported.

[0372] In certain embodiments, bicyclic nucleosides are provided having Formula VI:



VI

wherein:

[0373] Bx is a heterocyclic base moiety;

[0374] T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

[0375] each q_i, q_j, q_k and q_l is, independently, H, halogen, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_1-C_{12} alkoxyl, substituted C_1-C_{12} alkoxyl, OJ_j, SJ_j, SOJ_j, SO_2J_j, NJ_jJ_k, N_3, CN, C(=O)OJ_j, C(=O)NJ_jJ_k, C(=O)J_j, O—C(=O)NJ_jJ_k, N(H)C(=NH)NJ_jJ_k, N(H)C(=O)NJ_jJ_k or N(H)C(=S)NJ_jJ_k; and

[0376] q_i and q_j or q_l and q_k together are =C(q_g)(q_h), wherein q_g and q_h are each, independently, H, halogen, C_1-C_{12} alkyl or substituted C_1-C_{12} alkyl.

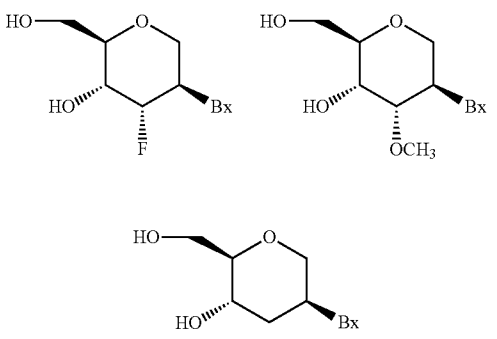
[0377] One carbocyclic bicyclic nucleoside having a 4'-$(CH_2)_3$-2' bridge and the alkenyl analog bridge 4'-CH=CH—CH_2-2' have been described (Freier et al., *Nucleic Acids Research,* 1997, 25(22), 4429-4443 and Albaek et al., *J. Org. Chem.,* 2006, 71, 7731-7740). The synthesis and preparation of carbocyclic bicyclic nucleosides along with their oligomerization and biochemical studies have also been described (Srivastava et al., *J. Am. Chem. Soc.,* 2007, 129(26), 8362-8379).

[0378] As used herein, "4'-2' bicyclic nucleoside" or "4' to 2' bicyclic nucleoside" refers to a bicyclic nucleoside comprising a furanose ring comprising a bridge connecting two carbon atoms of the furanose ring connects the 2' carbon atom and the 4' carbon atom of the sugar ring.

[0379] As used herein, "monocylic nucleosides" refer to nucleosides comprising modified sugar moieties that are not bicyclic sugar moieties. In certain embodiments, the sugar moiety, or sugar moiety analogue, of a nucleoside may be modified or substituted at any position.

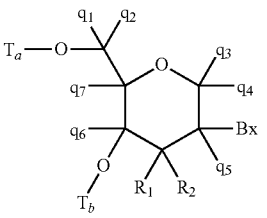
[0380] As used herein, "2'-modified sugar" means a furanosyl sugar modified at the 2' position. In certain embodiments, such modifications include substituents selected from: a halide, including, but not limited to substituted and unsubstituted alkoxy, substituted and unsubstituted thioalkyl, substituted and unsubstituted amino alkyl, substituted and unsubstituted alkyl, substituted and unsubstituted allyl, and substituted and unsubstituted alkynyl. In certain embodiments, 2' modifications are selected from substituents including, but not limited to: $O[(CH_2)_nO]_mCH_3$, $O(CH_2)_nNH_2$, $O(CH_2)$—CH_3, $O(CH_2)_nF$, $O(CH_2)_nONH_2$, $OCH_2C(=O)N(H)CH_3$, and $O(CH_2)_nON[(CH_2)_nCH_3]_2$, where n and m are from 1 to about 10. Other 2'-substituent groups can also be selected from: C_1-C_{12} alkyl, substituted alkyl, alkenyl, alkynyl, alkaryl, aralkyl, O-alkaryl or O-aralkyl, SH, SCH_3, OCN, Cl, Br, CN, F, CF_3, OCF_3, $SOCH_3$, SO_2CH_3, ONO_2, NO_2, N_3, NH_2, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, substituted silyl, an RNA cleaving group, a reporter group, an intercalator, a group for improving pharmacokinetic properties, or a group for improving the pharmacodynamic properties of an antisense compound, and other substituents having similar properties. In certain embodiments, modified nucleosides comprise a 2'-MOE side chain (Baker et al., *J. Biol. Chem.,* 1997, 272, 11944-12000). Such 2'-MOE substitution have been described as having improved binding affinity compared to unmodified nucleosides and to other modified nucleosides, such as 2'-O-methyl, O-propyl, and O-aminopropyl. Oligonucleotides having the 2'-MOE substituent also have been shown to be antisense inhibitors of gene expression with promising features for in vivo use (Martin, *Helv. Chim. Acta,* 1995, 78, 486-504; Altmann et al., *Chimia,* 1996, 50, 168-176; Altmann et al., *Biochem. Soc. Trans.,* 1996, 24, 630-637; and Altmann et al., *Nucleosides Nucleotides,* 1997, 16, 917-926).

[0381] As used herein, a "modified tetrahydropyran nucleoside" or "modified THP nucleoside" means a nucleoside having a six-membered tetrahydropyran "sugar" substituted in for the pentofuranosyl residue in normal nucleosides (a sugar surrogate). Modified THP nucleosides include, but are not limited to, what is referred to in the art as hexitol nucleic acid (HNA), anitol nucleic acid (ANA), manitol nucleic acid (MNA) (see Leumann, *Bioorg. Med. Chem.,* 2002, 10, 841-854) or fluoro HNA (F-HNA) having a tetrahydropyran ring system as illustrated below:



[0382] In certain embodiments, sugar surrogates are selected having Formula VII:

VII



wherein independently for each of said at least one tetrahydropyran nucleoside analog of Formula VII:

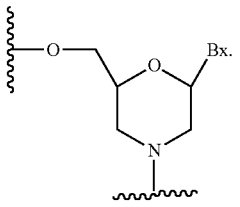
[0383] Bx is a heterocyclic base moiety;

[0384] T_a and T_b are each, independently, an internucleoside linking group linking the tetrahydropyran nucleoside analog to the antisense compound or one of T_a and T_b is an internucleoside linking group linking the tetrahydropyran nucleoside analog to the antisense compound and the other of T_a and T_b is H, a hydroxyl protecting group, a linked conjugate group or a 5' or 3'-terminal group;

[0385] q_1, q_2, q_3, q_4, q_5, q_6 and q_7 are each independently, H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl or substituted C_2-C_6 alkynyl; and each of R_1 and R_2 is selected from hydrogen, hydroxyl, halogen, substituted or unsubstituted alkoxy, NJ_1J_2, SJ_1, N_3, $OC(=X)J_1$, $OC(=X)NJ_1J_2$, $NJ_3C(=X)NJ_1J_2$ and CN, wherein X is O, S or NJ_1 and each J_1, J_2 and J_3 is, independently, H or C_1-C_6 alkyl.

[0386] In certain embodiments, the modified THP nucleosides of Formula VII are provided wherein q_1, q_2, q_3, q_4, q_5, q_6 and q_7 are each H. In certain embodiments, at least one of q_1, q_2, q_3, q_4, q_5, q_6 and q_7 is other than H. In certain embodiments, at least one of q_1, q_2, q_3, q_4, q_5, q_6 and q_7 is methyl. In certain embodiments, THP nucleosides of Formula VII are provided wherein one of R_1 and R_2 is fluoro. In certain embodiments, R_1 is fluoro and R_2 is H; R_1 is methoxy and R_2 is H, and R_1 is methoxyethoxy and R_2 is H.

[0387] In certain embodiments, sugar surrogates comprise rings having more than 5 atoms and more than one heteroatom. For example nucleosides comprising morpholino sugar moieties and their use in oligomeric compounds has been reported (see for example: Braasch et al., Biochemistry, 2002, 41, 4503-4510; and U.S. Pat. Nos. 5,698,685; 5,166,315; 5,185,444; and U.S. Pat. No. 5,034,506). As used here, the term "morpholino" means a sugar surrogate having the following formula:

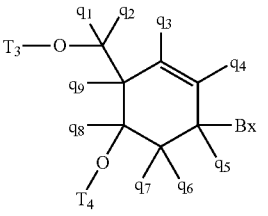


In certain embodiments, morpholinos may be modified, for example by adding or altering various substituent groups from the above morpholino structure. Such sugar surrogates are referred to herein as "modified morpholinos."

[0388] Combinations of modifications are also provided without limitation, such as 2'-F-5'-methyl substituted nucleosides (see PCT International Application WO 2008/101157 published on Aug. 21, 2008 for other disclosed 5', 2'-bis substituted nucleosides) and replacement of the ribosyl ring oxygen atom with S and further substitution at the 2'-position (see published U.S. Patent Application US2005-0130923, published on Jun. 16, 2005) or alternatively 5'-substitution of a bicyclic nucleic acid (see PCT International Application WO 2007/134181, published on Nov. 22, 2007 wherein a 4'-CH_2—O-2' bicyclic nucleoside is further substituted at the 5' position with a 5'-methyl or a 5'-vinyl group). The synthesis and preparation of carbocyclic bicyclic nucleosides along with their oligomerization and biochemical studies have also been described (see, e.g., Srivastava et al., *J. Am. Chem. Soc.* 2007, 129(26), 8362-8379).

[0389] In certain embodiments, antisense compounds comprise one or more modified cyclohexenyl nucleosides, which is a nucleoside having a six-membered cyclohexenyl in place of the pentofuranosyl residue in naturally occurring nucleosides. Modified cyclohexenyl nucleosides include, but are not limited to those described in the art (see for example commonly owned, published PCT Application WO 2010/036696, published on Apr. 10, 2010, Robeyns et al., *J. Am. Chem. Soc.*, 2008, 130(6), 1979-1984; Horvath et al., *Tetrahedron Letters*, 2007, 48, 3621-3623; Nauwelaerts et al., *J. Am. Chem. Soc.*, 2007, 129(30), 9340-9348; Gu et al., *Nucleosides, Nucleotides & Nucleic Acids*, 2005, 24(5-7), 993-998; Nauwelaerts et al., *Nucleic Acids Research*, 2005, 33(8), 2452-2463; Robeyns et al., *Acta Crystallographica, Section F: Structural Biology and Crystallization Communications*, 2005, F61(6), 585-586; Gu et al., *Tetrahedron*, 2004, 60(9), 2111-2123; Gu et al., *Oligonucleotides*, 2003, 13(6), 479-489; Wang et al., *J. Org. Chem.*, 2003, 68, 4499-4505; Verbeure et al., *Nucleic Acids Research*, 2001, 29(24), 4941-4947; Wang et al., *J. Org. Chem.*, 2001, 66, 8478-82; Wang et al., *Nucleosides, Nucleotides & Nucleic Acids*, 2001, 20(4-7), 785-788; Wang et al., J. *Am. Chem.*, 2000, 122, 8595-8602; Published PCT application, WO 06/047842; and Published PCT Application WO 01/049687; the text of each is incorporated by reference herein, in their entirety). Certain modified cyclohexenyl nucleosides have Formula X.

X



[0390] wherein independently for each of said at least one cyclohexenyl nucleoside analog of Formula X:

[0391] Bx is a heterocyclic base moiety;

[0392] T_3 and T_4 are each, independently, an internucleoside linking group linking the cyclohexenyl nucleoside analog to an antisense compound or one of T_3 and T_4 is an internucleoside linking group linking the tetrahydropyran nucleoside analog to an antisense compound and the other of

T_3 and T_4 is H, a hydroxyl protecting group, a linked conjugate group, or a 5'- or 3'-terminal group; and

[0393] q_1, q_2, q_3, q_4, q_5, q_6, q_7, q_8 and q_9 are each, independently, H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl, substituted C_2-C_6 alkynyl or other sugar substituent group.

[0394] As used herein, "2'-modified" or "2'-substituted" refers to a nucleoside comprising a sugar comprising a substituent at the 2' position other than H or OH. 2'-modified nucleosides, include, but are not limited to, bicyclic nucleosides wherein the bridge connecting two carbon atoms of the sugar ring connects the 2' carbon and another carbon of the sugar ring; and nucleosides with non-bridging 2' substituents, such as allyl, amino, azido, thio, O-allyl, O—C_1-C_{10} alkyl, —OCF_3, O—$(CH_2)_2$—O—CH_3, 2'-$O(CH_2)_2SCH_3$, O—$(CH_2)_2$—O—$N(R_m)(R_n)$, or O—CH_2—C(=O)—$N(R_m)(R_n)$, where each R_m and R_n is, independently, H or substituted or unsubstituted C_1-C_{10} alkyl. 2'-modified nucleosides may further comprise other modifications, for example at other positions of the sugar and/or at the nucleobase.

[0395] As used herein, "2'-F" refers to a nucleoside comprising a sugar comprising a fluoro group at the 2' position of the sugar ring.

[0396] As used herein, "2'-OMe" or "2'-OCH_3" or "2'-O-methyl" each refers to a nucleoside comprising a sugar comprising an —OCH_3 group at the 2' position of the sugar ring.

[0397] As used herein, "MOE" or "2'-MOE" or "2'-$OCH_2CH_2OCH_3$" or "2'-O-methoxyethyl" each refers to a nucleoside comprising a sugar comprising a —$OCH_2CH_2OCH_3$ group at the 2' position of the sugar ring.

[0398] As used herein, "oligonucleotide" refers to a compound comprising a plurality of linked nucleosides. In certain embodiments, one or more of the plurality of nucleosides is modified. In certain embodiments, an oligonucleotide comprises one or more ribonucleosides (RNA) and/or deoxyribonucleosides (DNA).

[0399] Many other bicyclo and tricyclo sugar surrogate ring systems are also known in the art that can be used to modify nucleosides for incorporation into antisense compounds (see for example review article: Leumann, *Bioorg. Med. Chem.*, 2002, 10, 841-854). Such ring systems can undergo various additional substitutions to enhance activity.

[0400] Methods for the preparations of modified sugars are well known to those skilled in the art. Some representative U.S. patents that teach the preparation of such modified sugars include without limitation, U.S.: 4,981,957; 5,118,800; 5,319,080; 5,359,044; 5,393,878; 5,446,137; 5,466,786; 5,514,785; 5,519,134; 5,567,811; 5,576,427; 5,591,722; 5,597,909; 5,610,300; 5,627,053; 5,639,873; 5,646,265; 5,670,633; 5,700,920; 5,792,847 and 6,600,032 and International Application PCT/US2005/019219, filed Jun. 2, 2005 and published as WO 2005/121371 on Dec. 22, 2005, and each of which is herein incorporated by reference in its entirety.

[0401] In nucleotides having modified sugar moieties, the nucleobase moieties (natural, modified or a combination thereof) are maintained for hybridization with an appropriate nucleic acid target.

[0402] In certain embodiments, antisense compounds comprise one or more nucleosides having modified sugar moieties. In certain embodiments, the modified sugar moiety is 2'-MOE. In certain embodiments, the 2'-MOE modified nucleosides are arranged in a gapmer motif. In certain embodiments, the modified sugar moiety is a bicyclic nucleoside having a (4'-$CH(CH_3)$—O-2') bridging group. In certain embodiments, the (4'-$CH(CH_3)$—O-2') modified nucleosides are arranged throughout the wings of a gapmer motif.

Modified Nucleobases

[0403] Nucleobase (or base) modifications or substitutions are structurally distinguishable from, yet functionally interchangeable with, naturally occurring or synthetic unmodified nucleobases. Both natural and modified nucleobases are capable of participating in hydrogen bonding. Such nucleobase modifications can impart nuclease stability, binding affinity or some other beneficial biological property to antisense compounds. Modified nucleobases include synthetic and natural nucleobases such as, for example, 5-methylcytosine (5-me-C). Certain nucleobase substitutions, including 5-methylcytosine substitutions, are particularly useful for increasing the binding affinity of an antisense compound for a target nucleic acid. For example, 5-methylcytosine substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2° C. (Sanghvi, Y. S., Crooke, S. T. and Lebleu, B., eds., Antisense Research and Applications, CRC Press, Boca Raton, 1993, pp. 276-278).

[0404] Additional modified nucleobases include 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-halouracil and cytosine, 5-propynyl (—C≡C—CH3) uracil and cytosine and other alkynyl derivatives of pyrimidine bases, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl and other 8-substituted adenines and guanines, 5-halo particularly 5-bromo, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylguanine and 7-methyladenine, 2-F-adenine, 2-amino-adenine, 8-azaguanine and 8-azaadenine, 7-deazaguanine and 7-deazaadenine and 3-deazaguanine and 3-deazaadenine.

[0405] Heterocyclic base moieties can also include those in which the purine or pyrimidine base is replaced with other heterocycles, for example 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine and 2-pyridone. Nucleobases that are particularly useful for increasing the binding affinity of antisense compounds include 5-substituted pyrimidines, 6-azapyrimidines and N-2, N-6 and 0-6 substituted purines, including 2 aminopropyladenine, 5-propynyluracil and 5-propynylcytosine.

[0406] In certain embodiments, antisense compounds targeted to a CFB nucleic acid comprise one or more modified nucleobases. In certain embodiments, shortened or gap-widened antisense oligonucleotides targeted to a CFB nucleic acid comprise one or more modified nucleobases. In certain embodiments, the modified nucleobase is 5-methylcytosine. In certain embodiments, each cytosine is a 5-methylcytosine.

Conjugated Antisense Compounds

[0407] Antisense compounds may be covalently linked to one or more moieties or conjugates which enhance the activity, cellular distribution or cellular uptake of the resulting antisense oligonucleotides. Typical conjugate groups include cholesterol moieties and lipid moieties. Additional conjugate groups include carbohydrates, phospholipids, biotin, phenazine, folate, phenanthridine, anthraquinone, acridine, fluoresceins, rhodamines, coumarins, and dyes.

[0408] Antisense compounds can also be modified to have one or more stabilizing groups that are generally attached to one or both termini of antisense compounds to enhance properties such as, for example, nuclease stability. Included in stabilizing groups are cap structures. These terminal modifications protect the antisense compound having terminal nucleic acid from exonuclease degradation, and can help in delivery and/or localization within a cell. The cap can be present at the 5'-terminus (5'-cap), or at the 3'-terminus (3'-cap), or can be present on both termini. Cap structures are well known in the art and include, for example, inverted deoxy abasic caps. Further 3' and 5'-stabilizing groups that can be used to cap one or both ends of an antisense compound to impart nuclease stability include those disclosed in WO 03/004602 published on Jan. 16, 2003.

[0409] In certain embodiments, antisense compounds, including, but not limited to those particularly suited for use as ssRNA, are modified by attachment of one or more conjugate groups. In general, conjugate groups modify one or more properties of the attached oligonucleotide, including but not limited to pharmacodynamics, pharmacokinetics, stability, binding, absorption, cellular distribution, cellular uptake, charge and clearance. Conjugate groups are routinely used in the chemical arts and are linked directly or via an optional conjugate linking moiety or conjugate linking group to a parent compound such as an oligonucleotide. Conjugate groups includes without limitation, intercalators, reporter molecules, polyamines, polyamides, polyethylene glycols, thioethers, polyethers, cholesterols, thiocholesterols, cholic acid moieties, folate, lipids, phospholipids, biotin, phenazine, phenanthridine, anthraquinone, adamantane, acridine, fluoresceins, rhodamines, coumarins and dyes. Certain conjugate groups have been described previously, for example: cholesterol moiety (Letsinger et al., Proc. Natl. Acad. Sci. USA, 1989, 86, 6553-6556), cholic acid (Manoharan et al., Bioorg. Med. Chem. Let., 1994, 4, 1053-1060), a thioether, e.g., hexyl-S-tritylthiol (Manoharan et al., Ann. N.Y. Acad. Sci., 1992, 660, 306-309; Manoharan et al., Bioorg. Med. Chem. Let., 1993, 3, 2765-2770), a thiocholesterol (Oberhauser et al., Nucl. Acids Res., 1992, 20, 533-538), an aliphatic chain, e.g., do-decan-diol or undecyl residues (Saison-Behmoaras et al., EMBO J., 1991, 10, 1111-1118; Kabanov et al., FEBS Lett., 1990, 259, 327-330; Svinarchuk et al., Biochimie, 1993, 75, 49-54), a phospholipid, e.g., di-hexadecyl-rac-glycerol or triethyl-ammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate (Manoharan et al., Tetrahedron Lett., 1995, 36, 3651-3654; Shea et al., Nucl. Acids Res., 1990, 18, 3777-3783), a polyamine or a polyethylene glycol chain (Manoharan et al., Nucleosides & Nucleotides, 1995, 14, 969-973), or adamantane acetic acid (Manoharan et al., Tetrahedron Lett., 1995, 36, 3651-3654), a palmityl moiety (Mishra et al., Biochim Biophys. Acta, 1995, 1264, 229-237), or an octadecylamine or hexylamino-carbonyl-oxycholesterol moiety (Crooke et al., J. Pharmacol. Exp. Ther., 1996, 277, 923-937).

[0410] For additional conjugates including those useful for ssRNA and their placement within antisense compounds, see e.g., U.S. Application No. 61/583,963.

In Vitro Testing of Antisense Oligonucleotides

[0411] Described herein are methods for treatment of cells with antisense oligonucleotides, which can be modified appropriately for treatment with other antisense compounds.

[0412] Cells may be treated with antisense oligonucleotides when the cells reach approximately 60-80% confluency in culture.

[0413] One reagent commonly used to introduce antisense oligonucleotides into cultured cells includes the cationic lipid transfection reagent LIPOFECTIN (Invitrogen, Carlsbad, Calif.). Antisense oligonucleotides may be mixed with LIPOFECTIN in OPTI-MEM 1 (Invitrogen, Carlsbad, Calif.) to achieve the desired final concentration of antisense oligonucleotide and a LIPOFECTIN concentration that may range from 2 to 12 ug/mL per 100 nM antisense oligonucleotide.

[0414] Another reagent used to introduce antisense oligonucleotides into cultured cells includes LIPOFECTAMINE (Invitrogen, Carlsbad, Calif.). Antisense oligonucleotide is mixed with LIPOFECTAMINE in OPTI-MEM 1 reduced serum medium (Invitrogen, Carlsbad, Calif.) to achieve the desired concentration of antisense oligonucleotide and a LIPOFECTAMINE concentration that may range from 2 to 12 ug/mL per 100 nM antisense oligonucleotide.

[0415] Another technique used to introduce antisense oligonucleotides into cultured cells includes electroporation.

[0416] Yet another technique used to introduce antisense oligonucleotides into cultured cells includes free uptake of the oligonucleotides by the cells.

[0417] Cells are treated with antisense oligonucleotides by routine methods. Cells may be harvested 16-24 hours after antisense oligonucleotide treatment, at which time RNA or protein levels of target nucleic acids are measured by methods known in the art and described herein. In general, when treatments are performed in multiple replicates, the data are presented as the average of the replicate treatments.

[0418] The concentration of antisense oligonucleotide used varies from cell line to cell line. Methods to determine the optimal antisense oligonucleotide concentration for a particular cell line are well known in the art. Antisense oligonucleotides are typically used at concentrations ranging from 1 nM to 300 nM when transfected with LIPOFECTAMINE. Antisense oligonucleotides are used at higher concentrations ranging from 625 to 20,000 nM when transfected using electroporation.

RNA Isolation

[0419] RNA analysis can be performed on total cellular RNA or poly(A)+mRNA. Methods of RNA isolation are well known in the art. RNA is prepared using methods well known in the art, for example, using the TRIZOL Reagent (Invitrogen, Carlsbad, Calif.) according to the manufacturer's recommended protocols.

Certain Indications

[0420] Certain embodiments provided herein relate to methods of treating, preventing, or ameliorating a disease associated with dysregulation of the complement alternative pathway in a subject by administration of a CFB specific inhibitor, such as an antisense compound targeted to CFB.

[0421] Examples of renal diseases associated with dysregulation of the complement alternative pathway treatable, preventable, and/or ameliorable with the methods provided herein include C3 glomerulopathy, atypical hemolytic uremic syndrome (aHUS), dense deposit disease (DDD; also known as MPGN Type II or C3Neph), and CFHR5 nephropathy.

[0422] Additional renal diseases associated with dysregulation of the complement alternative pathway treatable, pre-

ventable, and/or ameliorable with the methods provided herein include IgA nephropathy; mesangiocapillary (membranoproliferative) glomerulonephritis (MPGN); autoimmune disorders including lupus nephritis and systemic lupus erythematosus (SLE); infection-induced glomerulonephritis (also known as Postinfectious glomerulonephritis); and renal ischemia-reperfusion injury, for example post-transplant renal ischemia-reperfusion injury.

[0423] Examples of non-renal disorders associated with dysregulation of the complement alternative pathway treatable and/or preventable with the methods provided herein include ocular diseases such as macular degeneration, for example age-related macular degeneration (AMD), including wet AMD and dry AMD, such as Geographic Atrophy; neuromyelitis optica; corneal disease, such as corneal inflammation; autoimmune uveitis; and diabetic retinopathy. It has been reported that complement system is involved in ocular diseases. Jha P, et al., *Mol Immunol* (2007) 44(16): 3901-3908. Additional examples of non-renal disorders associated with dysregulation of the complement alternative pathway treatable and/or preventable with the methods provided herein include ANCA-assocaited vasculitis, antiphospholipid syndrome (also known as antiphospholipid antibody syndrome (APS)), asthma, rheumatoid arthritis, Myasthenia Gravis, and multiple sclerosis.

[0424] Certain embodiments provided herein relate to methods of treating, preventing, or ameliorating a renal disease associated with dysregulation of the complement alternative pathway in a subject by administration of a CFB specific inhibitor, such as an antisense compound targeted to CFB. In certain embodiments, the renal disease is lupus nephritis, systemic lupus erythematosus (SLE), dense deposit disease (DDD), C3 glomerulonephritis (C3GN), CFHR5 nephropathy, or atypical hemolytic uremic syndrome (aHUS), or any combination thereof.

[0425] Certain embodiments provided herein relate to methods of treating, preventing, or ameliorating macular degeneration, such as age-related macular degeneration (AMD), in a subject by administration of a CFB specific inhibitor, such as an antisense compound targeted to CFB. In certain embodiments, the AMD is wet AMD or dry AMD. In certain embodiments, dry AMD can be Geographic Atrophy. Studies have demonstrated the association of complement alternative pathway dysregulation and AMD. Complement components are common constituents of ocular drusen, the extracellular material that accumulates in the macula of AMD patients. Furthermore, it has been reported that CFH and CFB variants account for nearly 75% of AMD cases in northern Europe and North America. It has also been found that a specific CFB polymorphism confers protection against AMD. Patel, N. et al., Eye (2008) 22(6):768-76. Additionally, CFB homozygous null mice have lower complement pathway activity, exhibit smaller ocular lesions, and choroidal neovascularization (CNV) after laser photocoagulation. Rohrer, B. et al., *Invest Ophthalmol Vis Sci.* (2009) 50(7):3056-64. Furthermore, CFB siRNA treatment protects mice from laser induced CNV. Bora, N S et al., *J Immunol.* (2006) 177(3): 1872-8. Studies have also shown that the kidney and eye share developmental pathways and structural features including basement membrane collagen IV protomer composition and vascularity. Savige et al., *J Am Soc Nephrol.* (2011) 22(8): 1403-15. There is evidence that the complement pathway is involved in renal and ocular diseases. For instance, inherited complement regulatory protein deficiency causes predisposition to atypical hemolytic uremic syndrome and AMD. Richards A et al., *Adv Immunol.* (2007) 96:141-77. Additionally, chronic kidney disease has been associated with AMD. Nitsch, D. et al., *Ophthalmic Epidemiol.* (2009) 16(3):181-6; Choi, J. et al, *Ophthalmic Epidemiol.* (2011) 18(6):259-63. Dense deposit disease (DDD), a kidney disease associated with dysregulated complement alternative pathway, is characterized by acute nephritic syndrome and ocular drusen. Cruz and Smith, *GeneReviews* (2007) Jul. 20. Moreover, mice harboring genetic deletion of a component of the complement alternative pathway have coexisting renal and ocular disease phenotypes. It has been reported that CFH homozygous null mice develop DDD and present retinal abnormalities and visual dysfunction. Pickering et al., *Nat Genet.* (2002) 31(4): 424-8. Mouse models of renal diseases associated with dysregulation of the complement alternative pathway are also accepted as models of AMD. Pennesi M E et al., *Mol Apects Med* (2012) 33:487-509. CFH null mice, for example, are an accepted model for renal diseases, such as DDD, and AMD. Furthermore, it has been reported that AMD is associated with the systemic source of complement factors, which accumulate locally in the eye to drive alternative pathway complement activation. Loyet et al., *Invest Ophthalmol Vis Sci.* (2012) 53(10):6628-37.

EXAMPLES

Non-Limiting Disclosure and Incorporation by Reference

[0426] While certain compounds, compositions and methods described herein have been described with specificity in accordance with certain embodiments, the following examples serve only to illustrate the compounds described herein and are not intended to limit the same. Each of the references recited in the present application is incorporated herein by reference in its entirety.

[0427] It is understood that the sequence set forth in each SEQ ID NO in the examples contained herein is independent of any modification to a sugar moiety, an internucleoside linkage, or a nucleobase. As such, antisense compounds defined by a SEQ ID NO may comprise, independently, one or more modifications to a sugar moiety, an internucleoside linkage, or a nucleobase. Antisense compounds described by Isis Number (Isis No) indicate a combination of nucleobase sequence and motif.

Example 1

Antisense Inhibition of Human Complement Factor B (CFB) in HepG2 Cells by MOE Gapmers

[0428] Antisense oligonucleotides were designed targeting human Complement Factor B (CFB) nucleic acid and were tested for their effects on CFB mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 20,000 cells per well were transfected using electroporation with 4,500 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 (forward sequence AGTCTCTGTGGCATGGTTTGG, designated herein as SEQ ID NO: 810; reverse sequence GGGCGAATGACTGAGATCTTG,

designated herein as SEQ ID NO: 811; probe sequence TACCGATTACCACAAGCAACCATGGCA, designated herein as SEQ ID NO: 812) was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0429] The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 5-10-5 MOE gapmers. The 5-10-5 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P═S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in the Tables below is targeted to either the human CFB mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_001710.5) or the human CFB genomic sequence, designated herein as SEQ ID NO: 2 (GENBANK Accession No. NT_007592.15 truncated from nucleotides 31852000 to 31861000), or both. 'n/a.' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity.

TABLE 1

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target Region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532608	20	39	Exon 1	GCTGAGCTGCCAGTCAAGGA	36	1741	1760	6
532609	26	45	Exon 1	GGCCCCGCTGAGCTGCCAGT	16	1747	1766	7
532610	45	64	Exon 1	CGGAACATCCAAGCGGGAGG	11	1766	1785	8
532611	51	70	Exon 1	CTTTCCCGGAACATCCAAGC	26	1772	1791	9
532612	100	119	Exon 1	ATCTGTGTTCTGGCACCTGC	25	1821	1840	10
532613	148	167	Exon 1	GTCACATTCCCTTCCCCTGC	39	1869	1888	11
532614	154	173	Exon 1	GACCTGGTCACATTCCCTTC	71	1875	1894	12
532615	160	179	Exon 1	GACCTAGACCTGGTCACATT	35	1881	1900	13
532616	166	185	Exon 1	ACTCCAGACCTAGACCTGGT	39	1887	1906	14
532617	172	191	Exon 1	GCTGAAACTCCAGACCTAGA	27	1893	1912	15
532618	178	197	Exon 1	GTCCAAGCTGAAACTCCAGA	29	1899	1918	16
532619	184	203	Exon 1	CTCAGTGTCCAAGCTGAAAC	21	1905	1924	17
532620	246	265	Exon 1	AGGAGAGAAGCTGGGCCTGG	31	1967	1986	18
532621	252	271	Exon 1	GAAGGCAGGAGAGAAGCTGG	25	1973	1992	19
532622	336	355	Exon 1-2 Junction	GTGGTGGTCACACCTCCAGA	28	n/a	n/a	20
532623	381	400	Exon 2	CCCTCCAGAGAGCAGGATCC	22	2189	2208	21
532624	387	406	Exon 2	TCTACCCCCTCCAGAGAGCA	37	2195	2214	22
532625	393	412	Exon 2	TTGATCTCTACCCCCTCCAG	30	2201	2220	23
532626	417	436	Exon 2	TGGAGAAGTCGGAAGGAGCC	35	2225	2244	24
532627	423	442	Exon 2	CCCTCTTGGAGAAGTCGGAA	37	2231	2250	25
532628	429	448	Exon 2	GCCTGGCCCTCTTGGAGAAG	0	2237	2256	26
532629	435	454	Exon 2	TCCAGTGCCTGGCCCTCTTG	26	2243	2262	27
532630	458	477	Exon 2	AGAAGCCAGAAGGACACACG	30	2266	2285	28
532631	464	483	Exon 2	ACGGGTAGAAGCCAGAAGGA	43	2272	2291	29
532632	480	499	Exon 2	CGTGTCTGCACAGGGTACGG	57	2288	2307	30

TABLE 1-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target Region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532633	513	532	Exon 2	AGGGTGCTCCAGGACCCCGT	27	2321	2340	31
532634	560	579	Exon 2-3 Junction	TTGCTCTGCACTCTGCCTTC	41	n/a	n/a	32
532635	600	619	Exon 3	TATTCCCCGTTCTCGAAGTC	67	2808	2827	33
532636	626	645	Exon 3	CATTGTAGTAGGGAGACCGG	24	2834	2853	34
532637	632	651	Exon 3	CACTCACATTGTAGTAGGGA	49	2840	2859	35
532638	638	657	Exon 3	TCTCATCACTCACATTGTAG	50	2846	2865	36
532639	644	663	Exon 3	AAGAGATCTCATCACTCACA	52	2852	2871	37
532640	650	669	Exon 3	AGTGGAAAGAGATCTCATCA	34	2858	2877	38
532641	656	675	Exon 3	CATAGCAGTGGAAAGAGATC	32	2864	2883	39
532642	662	681	Exon 3	AACCGTCATAGCAGTGGAAA	45	2870	2889	40
532643	668	687	Exon 3	GAGTGTAACCGTCATAGCAG	36	2876	2895	41
532644	674	693	Exon 3	CCCGGAGAGTGTAACCGTCA	30	2882	2901	42
532645	680	699	Exon 3	CAGAGCCCCGGAGAGTGTAA	27	2888	2907	43
532646	686	705	Exon 3	GATTGGCAGAGCCCCGGAGA	20	2894	2913	44
532647	692	711	Exon 3	AGGTGCGATTGGCAGAGCCC	28	2900	2919	45
532648	698	717	Exon 3	CTTGGCAGGTGCGATTGGCA	24	2906	2925	46
532649	704	723	Exon 3	CATTCACTTGGCAGGTGCGA	28	2912	2931	47
532650	729	748	Exon 3	ATCGCTGTCTGCCCACTCCA	44	2937	2956	48
532651	735	754	Exon 3	TCACAGATCGCTGTCTGCCC	44	2943	2962	49
532652	741	760	Exon 3	CCGTTGTCACAGATCGCTGT	27	2949	2968	50
532653	747	766	Exon 3-4 Junction	CCCGCTCCGTTGTCACAGAT	28	n/a	n/a	51
532654	753	772	Exon 3-4 Junction	CAGTACCCCGCTCCGTTGTC	13	n/a	n/a	52
532655	759	778	Exon 3-4 Junction	TTGGAGCAGTACCCCGCTCC	8	n/a	n/a	53
532656	789	808	Exon 4	ACCTTCCTTGTGCCAATGGG	40	3152	3171	54
532657	795	814	Exon 4	CTGCCCACCTTCCTTGTGCC	41	3158	3177	55
532658	818	837	Exon 4	CGCTGTCTTCAAGGCGGTAC	33	3181	3200	56
532659	835	854	Exon 4	GCTGCAGTGGTAGGTGACGC	32	3198	3217	57
532660	841	860	Exon 4	CCCCCGGCTGCAGTGGTAGG	17	3204	3223	58
532661	847	866	Exon 4	GGTAAGCCCCCGGCTGCAGT	28	3210	3229	59
532662	853	872	Exon 4	ACGCAGGGTAAGCCCCCGGC	13	3216	3235	60
532663	859	878	Exon 4	GGAGCCACGCAGGGTAAGCC	33	3222	3241	61
532664	866	885	Exon 4	GCCGCTGGGAGCCACGCAGG	10	3229	3248	62

TABLE 1-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target Region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532665	891	910	Exon 4	CAAGAGCCACCTTCCTGACA	17	3254	3273	63
532666	897	916	Exon 4	CCGCTCCAAGAGCCACCTTC	25	3260	3279	64
532667	903	922	Exon 4	TCCGTCCCGCTCCAAGAGCC	29	3266	3285	65
532668	909	928	Exon 4	GAAGGCTCCGTCCCGCTCCA	14	3272	3291	66
532669	915	934	Exon 4	TGGCAGGAAGGCTCCGTCCC	18	3278	3297	67
532670	921	940	Exon 4-5 Junction	GAGTCTTGGCAGGAAGGCTC	20	n/a	n/a	68
532671	927	946	Exon 4-5 Junction	ATGAAGGAGTCTTGGCAGGA	14	n/a	n/a	69
532672	956	975	Exon 5	CTTCGGCCACCTCTTGAGGG	45	3539	3558	70
532673	962	981	Exon 5	GGAAAGCTTCGGCCACCTCT	37	3545	3564	71
532674	968	987	Exon 5	AAGACAGGAAAGCTTCGGCC	28	3551	3570	72
532675	974	993	Exon 5	TCAGGGAAGACAGGAAAGCT	16	3557	3576	73
532676	996	1015	Exon 5	TCGACTCCTTCTATGGTCTC	31	3579	3598	74
532677	1033	1052	Exon 5-6 Junction	CTTCTGTTGTTCCCCTGGGC	36	n/a	n/a	75
532678	1068	1087	Exon 6	TTCATGGAGCCTGAAGGGTC	19	3752	3771	76
532679	1074	1093	Exon 6	TAGATGTTCATGGAGCCTGA	24	3758	3777	77
532680	1080	1099	Exon 6	ACCAGGTAGATGTTCATGGA	13	3764	3783	78
532681	1086	1105	Exon 6	TCTAGCACCAGGTAGATGTT	20	3770	3789	79
532682	1092	1111	Exon 6	GATCCATCTAGCACCAGGTA	33	3776	3795	80
532683	1098	1117	Exon 6	CTGTCTGATCCATCTAGCAC	44	3782	3801	81
532684	1104	1123	Exon 6	CCAATGCTGTCTGATCCATC	29	3788	3807	82
532685	1129	1148	Exon 6	TTTGGCTCCTGTGAAGTTGC	40	3813	3832	83

TABLE 2

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS No	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532686	1135	1154	Exon 6	ACACTTTTTGGCTCCTGTGA	91	3819	3838	84
532687	1141	1160	Exon 6	GACTAGACACTTTTTGGCTC	77	3825	3844	85
532688	1147	1166	Exon 6	TAAGTTGACTAGACACTTTT	70	3831	3850	86
532689	1153	1172	Exon 6	CTCAATTAAGTTGACTAGAC	61	3837	3856	87
532690	1159	1178	Exon 6-7 Junction	CACCTTCTCAATTAAGTTGA	57	3843	3862	88

TABLE 2-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS No	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532691	1165	1184	Exon 6-7 Junction	ACTTGCCACCTTCTCAATTA	56	n/a	n/a	89
532692	1171	1190	Exon 6-7 Junction	ACCATAACTTGCCACCTTCT	56	n/a	n/a	90
532693	1177	1196	Exon 7	CTTCACACCATAACTTGCCA	56	4153	4172	91
532694	1183	1202	Exon 7	TCTTGGCTTCACACCATAAC	55	4159	4178	92
532695	1208	1227	Exon 7	ATGTGGCATATGTCACTAGA	55	4184	4203	93
532696	1235	1254	Exon 7	CAGACACTTTGACCCAAATT	55	4211	4230	94
532697	1298	1317	Exon 7-8 Junction	GGTCTTCATAATTGATTTCA	53	n/a	n/a	95
532698	1304	1323	Exon 7-8 Junction	ACTTGTGGTCTTCATAATTG	53	n/a	n/a	96
532699	1310	1329	Exon 7-8 Junction	ACTTCAACTTGTGGTCTTCA	52	n/a	n/a	97
532700	1316	1335	Exon 8	TCCCTGACTTCAACTTGTGG	52	4609	4628	98
532701	1322	1341	Exon 8	TGTTAGTCCCTGACTTCAAC	52	4615	4634	99
532702	1328	1347	Exon 8	TCTTGGTGTTAGTCCCTGAC	51	4621	4640	100
532703	1349	1368	Exon 8	TGTACACTGCCTGGAGGGCC	51	4642	4661	101
532704	1355	1374	Exon 8	TCATGCTGTACACTGCCTGG	51	4648	4667	102
532705	1393	1412	Exon 8	GTTCCAGCCTTCAGGAGGGA	50	4686	4705	103
532706	1399	1418	Exon 8	GGTGCGGTTCCAGCCTTCAG	50	4692	4711	104
532707	1405	1424	Exon 8	ATGGCGGGTGCGGTTCCAGC	50	4698	4717	105
532708	1411	1430	Exon 8	GATGACATGGCGGGTGCGGT	49	4704	4723	106
532709	1417	1436	Exon 8	GAGGATGATGACATGGCGGG	49	4710	4729	107
532710	1443	1462	Exon 8-9 Junction	CCCATGTTGTGCAATCCATC	48	n/a	n/a	108
532711	1449	1468	Exon 9	TCCCCGCCCATGTTGTGCAA	48	5023	5042	109
532712	1455	1474	Exon 9	ATTGGGTCCCCGCCCATGTT	48	5029	5048	110
532713	1461	1480	Exon 9	ACAGTAATTGGGTCCCCGCC	48	5035	5054	111
532714	1467	1486	Exon 9	TCAATGACAGTAATTGGGTC	47	5041	5060	112
532715	1473	1492	Exon 9	ATCTCATCAATGACAGTAAT	47	5047	5066	113
532716	1479	1498	Exon 9	TCCCGGATCTCATCAATGAC	46	5053	5072	114
532717	1533	1552	Exon 9-10 Junction	ACATCCAGATAATCCTCCCT	46	n/a	n/a	115
532718	1539	1558	Exon 9-10 Junction	ACATAGACATCCAGATAATC	46	n/a	n/a	116
532719	1545	1564	Exon 9-10 Junction	CCAAACACATAGACATCCAG	46	n/a	n/a	117
532720	1582	1601	Exon 10	AGCATTGATGTTCACTTGGT	46	5231	5250	118

TABLE 2-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS No	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532721	1588	1607	Exon 10	AGCCAAAGCATTGATGTTCA	45	5237	5256	119
532722	1594	1613	Exon 10	CTTGGAAGCCAAAGCATTGA	45	5243	5262	120
532723	1600	1619	Exon 10	GTCTTTCTTGGAAGCCAAAG	45	5249	5268	121
532724	1606	1625	Exon 10	CTCATTGTCTTTCTTGGAAG	44	5255	5274	122
532725	1612	1631	Exon 10	ATGTTGCTCATTGTCTTTCT	44	5261	5280	123
532726	1618	1637	Exon 10	GAACACATGTTGCTCATTGT	44	5267	5286	124
532727	1624	1643	Exon 10	GACTTTGAACACATGTTGCT	43	5273	5292	125
532728	1630	1649	Exon 10	ATCCTTGACTTTGAACACAT	43	5279	5298	126
532729	1636	1655	Exon 10	TTCCATATCCTTGACTTTGA	43	5285	5304	127
532730	1642	1661	Exon 10	CAGGTTTTCCATATCCTTGA	42	5291	5310	128
532731	1686	1705	Exon 11	CTCAGAGACTGGCTTTCATC	42	5827	5846	129
532732	1692	1711	Exon 11	CAGAGACTCAGAGACTGGCT	42	5833	5852	130
516252	1698	1717	Exon 11	ATGCCACAGAGACTCAGAGA	42	5839	5858	131
532733	1704	1723	Exon 11	CAAACCATGCCACAGAGACT	41	5845	5864	132
532734	1710	1729	Exon 11	TGTTCCCAAACCATGCCACA	41	5851	5870	133
532735	1734	1753	Exon 11	TTGTGGTAATCGGTACCCTT	41	5875	5894	134
532736	1740	1759	Exon 11	GGTTGCTTGTGGTAATCGGT	40	5881	5900	135
532737	1746	1765	Exon 11	TGCCATGGTTGCTTGTGGTA	40	5887	5906	136
532738	1752	1771	Exon 11	TTGGCCTGCCATGGTTGCTT	40	5893	5912	137
532739	1758	1777	Exon 11	GAGATCTTGGCCTGCCATGG	38	5899	5918	138
532740	1803	1822	Exon 12	ACAGCCCCCATACAGCTCTC	38	6082	6101	139
532741	1809	1828	Exon 12	GACACCACAGCCCCCATACA	38	6088	6107	140
532742	1815	1834	Exon 12	TACTCAGACACCACAGCCCC	38	6094	6113	141
532743	1821	1840	Exon 12	ACAAAGTACTCAGACACCAC	37	6100	6119	142
532744	1827	1846	Exon 12	GTCAGCACAAAGTACTCAGA	37	6106	6125	143
532745	1872	1891	Exon 12	TTGATTGAGTGTTCCTTGTC	36	6151	6170	144
532746	1878	1897	Exon 12	CTGACCTTGATTGAGTGTTC	35	6157	6176	145
532747	1909	1928	Exon 13	TATCTCCAGGTCCCGCTTCT	35	6403	6422	146
532748	1967	1986	Exon 13	GAATTCCTGCTTCTTTTTTC	32	6461	6480	147
532749	1973	1992	Exon 13	ATTCAGGAATTCCTGCTTCT	32	6467	6486	148
532750	1979	1998	Exon 13	CATAAAATTCAGGAATTCCT	32	6473	6492	149
532751	1985	2004	Exon 13	CATAGTCATAAAATTCAGGA	31	6479	6498	150
532752	2006	2025	Exon 13	TGAGCTTGATCAGGGCAACG	30	6500	6519	151
532753	2012	2031	Exon 13	TATTCTTGAGCTTGATCAGG	30	6506	6525	152

TABLE 2-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS No	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532754	2048	2067	Exon 13-14 Junction	GACAAATGGGCCTGATAGTC	30	n/a	n/a	153
532755	2070	2089	Exon 14	GTTGTTCCCTCGGTGCAGGG	29	6659	6678	154
532756	2076	2095	Exon 14	GCTCGAGTTGTTCCCTCGGT	28	6665	6684	155
532757	2082	2101	Exon 14	CTCAAAGCTCGAGTTGTTCC	28	6671	6690	156
532758	2088	2107	Exon 14	GGAAGCCTCAAAGCTCGAGT	25	6677	6696	157
532759	2094	2113	Exon 14	GTTGGAGGAAGCCTCAAAGC	23	6683	6702	158
532760	2100	2119	Exon 14	GTGGTAGTTGGAGGAAGCCT	23	6689	6708	159
532761	2106	2125	Exon 14	TGGCAAGTGGTAGTTGGAGG	18	6695	6714	160
532762	2112	2131	Exon 14	TGTTGCTGGCAAGTGGTAGT	14	6701	6720	161

TABLE 3

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target Region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532812	n/a	n/a	Exon 1	TCCAGCTCACTCCCCTGTTG	19	1593	1612	162
532813	n/a	n/a	Exon 1	TAAGGATCCAGCTCACTCCC	40	1599	1618	163
532814	n/a	n/a	Exon 1	CAGAAATAAGGATCCAGCTC	39	1605	1624	164
532815	n/a	n/a	Exon 1	AGGGACCAGAAATAAGGATC	0	1611	1630	165
532816	n/a	n/a	Exon 1	CCACTTAGGGACCAGAAATA	27	1617	1636	166
532817	n/a	n/a	Exon 1	TCCAGGACTCTCCCCTTCAG	39	1682	1701	167
532818	n/a	n/a	Exon 1	AAGTCCCACCCTTTGCTGCC	15	1707	1726	168
532819	n/a	n/a	Exon 1	CTGCAGAAGTCCCACCCTTT	26	1713	1732	169
532820	n/a	n/a	Exon 1	CAGAAACTGCAGAAGTCCCA	8	1719	1738	170
532821	n/a	n/a	Exon 2-Intron 2	AACCTCTGCACTCTGCCTTC	39	2368	2387	171
532822	n/a	n/a	Exon 2-Intron 2	CCCTCAAACCTCTGCACTCT	3	2374	2393	172
532823	n/a	n/a	Exon 2-Intron 2	TCATTGCCCTCAAACCTCTG	19	2380	2399	173
532824	n/a	n/a	Intron 2	CCACACTCATTGCCCTCAAA	37	2386	2405	174
532825	n/a	n/a	Intron 2	CACTGCCCACACTCATTGCC	23	2392	2411	175
532826	n/a	n/a	Intron 2	TTAGGCCACTGCCCACACTC	15	2398	2417	176
532827	n/a	n/a	Intron 2	CTAGTCCTGACCTTGCTGCC	28	2436	2455	177

TABLE 3-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target Region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532828	n/a	n/a	Intron 2	CTCATCCTAGTCCTGACCTT	25	2442	2461	178
532829	n/a	n/a	Intron 2	CCTAGTCTCATCCTAGTCCT	23	2448	2467	179
532830	n/a	n/a	Intron 2	ACCCTGCCTAGTCTCATCCT	30	2454	2473	180
532831	n/a	n/a	Intron 2	CTTGTCACCCTGCCTAGTCT	34	2460	2479	181
532832	n/a	n/a	Intron 2	GCCCACCTTGTCACCCTGCC	36	2466	2485	182
532833	n/a	n/a	Intron 2	CCTAAAACTGCTCCTACTCC	9	2492	2511	183
532834	n/a	n/a	Intron 4	GAGTCAGAAATGAGGTCAAA	19	3494	3513	184
532835	n/a	n/a	Intron 11	CCCTACTCCCATTTCACCTT	16	5971	5990	185
532836	n/a	n/a	Intron 8-Exon 9	TGTTGTGCAATCCTGCAGAA	25	5013	5032	186
532837	n/a	n/a	Intron 1	AAAGGCTGATGAAGCCTGGC	18	2123	2142	187
532838	n/a	n/a	Intron 7	CCTTTGACCACAAAGTGGCC	21	4461	4480	188
532839	n/a	n/a	Intron 12	AGGTACCACCTCTTTGTGGG	29	6362	6381	189
532840	n/a	n/a	Intron 1-Exon 2	TGGTGGTCACACCTGAAGAG	34	2143	2162	190
532763	2133	2152	Exon 14-15 Junction	GCAGGGAGCAGCTCTTCCTT	40	n/a	n/a	191
532764	2139	2158	Exon 15	TCCTGTGCAGGGAGCAGCTC	28	6927	6946	192
532765	2145	2164	Exon 15	TTGATATCCTGTGCAGGGAG	41	6933	6952	193
532766	2151	2170	Exon 15	AGAGCTTTGATATCCTGTGC	36	6939	6958	194
532767	2157	2176	Exon 15	ACAAACAGAGCTTTGATATC	33	6945	6964	195
532768	2163	2182	Exon 15	TCAGACACAAACAGAGCTTT	41	6951	6970	196
532769	2169	2188	Exon 15	TCCTCCTCAGACACAAACAG	49	6957	6976	197
532770	2193	2212	Exon 15	ACCTCCTTCCGAGTCAGCTT	61	6981	7000	198
532771	2199	2218	Exon 15	ATGTAGACCTCCTTCCGAGT	39	6987	7006	199
532772	2205	2224	Exon 15	TTCTTGATGTAGACCTCCTT	30	6993	7012	200
532773	2211	2230	Exon 15	TCCCCATTCTTGATGTAGAC	31	6999	7018	201
532774	2217	2236	Exon 15-16 Junction	TTCTTATCCCCATTCTTGAT	36	n/a	n/a	202
532775	2223	2242	Exon 15-16 Junction	CTGCCTTTCTTATCCCCATT	56	n/a	n/a	203
532776	2229	2248	Exon 15-16 Junction	TCACAGCTGCCTTTCTTATC	33	n/a	n/a	204
532777	2235	2254	Exon 16	TCTCTCTCACAGCTGCCTTT	38	7119	7138	205
532778	2241	2260	Exon 16	TGAGCATCTCTCTCACAGCT	51	7125	7144	206

TABLE 3-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target Region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532779	2247	2266	Exon 16	GCATATTGAGCATCTCTCTC	39	7131	7150	207
532780	2267	2286	Exon 16	TGACTTTGTCATAGCCTGGG	56	7151	7170	208
532781	2273	2292	Exon 16	TGTCCTTGACTTTGTCATAG	36	7157	7176	209
532782	2309	2328	Exon 16	CAGTACAAAGGAACCGAGGG	30	7193	7212	210
532783	2315	2334	Exon 16	CTCCTCCAGTACAAAGGAAC	21	7199	7218	211
532784	2321	2340	Exon 16	GACTCACTCCTCCAGTACAA	31	7205	7224	212
532785	2327	2346	Exon 16	CATAGGGACTCACTCCTCCA	30	7211	7230	213
532786	2333	2352	Exon 16	GGTCAGCATAGGGACTCACT	31	7217	7236	214
532787	2352	2371	Exon 16-17 Junction	TCACCTCTGCAAGTATTGGG	42	7236	7255	215
532788	2358	2377	Exon 16-17 Junction	CCAGAATCACCTCTGCAAGT	32	n/a	n/a	216
532789	2364	2383	Exon 16-17 Junction	GGGCCGCCAGAATCACCTCT	35	n/a	n/a	217
532790	2382	2401	Exon 17	CTCTTGTGAACTATCAAGGG	33	7347	7366	218
532791	2388	2407	Exon 17	CGACTTCTCTTGTGAACTAT	52	7353	7372	219
532792	2394	2413	Exon 17	ATGAAACGACTTCTCTTGTG	16	7359	7378	220
532793	2400	2419	Exon 17-18 Junction	ACTTGAATGAAACGACTTCT	45	7365	7384	221
532794	2406	2425	Exon 17-18 Junction	ACACCAACTTGAATGAAACG	18	n/a	n/a	222
532795	2427	2446	Exon 18	TCCACTACTCCCCAGCTGAT	30	7662	7681	223
532796	2433	2452	Exon 18	CAGACATCCACTACTCCCCA	38	7668	7687	224
532797	2439	2458	Exon 18	TTTTTGCAGACATCCACTAC	35	7674	7693	225
532798	2445	2464	Exon 18	TTCTGGTTTTTGCAGACATC	45	7680	7699	226
532799	2451	2470	Exon 18	TGCCGCTTCTGGTTTTTGCA	47	7686	7705	227
532800	2457	2476	Exon 18	TGCTTTTGCCGCTTCTGGTT	61	7692	7711	228
532801	2463	2482	Exon 18	GGTACCTGCTTTTGCCGCTT	47	7698	7717	229
532802	2469	2488	Exon 18	TGAGCAGGTACCTGCTTTTG	31	7704	7723	230
532803	2517	2536	Exon 18	TTCAGCCAGGGCAGCACTTG	41	7752	7771	231
532804	2523	2542	Exon 18	TTCTCCTTCAGCCAGGGCAG	44	7758	7777	232
532805	2529	2548	Exon 18	TGGAGTTTCTCCTTCAGCCA	46	7764	7783	233
532806	2535	2554	Exon 18	TCATCTTGGAGTTTCTCCTT	49	7770	7789	234
532807	2541	2560	Exon 18	AAATCCTCATCTTGGAGTTT	30	7776	7795	235

TABLE 3-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target Region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532808	2547	2566	Exon 18	AAACCCAAATCCTCATCTTG	20	7782	7801	236
532809	2571	2590	Exon 18	GTCCAGCAGGAAACCCCTTA	65	7806	7825	237
532810	2577	2596	Exon 18	GCCCCTGTCCAGCAGGAAAC	74	7812	7831	238
532811	2599	2618	Exon 18	AGCTGTTTTAATTCAATCCC	96	7834	7853	239

TABLE 4

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	% inhibition	SEQ ID NO:
532841	n/a	n/a	Intron 6-Exon 7	AACTTGCCACCTGTGGGTGA	4142	4161	11	240
532842	n/a	n/a	Exon 15-Intron 15	TCACCTTATCCCCATTCTTG	7007	7026	16	241
532843	n/a	n/a	Intron 11	TCAACTTTCACAAACCACCA	6015	6034	19	242
532844	n/a	n/a	Intron 16-Exon 17	CCGCCAGAATCACCTGCAAG	7326	7345	33	243
532845	n/a	n/a	Intron 10	AGGAGGAATGAAGAAGGCTT	5431	5450	29	244
532846	n/a	n/a	Intron 13	GCCTTTCCTCAGGGATCTGG	6561	6580	26	245
532847	n/a	n/a	Intron 4	AAATGTCTGGGAGTGTCAGG	3477	3496	18	246
532848	n/a	n/a	Intron 15	GCCTAGAGTGCCTCCTTAGG	7038	7057	20	247
532849	n/a	n/a	Intron 17	GGCATCTCCCCAGATAGGAA	7396	7415	16	248
532850	n/a	n/a	Intron 6	AGGGAGCTAGTCCTGGAAGA	3906	3925	14	249
532851	n/a	n/a	Intron 1-Exon 2	ACACCTGAAGAGAAAGGCTG	2135	2154	6	250
532852	n/a	n/a	Intron 7	CCCTTTGACCACAAAGTGGC	4462	4481	25	251
532853	n/a	n/a	Intron 7	GCCCTCAAGGTAGTCTCATG	4354	4373	26	252
532854	n/a	n/a	Intron 6	AAGGGAAGGAGGACAGAATA	3977	3996	18	253
532855	n/a	n/a	Intron 1	AAAGGCCAAGGAGGGATGCT	2099	2118	9	254
532856	n/a	n/a	Exon 8-Intron 8	AGAGGTCCCTTCTGACCATC	4736	4755	4	255
532857	n/a	n/a	Intron 8	GCTGGGACAGGAGAGAGGTC	4749	4768	0	256
532858	n/a	n/a	Intron 4	TCAAATGTCTGGGAGTGTCA	3479	3498	13	257
532859	n/a	n/a	Intron 10	AGAAGGAGAATGTGCTGAAA	5801	5820	20	258
532860	n/a	n/a	Intron 17	TGCTGACCACTTGGCATCTC	7408	7427	20	259
532861	n/a	n/a	Intron 11	CAACTTTCACAAACCACCAT	6014	6033	18	260
532862	n/a	n/a	Intron 10	AGCTCTGTGATTCTAAGGTT	5497	5516	15	261

TABLE 4-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	% inhibition	SEQ ID NO:
532863	n/a	n/a	Intron 6-Exon 7	CCACCTGTGGGTGAGGAGAA	4136	4155	16	262
532864	n/a	n/a	Exon 17-Intron 17	GAGGACTCACTTGAATGAAA	7373	7392	21	263
532865	n/a	n/a	Intron 6	TGGAATGATCAGGGAGCTAG	3916	3935	30	264
532866	n/a	n/a	Intron 5	GTCCCTTCTCCATTTTCCCC	3659	3678	26	265
532867	n/a	n/a	Intron 7	TCAACTTTTTAAGTTAATCA	4497	4516	14	266
532868	n/a	n/a	Intron 6	GGGTGAGGAGAACAAGGCGC	4128	4147	21	267
532869	n/a	n/a	Intron 7	CTTCCAAGCCATCTTTTAAC	4553	4572	5	268
532870	n/a	n/a	Exon 17-Intron 17	AGGACTCACTTGAATGAAAC	7372	7391	18	269
532871	n/a	n/a	Intron 10	TTCCAGGCAACTAGAGCTTC	5412	5431	15	270
532872	n/a	n/a	Exon 1	CAGAGTCCAGCCACTGTTTG	1557	1576	13	271
532873	n/a	n/a	Intron 17-Exon 18	CCAACCTGCAGAGGCAGTGG	7638	7657	23	272
532874	n/a	n/a	Intron 16	TGCAAGGAGAGGAGAAGCTG	7312	7331	10	273
532875	n/a	n/a	Exon 9-Intron 9	CTAGGCAGGTTACTCACCCA	5120	5139	21	274
532876	n/a	n/a	Intron 6-Exon 7	CACCATAACTTGCCACCTGT	4148	4167	41	275
532877	n/a	n/a	Intron 12	TAGGTACCACCTCTTTGTGG	6363	6382	27	276
532878	n/a	n/a	Intron 11	CTTGACCTCACCTCCCCCAA	5954	5973	13	277
532879	n/a	n/a	Intron 12	CCACCTCTTTGTGGGCAGCT	6357	6376	33	278
532880	n/a	n/a	Intron 11	TTCACAAACCACCATCTCTT	6009	6028	8	279
532881	n/a	n/a	Exon 3-Intron 3	TTCTCACCTCCGTTGTCACA	2958	2977	17	280
532882	n/a	n/a	Intron 12	GAAAGTGGGAGGTGTTGCCT	6225	6244	19	281
532883	n/a	n/a	Intron 1	ACAGCAGGAAGGGAAGGTTA	2075	2094	34	282
532884	n/a	n/a	Intron 17	CATGCTGACCACTTGGCATC	7410	7429	18	283
532885	n/a	n/a	Exon 4-Intron 4	GGTCACCTTGGCAGGAAGGC	3286	3305	0	284
532886	n/a	n/a	Intron 8	GTATAGTGTTACAAGTGGAC	4804	4823	13	285
532887	n/a	n/a	Intron 7	GGACTTCCCTTTGACCACAA	4468	4487	18	286
532888	n/a	n/a	Intron 11	TCACCTTGACCTCACCTCCC	5958	5977	20	287
532889	n/a	n/a	Intron 15	TAGAGTGCCTCCTTAGGATG	7035	7054	27	288
532890	n/a	n/a	Intron 7	TGACTTCAACTTGTGGTCTG	4605	4624	16	289
532891	n/a	n/a	Intron 10	CAGAGAAGGAGAATGTGCTG	5804	5823	25	290
532892	n/a	n/a	Intron 14-Exon 15	AGGGAGCAGCTCTTCCTCTG	6919	6938	47	291

TABLE 4-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	% inhibition	SEQ ID NO:
532893	n/a	n/a	Intron 5-Exon 6	TGTTCCCCTGGGTGCCAGGA	3710	3729	24	292
532894	n/a	n/a	Intron 10	GGCCTGGCTGTTTTCAAGCC	5612	5631	15	293
532895	n/a	n/a	Intron 10-Exon 11	GACTGGCTTTCATCTGGCAG	5821	5840	25	294
532896	n/a	n/a	Intron 10	GAAGGCTTTCCAGGCAACTA	5419	5438	19	295
532897	n/a	n/a	Exon 17-Intron 17	TCACTTGAATGAAACGACTT	7367	7386	11	296
532898	n/a	n/a	Intron 1	GGCCCCAAAAGGCCAAGGAG	2106	2125	5	297
532899	n/a	n/a	Intron 16-Exon 17	AATCACCTGCAAGGAGAGGA	7319	7338	19	298
532900	n/a	n/a	Intron 12	GACCTTCAGTTGCATCCTTA	6183	6202	25	299
532901	n/a	n/a	Intron 1	TGATGAAGCCTGGCCCCAAA	2117	2136	0	300
532902	n/a	n/a	Intron 12	TAGAAAGTGGGAGGTGTTGC	6227	6246	0	301
532903	n/a	n/a	Intron 12	CCCATCCCTGACTGGTCTGG	6295	6314	14	302
532904	n/a	n/a	Intron 8	CCATGGGTATAGTGTTACAA	4810	4829	13	303
532905	n/a	n/a	Intron 2	GTGTTCTCTTGACTTCCAGG	2586	2605	23	304
532906	n/a	n/a	Intron 13	GGCCTGCTCCTCACCCCAGT	6597	6616	27	305
532907	n/a	n/a	Intron 10	GAGGCCTGGCTGTTTTCAAG	5614	5633	32	306
532908	n/a	n/a	Exon 1	GACTCTCCCCTTCAGTACCT	1677	1696	16	307
532909	n/a	n/a	Intron 8	CATGGGTATAGTGTTACAAG	4809	4828	10	308
532910	n/a	n/a	Intron 10	GAAGGAGAATGTGCTGAAAA	5800	5819	0	309
532911	n/a	n/a	Intron 7	TCACCTGGTCTTCCAAGCCA	4562	4581	0	310
532912	n/a	n/a	Intron 17	CTCCCCAGATAGGAAAGGGA	7391	7410	0	311
532913	n/a	n/a	Exon 17-Intron 17	GGACTCACTTGAATGAAACG	7371	7390	0	312
532914	n/a	n/a	Intron 16-Exon 17	GGCCGCCAGAATCACCTGCA	7328	7347	30	313
532915	n/a	n/a	Exon 17-Intron 17	CTCACTTGAATGAAACGACT	7368	7387	22	314
532916	n/a	n/a	Intron 13	CTTTCCCAGCCTTTCCTCAG	6569	6588	28	315
532918	n/a	n/a	Intron 12	AGAAAGTGGGAGGTGTTGCC	6226	6245	3	316
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	7839	7858	90	317

TABLE 5

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	% inhibition	SEQ ID NO:
532919	n/a	n/a	Exon 1	CCAGGACTCTCCCCTTCAGT	1681	1700	4	318
532920	n/a	n/a	Intron 6	AGGGAAGGAGGACAGAATAG	3976	3995	25	319
532921	n/a	n/a	Intron 4	GAAATGAGGTCAAATGTCTG	3488	3507	30	320
532922	n/a	n/a	Intron 4	GGAGAGTCAGAAATGAGGTC	3497	3516	25	321
532923	n/a	n/a	Intron 12	GTAGAAAGTGGGAGGTGTTG	6228	6247	26	322
532924	n/a	n/a	Intron 10	TAGAAAGATCTCTGAAGTGC	5521	5540	24	323
532925	n/a	n/a	Intron 13	CTGCTCCTCACCCCAGTCCT	6594	6613	26	324
532926	n/a	n/a	Intron 11	CTACTGGGATTCTGTGCTTA	5927	5946	30	325
532927	n/a	n/a	Intron 1	CCCAAAAGGCCAAGGAGGGA	2103	2122	13	326
532928	n/a	n/a	Intron 17	TGACCACTTGGCATCTCCCC	7405	7424	27	327
532929	n/a	n/a	Intron 16-Exon 17	CCTGCAAGGAGAGGAGAAGC	7314	7333	29	328
532930	n/a	n/a	Exon 16-Intron 16	CTCTCACCTCTGCAAGTATT	7239	7258	44	329
532931	n/a	n/a	Intron 1	CCCCAAAAGGCCAAGGAGGG	2104	2123	21	330
532932	n/a	n/a	Intron 7	GTCTTCCAAGCCATCTTTTA	4555	4574	20	331
532933	n/a	n/a	Intron 8	GTTACAAGTGGACTTAAGGG	4797	4816	30	332
532934	n/a	n/a	Intron 8-Exon 9	CCCATGTTGTGCAATCCTGC	5017	5036	30	333
532935	n/a	n/a	Intron 15	GAGGTGGGAAGCATGGAGAA	7091	7110	17	334
532936	n/a	n/a	Intron 14	TGCTCCCACCACTGTCATCT	6874	6893	21	335
532937	n/a	n/a	Exon 9-Intron 9	AGGCAGGTTACTCACCCAGA	5118	5137	18	336
532938	n/a	n/a	Intron 11	TACTGGGATTCTGTGCTTAC	5926	5945	15	337
532939	n/a	n/a	Intron 13	GCCTTTCCCAGCCTTTCCTC	6571	6590	27	338
532940	n/a	n/a	Intron 8-Exon 9	GTGCAATCCTGCAGAAGAGA	5009	5028	21	339
532941	n/a	n/a	Intron 8	ACAGGAGAGAGGTCCCTTCT	4743	4762	20	340
532942	n/a	n/a	Intron 10	CCCAAAAGGAGAAAGGGAAA	5717	5736	14	341
532943	n/a	n/a	Intron 2	AAGCCCAGGGTAAATGCTTA	2557	2576	32	342
532944	n/a	n/a	Intron 1	GATGAAGCCTGGCCCCAAAA	2116	2135	22	343
532945	n/a	n/a	Intron 10	TGGCAGAGAAGGAGAATGTG	5807	5826	22	344
532946	n/a	n/a	Intron 13	TTCCCAGCCTTTCCTCAGGG	6567	6586	35	345
532947	n/a	n/a	Intron 10	GGCAGAGAAGGAGAATGTGC	5806	5825	30	346
532948	n/a	n/a	Intron 10	ACAGTGCCAGGAAACAAGAA	5471	5490	25	347
532949	n/a	n/a	Exon 9-Intron 9	TAGGCAGGTTACTCACCCAG	5119	5138	22	348
532950	n/a	n/a	Intron 2	TTCTCTTGACTTCCAGGGCT	2583	2602	22	349

TABLE 5-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	% inhibition	SEQ ID NO:
532951	n/a	n/a	Intron 13	CCTGCTCCTCACCCCAGTCC	6595	6614	16	350
532953	n/a	n/a	Intron 7	TCCCACTAACCTCCATTGCC	4422	4441	14	351
532954	n/a	n/a	Intron 7	TTCCCTTTGACCACAAAGTG	4464	4483	16	352
532955	n/a	n/a	Intron 9	CTGGGTCCTAGGCAGGTTAC	5127	5146	30	353
532956	n/a	n/a	Intron 10	TCCAGGCAACTAGAGCTTCA	5411	5430	20	354
532957	n/a	n/a	Intron 8-Exon 9	GCCCATGTTGTGCAATCCTG	5018	5037	45	355
532958	n/a	n/a	Intron 7	GGTTCCCACTAACCTCCATT	4425	4444	18	356
532959	n/a	n/a	Intron 3	AGGTAGAGAGCAAGAGTTAC	3052	3071	26	357
532960	n/a	n/a	Intron 7	CCACTAACCTCCATTGCCCA	4420	4439	10	358
532961	n/a	n/a	Intron 11	TCACAAACCACCATCTCTTA	6008	6027	40	359
532962	n/a	n/a	Exon 9-Intron 9	TACTCACCCAGATAATCCTC	5110	5129	27	360
532963	n/a	n/a	Intron 13	TGCTCCTCACCCCAGTCCTC	6593	6612	24	361
532964	n/a	n/a	Intron 15-Exon 16	TCTCACAGCTGCCTTTCTGT	7115	7134	25	362
532965	n/a	n/a	Exon 17-Intron 17	GAAAGGGAGGACTCACTTGA	7379	7398	11	363
532966	n/a	n/a	Intron 7	CCATCTTTTAACCCCAGAGA	4545	4564	18	364
532967	n/a	n/a	Intron 13	TCCTCACCCCAGTCCTCCAG	6590	6609	27	365
532968	n/a	n/a	Intron 10	CTGGCAGAGAAGGAGAATGT	5808	5827	15	366
532969	n/a	n/a	Intron 17	TCTCCCCAGATAGGAAAGGG	7392	7411	23	367
532970	n/a	n/a	Intron 14	ACTTCAGCTGCTCCCACCAC	6882	6901	18	368
532971	n/a	n/a	Intron 1	GACAGCAGGAAGGGAAGGTT	2076	2095	13	369
532972	n/a	n/a	Intron 13-Exon 14	GGAGACAAATGGGCCTATAA	6640	6659	33	370
532973	n/a	n/a	Intron 14	CTGCTCCCACCACTGTCATC	6875	6894	11	371
532974	n/a	n/a	Intron 10	AGGAATGAAGAAGGCTTTCC	5428	5447	21	372
532975	n/a	n/a	Intron 14	GGGATCTCATCCTTATCCTC	6741	6760	31	373
532976	n/a	n/a	Intron 9	GTGCTGGGTCCTAGGCAGGT	5130	5149	16	374
532977	n/a	n/a	Intron 1	CAAAAGGCCAAGGAGGGATG	2101	2120	14	375
532978	n/a	n/a	Intron 17	CCATGCTGACCACTTGGCAT	7411	7430	20	376
532979	n/a	n/a	Intron 8	GGAGGCTGGGACAGGAGAGA	4753	4772	25	377
532980	n/a	n/a	Intron 14-Exon 15	GGAGCAGCTCTTCCTCTGGA	6917	6936	36	378
532981	n/a	n/a	Exon 3-Intron 3	TCTCACCTCCGTTGTCACAG	2957	2976	20	379
532982	n/a	n/a	Intron 13	CAGTCCTCCAGCCTTTCCCA	6581	6600	21	380

TABLE 5-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	% inhibition	SEQ ID NO:
532983	n/a	n/a	Intron 13	AGTCCTCCAGCCTTTCCCAG	6580	6599	22	381
532984	n/a	n/a	Intron 4-Exon 5	TGAAGGAGTCTGGGAGAGTC	3509	3528	12	382
532985	n/a	n/a	Intron 16-Exon 17	CAGAATCACCTGCAAGGAGA	7322	7341	20	383
532986	n/a	n/a	Exon 17-Intron 17	TAGGAAAGGGAGGACTCACT	7382	7401	3	384
532987	n/a	n/a	Exon 4-Intron 4	ACCTTGGCAGGAAGGCTCCG	3282	3301	12	385
532988	n/a	n/a	Intron 13-Exon 14	GAGACAAATGGGCCTATAAA	6639	6658	15	386
532989	n/a	n/a	Intron 1	CTGAAGAGAAAGGCTGATGA	2131	2150	17	387
532990	n/a	n/a	Intron 6	AATGATCAGGGAGCTAGTCC	3913	3932	30	388
532991	n/a	n/a	Intron 17	CTTAGCTGACCTAAAGGAAT	7557	7576	22	389
532992	n/a	n/a	Intron 8	TGGGTATAGTGTTACAAGTG	4807	4826	17	390
532993	n/a	n/a	Intron 1	TGAAGAGAAAGGCTGATGAA	2130	2149	19	391
532994	n/a	n/a	Intron 8	GTGTTACAAGTGGACTTAAG	4799	4818	25	392
532995	n/a	n/a	Intron 6	ACCTGTGGGTGAGGAGAACA	4134	4153	24	393
532996	n/a	n/a	Exon 9-Intron 9	TCACCCAGATAATCCTCCCT	5107	5126	36	394
532952	2608	2627	Exon 18	TGTTGTCGCAGCTGTTTTAA	7843	7862	90	395

Example 2

Antisense Inhibition of Human Complement Factor B (CFB) in HepG2 Cells by MOE Gapmers

[0430] Additional antisense oligonucleotides were designed targeting human Complement Factor B (CFB) nucleic acid and were tested for their effects on CFB mRNA in vitro. Cultured HepG2 cells at a density of 20,000 cells per well were transfected using electroporation with 4,500 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3460_MGB (forward sequence CGAAGCAGCTCAATGAAATCAA, designated herein as SEQ ID NO: 813; reverse sequence TGCCTGGAGGGCCTTCTT, designated herein as SEQ ID NO: 814; probe sequence AGACCACAAGTTGAAGTC, designated herein as SEQ ID NO: 815) was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0431] The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 5-10-5 MOE gapmers. The 5-10-5 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P═S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in the Tables below is targeted to either the human CFB mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_001710.5) or the human CFB genomic sequence, designated herein as SEQ ID NO: 2 (GENBANK Accession No. NT_007592.15 truncated from nucleotides 31852000 to 31861000), or both. 'n/a.' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity.

TABLE 6

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532686	1135	1154	Exon 6	ACACTTTTTGGCTCCTGTGA	48	3819	3838	84
532687	1141	1160	Exon 6	GACTAGACACTTTTTGGCTC	63	3825	3844	85
532688	1147	1166	Exon 6	TAAGTTGACTAGACACTTTT	47	3831	3850	86
532689	1153	1172	Exon 6	CTCAATTAAGTTGACTAGAC	57	3837	3856	87
532690	1159	1178	Exon 6-7 Junction	CACCTTCTCAATTAAGTTGA	49	3843	3862	88
532691	1165	1184	Exon 6-7 Junction	ACTTGCCACCTTCTCAATTA	33	n/a	n/a	89
532692	1171	1190	Exon 6-7 Junction	ACCATAACTTGCCACCTTCT	67	n/a	n/a	90
532693	1177	1196	Exon 7	CTTCACACCATAACTTGCCA	56	4153	4172	91
532694	1183	1202	Exon 7	TCTTGGCTTCACACCATAAC	50	4159	4178	92
532695	1208	1227	Exon 7	ATGTGGCATATGTCACTAGA	53	4184	4203	93
532696	1235	1254	Exon 7	CAGACACTTTGACCCAAATT	52	4211	4230	94
532697	1298	1317	Exon 7-8 Junction	GGTCTTCATAATTGATTTCA	59	n/a	n/a	95
532698	1304	1323	Exon 7-8 Junction	ACTTGTGGTCTTCATAATTG	52	n/a	n/a	96
532699	1310	1329	Exon 7-8 Junction	ACTTCAACTTGTGGTCTTCA	85	n/a	n/a	97
532700	1316	1335	Exon 8	TCCCTGACTTCAACTTGTGG	96	4609	4628	98
532701	1322	1341	Exon 8	TGTTAGTCCCTGACTTCAAC	56	4615	4634	99
532702	1328	1347	Exon 8	TCTTGGTGTTAGTCCCTGAC	86	4621	4640	100
532703	1349	1368	Exon 8	TGTACACTGCCTGGAGGGCC	35	4642	4661	101
532704	1355	1374	Exon 8	TCATGCTGTACACTGCCTGG	12	4648	4667	102
532705	1393	1412	Exon 8	GTTCCAGCCTTCAGGAGGGA	27	4686	4705	103
532706	1399	1418	Exon 8	GGTGCGGTTCCAGCCTTCAG	67	4692	4711	104
532707	1405	1424	Exon 8	ATGGCGGGTGCGGTTCCAGC	26	4698	4717	105
532708	1411	1430	Exon 8	GATGACATGGCGGGTGCGGT	28	4704	4723	106
532709	1417	1436	Exon 8	GAGGATGATGACATGGCGGG	6	4710	4729	107
532710	1443	1462	Exon 8-9 Junction	CCCATGTTGTGCAATCCATC	35	n/a	n/a	108
532711	1449	1468	Exon 9	TCCCCGCCCATGTTGTGCAA	28	5023	5042	109
532712	1455	1474	Exon 9	ATTGGGTCCCCGCCCATGTT	19	5029	5048	110
532713	1461	1480	Exon 9	ACAGTAATTGGGTCCCCGCC	29	5035	5054	111
532714	1467	1486	Exon 9	TCAATGACAGTAATTGGGTC	49	5041	5060	112
532715	1473	1492	Exon 9	ATCTCATCAATGACAGTAAT	45	5047	5066	113
532716	1479	1498	Exon 9	TCCCGGATCTCATCAATGAC	54	5053	5072	114

TABLE 6-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532717	1533	1552	Exon 9-10 Junction	ACATCCAGATAATCCTCCCT	22	n/a	n/a	115
532718	1539	1558	Exon 9-10 Junction	ACATAGACATCCAGATAATC	8	n/a	n/a	116
532719	1545	1564	Exon 9-10 Junction	CCAAACACATAGACATCCAG	30	n/a	n/a	117
532720	1582	1601	Exon 10	AGCATTGATGTTCACTTGGT	62	5231	5250	118
532721	1588	1607	Exon 10	AGCCAAAGCATTGATGTTCA	46	5237	5256	119
532722	1594	1613	Exon 10	CTTGGAAGCCAAAGCATTGA	35	5243	5262	120
532723	1600	1619	Exon 10	GTCTTTCTTGGAAGCCAAAG	43	5249	5268	121
532724	1606	1625	Exon 10	CTCATTGTCTTTCTTGGAAG	40	5255	5274	122
532725	1612	1631	Exon 10	ATGTTGCTCATTGTCTTTCT	49	5261	5280	123
532726	1618	1637	Exon 10	GAACACATGTTGCTCATTGT	68	5267	5286	124
532727	1624	1643	Exon 10	GACTTTGAACACATGTTGCT	54	5273	5292	125
532728	1630	1649	Exon 10	ATCCTTGACTTTGAACACAT	61	5279	5298	126
532729	1636	1655	Exon 10	TTCCATATCCTTGACTTTGA	55	5285	5304	127
532730	1642	1661	Exon 10	CAGGTTTTCCATATCCTTGA	51	5291	5310	440
532731	1686	1705	Exon 10-11 Junction	CTCAGAGACTGGCTTTCATC	41	5827	5846	129
532732	1692	1711	Exon 11	CAGAGACTCAGAGACTGGCT	59	5833	5852	130
516252	1698	1717	Exon 11	ATGCCACAGAGACTCAGAGA	57	5839	5858	131
532733	1704	1723	Exon 11	CAAACCATGCCACAGAGACT	34	5845	5864	132
532734	1710	1729	Exon 11	TGTTCCCAAACCATGCCACA	51	5851	5870	133
532735	1734	1753	Exon 11	TTGTGGTAATCGGTACCCTT	50	5875	5894	134
532736	1740	1759	Exon 11	GGTTGCTTGTGGTAATCGGT	64	5881	5900	135
532737	1746	1765	Exon 11	TGCCATGGTTGCTTGTGGTA	40	5887	5906	136
532738	1752	1771	Exon 11	TTGGCCTGCCATGGTTGCTT	49	5893	5912	137
532739	1758	1777	Exon 11	GAGATCTTGGCCTGCCATGG	47	5899	5918	138
532740	1803	1822	Exon 12	ACAGCCCCCATACAGCTCTC	48	6082	6101	139
532741	1809	1828	Exon 12	GACACCACAGCCCCCATACA	40	6088	6107	140
532742	1815	1834	Exon 12	TACTCAGACACCACAGCCCC	33	6094	6113	141
532743	1821	1840	Exon 12	ACAAAGTACTCAGACACCAC	39	6100	6119	142
532744	1827	1846	Exon 12	GTCAGCACAAAGTACTCAGA	45	6106	6125	143
532745	1872	1891	Exon 12	TTGATTGAGTGTTCCTTGTC	42	6151	6170	144
532746	1878	1897	Exon 12	CTGACCTTGATTGAGTGTTC	53	6157	6176	145

TABLE 6-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 and 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
532747	1909	1928	Exon 13	TATCTCCAGGTCCCGCTTCT	31	6403	6422	146
532748	1967	1986	Exon 13	GAATTCCTGCTTCTTTTTTC	30	6461	6480	147
532749	1973	1992	Exon 13	ATTCAGGAATTCCTGCTTCT	40	6467	6486	148
532750	1979	1998	Exon 13	CATAAAATTCAGGAATTCCT	45	6473	6492	149
532751	1985	2004	Exon 13	CATAGTCATAAAATTCAGGA	43	6479	6498	150
532752	2006	2025	Exon 13	TGAGCTTGATCAGGGCAACG	61	6500	6519	151
532753	2012	2031	Exon 13	TATTCTTGAGCTTGATCAGG	47	6506	6525	152
532754	2048	2067	Exon 13-14 Junction	GACAAATGGGCCTGATAGTC	35	n/a	n/a	153
532755	2070	2089	Exon 14	GTTGTTCCCTCGGTGCAGGG	43	6659	6678	154
532756	2076	2095	Exon 14	GCTCGAGTTGTTCCCTCGGT	51	6665	6684	155
532757	2082	2101	Exon 14	CTCAAAGCTCGAGTTGTTCC	36	6671	6690	156
532758	2088	2107	Exon 14	GGAAGCCTCAAAGCTCGAGT	54	6677	6696	157
532759	2094	2113	Exon 14	GTTGGAGGAAGCCTCAAAGC	52	6683	6702	158
532760	2100	2119	Exon 14	GTGGTAGTTGGAGGAAGCCT	22	6689	6708	159
532761	2106	2125	Exon 14	TGGCAAGTGGTAGTTGGAGG	34	6695	6714	160
532762	2112	2131	Exon 14	TGTTGCTGGCAAGTGGTAGT	52	6701	6720	161

Example 3

Antisense Inhibition of Human Complement Factor B (CFB) in HepG2 Cells by MOE Gapmers

[0432] Additional antisense oligonucleotides were designed targeting human Complement Factor B (CFB) nucleic acid and were tested for their effects on CFB mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 20,000 cells per well were transfected using electroporation with 5,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0433] The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 5-10-5 MOE gapmers. The gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines. "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in the Tables below is targeted to either the human CFB mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_001710.5) or the human CFB genomic sequence, designated herein as SEQ ID NO: 2 (GENBANK Accession No. NT_007592.15 truncated from nucleotides 31852000 to 31861000), or both. 'n/a.' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity. In case the sequence alignment for a target gene in a particular table is not shown, it is understood that none of the oligonucleotides presented in that table align with 100% complementarity with that target gene.

TABLE 7

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO:
588570	150	169	Exon 1	TGGTCACATTCCCTTCCCCT	54	396
588571	152	171	Exon 1	CCTGGTCACATTCCCTTCCC	63	397
532614	154	173	Exon 1	GACCTGGTCACATTCCCTTC	64	12
588572	156	175	Exon 1	TAGACCTGGTCACATTCCCT	62	398
588573	158	177	Exon 1	CCTAGACCTGGTCACATTCC	53	399
588566	2189	2208	Exon 15	CCTTCCGAGTCAGCTTTTTC	60	400
588567	2191	2210	Exon 15	CTCCTTCCGAGTCAGCTTTT	61	401
532770	2193	2212	Exon 15	ACCTCCTTCCGAGTCAGCTT	77	198
588568	2195	2214	Exon 15	AGACCTCCTTCCGAGTCAGC	72	402
588569	2197	2216	Exon 15	GTAGACCTCCTTCCGAGTCA	46	403
588574	2453	2472	Exon 18	TTTGCCGCTTCTGGTTTTTG	46	404
588575	2455	2474	Exon 18	CTTTTGCCGCTTCTGGTTTT	41	405
532800	2457	2476	Exon 18	TGCTTTTGCCGCTTCTGGTT	69	228
588576	2459	2478	Exon 18	CCTGCTTTTGCCGCTTCTGG	61	406
588577	2461	2480	Exon 18	TACCTGCTTTTGCCGCTTCT	51	407
516350	2550	2569	Exon 18	AGAAAACCCAAATCCTCATC	71	408
588509	2551	2570	Exon 18	TAGAAAACCCAAATCCTCAT	58	409
588510	2552	2571	Exon 18	ATAGAAAACCCAAATCCTCA	57	410
588511	2553	2572	Exon 18	TATAGAAAACCCAAATCCTC	57	411
588512	2554	2573	Exon 18	TTATAGAAAACCCAAATCCT	44	412
588513	2555	2574	Exon 18	CTTATAGAAAACCCAAATCC	37	413
588514	2556	2575	Exon 18	CCTTATAGAAAACCCAAATC	50	414
588515	2557	2576	Exon 18	CCCTTATAGAAAACCCAAAT	45	415
588516	2558	2577	Exon 18	CCCCTTATAGAAAACCCAAA	60	416
588517	2559	2578	Exon 18	ACCCCTTATAGAAAACCCAA	67	417
588518	2560	2579	Exon 18	AACCCCTTATAGAAAACCCA	57	418
588519	2561	2580	Exon 18	AAACCCCTTATAGAAAACCC	61	419
588520	2562	2581	Exon 18	GAAACCCCTTATAGAAAACC	27	420
588521	2563	2582	Exon 18	GGAAACCCCTTATAGAAAAC	25	421
588522	2564	2583	Exon 18	AGGAAACCCCTTATAGAAAA	36	422
588523	2565	2584	Exon 18	CAGGAAACCCCTTATAGAAA	36	423
588524	2566	2585	Exon 18	GCAGGAAACCCCTTATAGAA	46	424
588525	2567	2586	Exon 18	AGCAGGAAACCCCTTATAGA	38	425
588526	2568	2587	Exon 18	CAGCAGGAAACCCCTTATAG	47	426
588527	2569	2588	Exon 18	CCAGCAGGAAACCCCTTATA	68	427
588528	2570	2589	Exon 18	TCCAGCAGGAAACCCCTTAT	63	428

TABLE 7-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO:
532809	2571	2590	Exon 18	GTCCAGCAGGAAACCCCTTA	85	237
588529	2572	2591	Exon 18	TGTCCAGCAGGAAACCCCTT	76	429
588530	2573	2592	Exon 18	CTGTCCAGCAGGAAACCCCT	74	430
588531	2574	2593	Exon 18	CCTGTCCAGCAGGAAACCCC	75	431
588532	2575	2594	Exon 18	CCCTGTCCAGCAGGAAACCC	73	432
588533	2576	2595	Exon 18	CCCCTGTCCAGCAGGAAACC	82	433
532810	2577	2596	Exon 18	GCCCCTGTCCAGCAGGAAAC	88	238
588534	2578	2597	Exon 18	CGCCCCTGTCCAGCAGGAAA	86	434
588535	2579	2598	Exon 18	ACGCCCCTGTCCAGCAGGAA	86	435
588536	2580	2599	Exon 18	CACGCCCCTGTCCAGCAGGA	93	436
588537	2581	2600	Exon 18	CCACGCCCCTGTCCAGCAGG	92	437
588538	2582	2601	Exon 18	CCCACGCCCCTGTCCAGCAG	94	438
588539	2583	2602	Exon 18	TCCCACGCCCCTGTCCAGCA	96	439
588540	2584	2603	Exon 18	ATCCCACGCCCCTGTCCAGC	88	440
588541	2585	2604	Exon 18	AATCCCACGCCCCTGTCCAG	79	441
588542	2586	2605	Exon 18	CAATCCCACGCCCCTGTCCA	83	442
588543	2587	2606	Exon 18	TCAATCCCACGCCCCTGTCC	86	443
588544	2588	2607	Exon 18	TTCAATCCCACGCCCCTGTC	90	444
588545	2589	2608	Exon 18	ATTCAATCCCACGCCCCTGT	92	445
588546	2590	2609	Exon 18	AATTCAATCCCACGCCCCTG	92	446
588547	2591	2610	Exon 18	TAATTCAATCCCACGCCCCT	88	447
588548	2592	2611	Exon 18	TTAATTCAATCCCACGCCCC	93	448
588549	2593	2612	Exon 18	TTTAATTCAATCCCACGCCC	88	449
588550	2594	2613	Exon 18	TTTTAATTCAATCCCACGCC	89	450
588551	2595	2614	Exon 18	GTTTTAATTCAATCCCACGC	94	451
588552	2596	2615	Exon 18	TGTTTTAATTCAATCCCACG	93	452
588553	2597	2616	Exon 18	CTGTTTTAATTCAATCCCAC	96	453
588554	2598	2617	Exon 18	GCTGTTTTAATTCAATCCCA	98	454
532811	2599	2618	Exon 18	AGCTGTTTTAATTCAATCCC	97	239
532811	2599	2618	Exon 18	AGCTGTTTTAATTCAATCCC	95	239
588555	2600	2619	Exon 18	CAGCTGTTTTAATTCAATCC	93	455
588556	2601	2620	Exon 18	GCAGCTGTTTTAATTCAATC	96	456
588557	2602	2621	Exon 18	CGCAGCTGTTTTAATTCAAT	98	457
588558	2603	2622	Exon 18	TCGCAGCTGTTTTAATTCAA	95	458
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	97	317

TABLE 7-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO:
588559	2605	2624	Exon 18	TGTCGCAGCTGTTTTAATTC	95	459
588560	2606	2625	Exon 18	TTGTCGCAGCTGTTTTAATT	92	460
588561	2607	2626	Exon 18	GTTGTCGCAGCTGTTTTAAT	93	461
532952	2608	2627	Exon 18	TGTTGTCGCAGCTGTTTTAA	88	395
588562	2609	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTTTTA	90	462
588563	2610	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGTTTT	89	463
588564	2611	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTGTTT	92	464
588565	2612	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCTGTT	88	465

TABLE 8

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO 2: start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588685	n/a	n/a	Exon 1	GGATCCAGCTCACTCCCCTG	48	1596	1615	466
588686	n/a	n/a	Exon 1	AAATAAGGATCCAGCTCACT	29	1602	n/a	467
588688	n/a	n/a	Exon 1	GACCAGAAATAAGGATCCAG	58	1608	1627	468
588690	n/a	n/a	Exon 1	CTTAGGGACCAGAAATAAGG	45	1614	1633	469
588692	n/a	n/a	Exon 1	CACCCACTTAGGGACCAGAA	36	1620	1639	470
588694	n/a	n/a	Exon 1	ACCACCCACTTAGGGACCAG	47	1622	1641	471
588696	n/a	n/a	Exon 1	AGGTCCAGGACTCTCCCCTT	96	1685	1704	472
588698	n/a	n/a	Exon 1	AAGGTCCAGGACTCTCCCCT	96	1686	1705	473
588700	n/a	n/a	Exon 1	AAACTGCAGAAGTCCCACCC	2	1716	1735	474
588586	30	49	Exon 1	GGAGGGCCCCGCTGAGCTGC	59	1751	1770	475
588587	48	67	Exon 1	TCCCGGAACATCCAAGCGGG	45	1769	1788	476
588588	56	75	Exon 1	CATCACTTTCCCGGAACATC	39	1777	n/a	477
588589	151	170	Exon 1	CTGGTCACATTCCCTTCCCC	29	1872	1891	478
588590	157	176	Exon 1	CTAGACCTGGTCACATTCCC	47	1878	1897	479
588591	339	358	Exon 1-2 Junction	GGAGTGGTGGTCACACCTCC	44	n/a	n/a	480
588592	384	403	Exon 2	ACCCCCTCCAGAGAGCAGGA	43	2192	2211	481
588593	390	409	Exon 2	ATCTCTACCCCCTCCAGAGA	34	2198	2217	482
588594	467	486	Exon 2	GGTACGGGTAGAAGCCAGAA	17	2275	2294	483

TABLE 8-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO 2: start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588595	671	690	Exon 3	GGAGAGTGTAACCGTCATAG	37	2879	2898	484
588596	689	708	Exon 3	TGCGATTGGCAGAGCCCCGG	18	2897	2916	485
588597	695	714	Exon 3	GGCAGGTGCGATTGGCAGAG	32	2903	2922	486
588598	707	726	Exon 3	GGCCATTCACTTGGCAGGTG	45	2915	2934	487
588599	738	757	Exon 3	TTGTCACAGATCGCTGTCTG	52	2946	2965	488
588600	924	943	Exon 4-5 Junction	AAGGAGTCTTGGCAGGAAGG	39	n/a	n/a	489
588601	931	950	Exon 4-5 Junction	GTACATGAAGGAGTCTTGGC	37	n/a	n/a	490
588602	959	978	Exon 5	AAGCTTCGGCCACCTCTTGA	21	3542	3561	491
588603	1089	1108	Exon 6	CCATCTAGCACCAGGTAGAT	22	3773	3792	492
588604	1108	1127	Exon 6	GGCCCCAATGCTGTCTGATC	21	3792	3811	493
588606	1150	1169	Exon 6	AATTAAGTTGACTAGACACT	56	3834	3853	494
588608	1162	1181	Exon 6-7 Junction	TGCCACCTTCTCAATTAAGT	50	19	495	
588578	1167	1186	Exon 6-7 Junction	TAACTTGCCACCTTCTCAAT	23	n/a	n/a	496
588579	1169	1188	Exon 6-7 Junction	CATAACTTGCCACCTTCTCA	23	n/a	n/a	497
532692	1171	1190	Exon 6-7 Junction	ACCATAACTTGCCACCTTCT	15	n/a	n/a	90
588580	1173	1192	Exon 6-7 Junction	ACACCATAACTTGCCACCTT	16	n/a	n/a	498
588581	1175	1194	Exon 6-7 Junction	TCACACCATAACTTGCCACC	14	4151	4170	499
588610	1319	1338	Exon 8	TAGTCCCTGACTTCAACTTG	50	4612	4631	500
588612	1325	1344	Exon 8	TGGTGTTAGTCCCTGACTTC	47	4618	4637	501
588614	1396	1415	Exon 8	GCGGTTCCAGCCTTCAGGAG	47	4689	4708	502
588616	1421	1440	Exon 8	TCATGAGGATGATGACATGG	51	4714	4733	503
588618	1446	1465	Exon 9	CCGCCCATGTTGTGCAATCC	18	5020	5039	504
588620	1458	1477	Exon 9	GTAATTGGGTCCCCGCCCAT	40	5032	5051	505
588623	1482	1501	Exon 9	AAGTCCCGGATCTCATCAAT	40	5056	5075	506
588624	1542	1561	Exon 9-10 Junction	AACACATAGACATCCAGATA	45	n/a	n/a	507
588626	1585	1604	Exon 10	CAAAGCATTGATGTTCACTT	43	5234	5253	508
588628	1621	1640	Exon 10	TTTGAACACATGTTGCTCAT	45	5270	5289	509
588631	1646	1665	Exon 10	CTTCCAGGTTTTCCATATCC	53	5295	5314	510
588632	1647	1666	Exon 10	TCTTCCAGGTTTTCCATATC	56	5296	5315	511

TABLE 8-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO 2: start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588634	1689	1708	Exon 11	AGACTCAGAGACTGGCTTTC	35	5830	5849	512
588636	1749	1768	Exon 11	GCCTGCCATGGTTGCTTGTG	55	5890	5909	513
588638	1763	1782	Exon 11	TGACTGAGATCTTGGCCTGC	78	5904	5923	514
588640	1912	1931	Exon 13	TTCTATCTCCAGGTCCCGCT	95	6406	6425	515
588642	1982	2001	Exon 13	AGTCATAAAATTCAGGAATT	44	6476	6495	516
588645	2073	2092	Exon 14	CGAGTTGTTCCCTCGGTGCA	40	6662	6681	517
588646	2085	2104	Exon 14	AGCCTCAAAGCTCGAGTTGT	57	6674	6693	518
588648	2091	2110	Exon 14	GGAGGAAGCCTCAAAGCTCG	48	6680	6699	519
588651	2097	2116	Exon 14	GTAGTTGGAGGAAGCCTCAA	40	6686	6705	520
588652	2103	2122	Exon 14	CAAGTGGTAGTTGGAGGAAG	43	6692	6711	521
588654	2166	2185	Exon 15	TCCTCAGACACAAACAGAGC	13	6954	6973	522
588656	2172	2191	Exon 15	TTCTCCTCCTCAGACACAAA	55	6960	6979	523
588658	2196	2215	Exon 15	TAGACCTCCTTCCGAGTCAG	44	6984	7003	524
588660	2202	2221	Exon 15	TTGATGTAGACCTCCTTCCG	50	6990	7009	525
588582	2219	2238	Exon 15-16 Junction	CTTTCTTATCCCCATTCTTG	19	n/a	n/a	526
588583	2221	2240	Exon 15-16 Junction	GCCTTTCTTATCCCCATTCT	14	n/a	n/a	527
532775	2223	2242	Exon 15-16 Junction	CTGCCTTTCTTATCCCCATT	3	n/a	n/a	203
588584	2225	2244	Exon 15-16 Junction	AGCTGCCTTTCTTATCCCCA	18	n/a	n/a	528
588662	2226	2245	Exon 15-16 Junction	CAGCTGCCTTTCTTATCCCC	27	n/a	n/a	529
588585	2227	2246	Exon 15-16 Junction	ACAGCTGCCTTTCTTATCCC	59	n/a	n/a	530
588664	2238	2257	Exon 16	GCATCTCTCTCACAGCTGCC	49	7122	7141	531
588666	2276	2295	Exon 16	AGATGTCCTTGACTTTGTCA	41	7160	7179	532
588668	2330	2349	Exon 16	CAGCATAGGGACTCACTCCT	41	7214	7233	533
588670	2361	2380	Exon 16-17 Junction	CCGCCAGAATCACCTCTGCA	43	n/a	n/a	534
588672	2397	2416	Exon 17	TGAATGAAACGACTTCTCTT	52	7362	7381	535
588674	2430	2449	Exon 18	ACATCCACTACTCCCCAGCT	39	7665	7684	536
588676	2448	2467	Exon 18	CGCTTCTGGTTTTTGCAGAC	69	7683	7702	537

TABLE 8-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO 2: start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588678	2454	2473	Exon 18	TTTTGCCGCTTCTGGTTTTT	46	7689	7708	538
588680	2466	2485	Exon 18	GCAGGTACCTGCTTTTGCCG	47	7701	7720	539
588682	2532	2551	Exon 18	TCTTGGAGTTTCTCCTTCAG	58	7767	7786	540
532811	2599	2618	Exon 18	AGCTGTTTTAATTCAATCCC	10	7834	7853	239
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	11	7839	7858	317

Example 4

Antisense Inhibition of Human Complement Factor B (CFB) in HepG2 Cells by MOE Gapmers

[0434] Antisense oligonucleotides were designed targeting human Complement Factor B (CFB) nucleic acid and were tested for their effects on CFB mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 20,000 cells per well were transfected using electroporation with 3,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0435] The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 4-8-5 MOE, 5-9-5 MOE, 5-10-5 MOE, 3-10-4 MOE, 3-10-7 MOE, 6-7-6-MOE, 6-8-6 MOE, or 5-7-5 MOE gapmers, or as deoxy, MOE, and cEt oligonucleotides.

[0436] The 4-8-5 MOE gapmers are 17 nucleosides in length, wherein the central gap segment comprises of eight 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising four and five nucleosides respectively. The 5-9-5 MOE gapmers are 19 nucleosides in length, wherein the central gap segment comprises of nine 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 5-10-5 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 5-7-5 MOE gapmers are 17 nucleosides in length, wherein the central gap segment comprises of seven 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 3-10-4 MOE gapmers are 17 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising three and four nucleosides respectively. The 3-10-7 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising three and seven nucleosides respectively. The 6-7-6 MOE gapmers are 19 nucleosides in length, wherein the central gap segment comprises of seven 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising six nucleosides each. The 6-8-6 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of eight 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising six nucleosides each. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines.

[0437] The deoxy, MOE and cEt oligonucleotides are 16 nucleosides in length wherein the nucleoside have either a MOE sugar modification, an cEt sugar modification, or a deoxy modification. The 'Chemistry' column describes the sugar modifications of each oligonucleotide. 'k' indicates an cEt sugar modification; 'd' indicates deoxyribose; and 'e' indicates a MOE modification.

[0438] "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in the Tables below is targeted to either the human CFB mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_001710.5) or the human CFB genomic sequence, designated herein as SEQ ID NO: 2 (GENBANK Accession No. NT_007592.15 truncated from nucleotides 31852000 to 31861000), or both. 'n/a' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity.

TABLE 9

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 Start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 Start site	SEQ ID NO: 2 Stop site	Motif	SEQ ID NO:
532811	2599	2618	Exon 18	AGCTGTTTTAATTCAATCCC	10	7834	7853	eeeeeddddddddddeeeee	239
588884	48	63	Exon 1	GGAACATCCAAGCGGG	79	1769	1784	eekddddddddddkke	541
588872	154	169	Exon 1	TGGTCACATTCCCTTC	91	1875	1890	eekddddddddddkke	542
588873	156	171	Exon 1	CCTGGTCACATTCCCT	91	1877	1892	eekddddddddddkke	543
588874	158	173	Exon 1	GACCTGGTCACATTCC	91	1879	1894	eekddddddddddkke	544
588878	1171	1186	Exon 6-7 Junction	TAACTTGCCACCTTCT	92	n/a	n/a	eekddddddddddkke	545
588879	1173	1188	Exon 6-7 Junction	CATAACTTGCCACCTT	94	n/a	n/a	eekddddddddddkke	546
588880	1175	1190	Exon 6-7 Junction	ACCATAACTTGCCACC	89	4151	4166	eekddddddddddkke	547
588869	2193	2208	Exon 15	CCTTCCGAGTCAGCTT	17	6981	6996	eekddddddddddkke	548
588870	2195	2210	Exon 15	CTCCTTCCGAGTCAGC	78	6983	6998	eekddddddddddkke	549
588871	2197	2212	Exon 15	ACCTCCTTCCGAGTCA	80	6985	7000	eekddddddddddkke	550
588881	2223	2238	Exon 15-16 Junction	CTTTCTTATCCCCATT	93	n/a	n/a	eekddddddddddkke	551
588882	2225	2240	Exon 15-16 Junction	GCCTTTCTTATCCCCA	88	n/a	n/a	eekddddddddddkke	552
588883	2227	2242	Exon 15-16 Junction	CTGCCTTTCTTATCCC	90	n/a	n/a	eekddddddddddkke	553
588875	2457	2472	Exon 18	TTTGCCGCTTCTGGTT	81	7692	7707	eekddddddddddkke	554
588876	2459	2474	Exon 18	CTTTTGCCGCTTCTGG	95	7694	7709	eekddddddddddkke	555
588877	2461	2476	Exon 18	TGCTTTTGCCGCTTCT	91	7696	7711	eekddddddddddkke	556
588807	2551	2566	Exon 18	AAACCCAAATCCTCAT	82	7786	7801	eekddddddddddkke	557
588808	2553	2568	Exon 18	GAAAACCCAAATCCTC	69	7788	7803	eekddddddddddkke	558
588809	2555	2570	Exon 18	TAGAAAACCCAAATCC	51	7790	7805	eekddddddddddkke	559
588810	2556	2571	Exon 18	ATAGAAAACCCAAATC	23	7791	7806	eekddddddddddkke	560
588811	2559	2574	Exon 18	CTTATAGAAAACCCAA	13	7794	7809	eekddddddddddkke	561
588812	2560	2575	Exon 18	CCTTATAGAAAACCCA	29	7795	7810	eekddddddddddkke	562
588813	2561	2576	Exon 18	CCCTTATAGAAAACCC	53	7796	7811	eekddddddddddkke	563
588814	2562	2577	Exon 18	CCCCTTATAGAAAACC	86	7797	7812	eekddddddddddkke	564
588815	2563	2578	Exon 18	ACCCCTTATAGAAAAC	76	7798	7813	eekddddddddddkke	565
588816	2564	2579	Exon 18	AACCCCTTATAGAAAA	33	7799	7814	eekddddddddddkke	566
588817	2565	2580	Exon 18	AAACCCCTTATAGAAA	48	7800	7815	eekddddddddddkke	567
588818	2566	2581	Exon 18	GAAACCCCTTATAGAA	44	7801	7816	eekddddddddddkke	568
588819	2567	2582	Exon 18	GGAAACCCCTTATAGA	74	7802	7817	eekddddddddddkke	569
588820	2568	2583	Exon 18	AGGAAACCCCTTATAG	68	7803	7818	eekddddddddddkke	570

TABLE 9-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 Start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 Start site	SEQ ID NO: 2 Stop site	Motif	SEQ ID NO:
588821	2569	2584	Exon 18	CAGGAAACCCCTTATA	45	7804	7819	eekddddddddddkke	571
588822	2570	2585	Exon 18	GCAGGAAACCCCTTAT	50	7805	7820	eekddddddddddkke	572
588823	2571	2586	Exon 18	AGCAGGAAACCCCTTA	54	7806	7821	eekddddddddddkke	573
588824	2572	2587	Exon 18	CAGCAGGAAACCCCTT	35	7807	7822	eekddddddddddkke	574
588825	2573	2588	Exon 18	CCAGCAGGAAACCCCT	11	7808	7823	eekddddddddddkke	575
588826	2574	2589	Exon 18	TCCAGCAGGAAACCCC	19	7809	7824	eekddddddddddkke	576
588827	2575	2590	Exon 18	GTCCAGCAGGAAACCC	42	7810	7825	eekddddddddddkke	577
588828	2576	2591	Exon 18	TGTCCAGCAGGAAACC	0	7811	7826	eekddddddddddkke	578
588829	2577	2592	Exon 18	CTGTCCAGCAGGAAAC	49	7812	7827	eekddddddddddkke	579
588830	2578	2593	Exon 18	CCTGTCCAGCAGGAAA	11	7813	7828	eekddddddddddkke	580
588831	2579	2594	Exon 18	CCCTGTCCAGCAGGAA	20	7814	7829	eekddddddddddkke	581
588832	2580	2595	Exon 18	CCCCTGTCCAGCAGGA	19	7815	7830	eekddddddddddkke	582
588833	2581	2596	Exon 18	GCCCCTGTCCAGCAGG	12	7816	7831	eekddddddddddkke	583
588834	2582	2597	Exon 18	CGCCCCTGTCCAGCAG	10	7817	7832	eekddddddddddkke	584
588835	2583	2598	Exon 18	ACGCCCCTGTCCAGCA	13	7818	7833	eekddddddddddkke	585
588836	2584	2599	Exon 18	CACGCCCCTGTCCAGC	13	7819	7834	eekddddddddddkke	586
588837	2585	2600	Exon 18	CCACGCCCCTGTCCAG	39	7820	7835	eekddddddddddkke	587
588838	2586	2601	Exon 18	CCCACGCCCCTGTCCA	54	7821	7836	eekddddddddddkke	588
588839	2587	2602	Exon 18	TCCCACGCCCCTGTCC	51	7822	7837	eekddddddddddkke	589
588840	2588	2603	Exon 18	ATCCCACGCCCCTGTC	65	7823	7838	eekddddddddddkke	590
588841	2589	2604	Exon 18	AATCCCACGCCCCTGT	59	7824	7839	eekddddddddddkke	591
588842	2590	2605	Exon 18	CAATCCCACGCCCCTG	70	7825	7840	eekddddddddddkke	592
588843	2591	2606	Exon 18	TCAATCCCACGCCCCT	0	7826	7841	eekddddddddddkke	593
588844	2592	2607	Exon 18	TTCAATCCCACGCCCC	48	7827	7842	eekddddddddddkke	594
588845	2593	2608	Exon 18	ATTCAATCCCACGCCC	46	7828	7843	eekddddddddddkke	595
588846	2594	2609	Exon 18	AATTCAATCCCACGCC	67	7829	7844	eekddddddddddkke	596
588847	2595	2610	Exon 18	TAATTCAATCCCACGC	75	7830	7845	eekddddddddddkke	597
588848	2596	2611	Exon 18	TTAATTCAATCCCACG	76	7831	7846	eekddddddddddkke	598
588849	2597	2612	Exon 18	TTTAATTCAATCCCAC	94	7832	7847	eekddddddddddkke	599
588850	2598	2613	Exon 18	TTTTAATTCAATCCCA	91	7833	7848	eekddddddddddkke	600
588851	2599	2614	Exon 18	GTTTTAATTCAATCCC	91	7834	7849	eekddddddddddkke	601
588852	2600	2615	Exon 18	TGTTTTAATTCAATCC	78	7835	7850	eekddddddddddkke	602
588853	2601	2616	Exon 18	CTGTTTTAATTCAATC	81	7836	7851	eekddddddddddkke	603
588854	2602	2617	Exon 18	GCTGTTTTAATTCAAT	63	7837	7852	eekddddddddddkke	604
588855	2603	2618	Exon 18	AGCTGTTTTAATTCAA	65	7838	7853	eekddddddddddkke	605

TABLE 9-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 Start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 Start site	SEQ ID NO: 2 Stop site	Motif	SEQ ID NO:
588856	2604	2619	Exon 18	CAGCTGTTTTAATTCA	76	7839	7854	eekddddddddddkke	606
588857	2605	2620	Exon 18	GCAGCTGTTTTAATTC	89	7840	7855	eekddddddddddkke	607
588858	2606	2621	Exon 18	CGCAGCTGTTTTAATT	89	7841	7856	eekddddddddddkke	608
588859	2607	2622	Exon 18	TCGCAGCTGTTTTAAT	89	7842	7857	eekddddddddddkke	609
588860	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	76	7843	7858	eekddddddddddkke	610
588861	2609	2624	Exon 18	TGTCGCAGCTGTTTTA	87	7844	7859	eekddddddddddkke	611
588862	2610	2625	Exon 18	TTGTCGCAGCTGTTTT	85	7845	7860	eekddddddddddkke	612
588863	2611	2626	Exon 18	GTTGTCGCAGCTGTTT	87	7846	7861	eekddddddddddkke	613
588864	2612	2627	Exon 18	TGTTGTCGCAGCTGTT	67	7847	7862	eekddddddddddkke	614
588865	2613	2628	Exon 18	TTGTTGTCGCAGCTGT	51	n/a	n/a	eekddddddddddkke	615
588866	2614	2629	Exon 18	TTTGTTGTCGCAGCTG	95	n/a	n/a	eekddddddddddkke	616
588867	2615	2630	Exon 18	TTTTGTTGTCGCAGCT	92	n/a	n/a	eekddddddddddkke	617
588868	2616	2631	Exon 18	TTTTTGTTGTCGCAGC	66	n/a	n/a	eekddddddddddkke	618

TABLE 10

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588685	n/a	n/a	Exon 1	GGATCCAGCTCACTCCCCTG	14	1596	1615	466
588686	n/a	n/a	Exon 1	AAATAAGGATCCAGCTCACT	2	1602	1621	467
588688	n/a	n/a	Exon 1	GACCAGAAATAAGGATCCAG	3	1608	1627	468
588690	n/a	n/a	Exon 1	CTTAGGGACCAGAAATAAGG	10	1614	1633	469
588692	n/a	n/a	Exon 1	CACCCACTTAGGGACCAGAA	23	1620	1639	470
588694	n/a	n/a	Exon 1	ACCACCCACTTAGGGACCAG	23	1622	1641	471
588696	n/a	n/a	Exon 1	AGGTCCAGGACTCTCCCCTT	15	1685	1704	472
588698	n/a	n/a	Exon 1	AAGGTCCAGGACTCTCCCCT	19	1686	1705	473
588700	n/a	n/a	Exon 1	AAACTGCAGAAGTCCCACCC	16	1716	1735	474
588586	30	49	Exon 1	GGAGGGCCCCGCTGAGCTGC	11	1751	1770	475
588587	48	67	Exon 1	TCCCGGAACATCCAAGCGGG	14	1769	1788	476
588588	56	75	Exon 1	CATCACTTTCCCGGAACATC	18	1777	1796	477
588589	151	170	Exon 1	CTGGTCACATTCCCTTCCCC	59	1872	1891	478
588590	157	176	Exon 1	CTAGACCTGGTCACATTCCC	59	1878	1897	479

TABLE 10-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588591	339	358	Exon 1-2 Junction	GGAGTGGTGGTCACACCTCC	45	n/a	n/a	480
588592	384	403	Exon 2	ACCCCCTCCAGAGAGCAGGA	39	2192	2211	481
588593	390	409	Exon 2	ATCTCTACCCCCTCCAGAGA	29	2198	2217	482
588594	467	486	Exon 2	GGTACGGGTAGAAGCCAGAA	47	2275	2294	483
588595	671	690	Exon 3	GGAGAGTGTAACCGTCATAG	44	2879	2898	484
588596	689	708	Exon 3	TGCGATTGGCAGAGCCCCGG	43	2897	2916	638
588597	695	714	Exon 3	GGCAGGTGCGATTGGCAGAG	34	2903	2922	486
588598	707	726	Exon 3	GGCCATTCACTTGGCAGGTG	17	2915	2934	487
588599	738	757	Exon 3	TTGTCACAGATCGCTGTCTG	37	2946	2965	488
588600	924	943	Exon 3-4 Junction	AAGGAGTCTTGGCAGGAAGG	18	n/a	n/a	489
588601	931	950	Exon 3-4 Junction	GTACATGAAGGAGTCTTGGC	32	n/a	n/a	490
588602	959	978	Exon 5	AAGCTTCGGCCACCTCTTGA	45	3542	3561	491
588603	1089	1108	Exon 6	CCATCTAGCACCAGGTAGAT	52	3773	3792	492
588604	1108	1127	Exon 6	GGCCCCAATGCTGTCTGATC	39	3792	3811	493
588606	1150	1169	Exon 6	AATTAAGTTGACTAGACACT	37	3834	3853	494
588608	1162	1181	Exon 6-7 Junction	TGCCACCTTCTCAATTAAGT	21	n/a	n/a	648
588578	1167	1186	Exon 6-7 Junction	TAACTTGCCACCTTCTCAAT	22	n/a	n/a	496
588579	1169	1188	Exon 6-7 Junction	CATAACTTGCCACCTTCTCA	21	n/a	n/a	497
532692	1171	1190	Exon 6-7 Junction	ACCATAACTTGCCACCTTCT	56	n/a	n/a	90
588580	1173	1192	Exon 6-7 Junction	ACACCATAACTTGCCACCTT	50	n/a	n/a	498
588581	1175	1194	Exon 7	TCACACCATAACTTGCCACC	50	4151	4170	499
588610	1319	1338	Exon 8	TAGTCCCTGACTTCAACTTG	47	4612	4631	500
588612	1325	1344	Exon 8	TGGTGTTAGTCCCTGACTTC	47	4618	4637	501
588614	1396	1415	Exon 8	GCGGTTCCAGCCTTCAGGAG	51	4689	4708	502
588616	1421	1440	Exon 8	TCATGAGGATGATGACATGG	18	4714	4733	503
588618	1446	1465	Exon 9	CCGCCCATGTTGTGCAATCC	40	5020	5039	504
588620	1458	1477	Exon 9	GTAATTGGGTCCCCGCCCAT	40	5032	5051	505
588623	1482	1501	Exon 9	AAGTCCCGGATCTCATCAAT	45	5056	5075	506
588624	1542	1561	Exon 9-10 Junction	AACACATAGACATCCAGATA	43	n/a	n/a	507

TABLE 10-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588626	1585	1604	Exon 10	CAAAGCATTGATGTTCACTT	45	5234	5253	508
588628	1621	1640	Exon 10	TTTGAACACATGTTGCTCAT	53	5270	5289	509
588631	1646	1665	Exon 10	CTTCCAGGTTTTCCATATCC	56	5295	5314	510
588632	1647	1666	Exon 10	TCTTCCAGGTTTTCCATATC	35	5296	5315	511
588634	1689	1708	Exon 11	AGACTCAGAGACTGGCTTTC	55	5830	5849	512
588636	1749	1768	Exon 11	GCCTGCCATGGTTGCTTGTG	78	5890	5909	513
588638	1763	1782	Exon 11	TGACTGAGATCTTGGCCTGC	95	5904	5923	514
588640	1912	1931	Exon 13	TTCTATCTCCAGGTCCCGCT	44	6406	6425	515
588642	1982	2001	Exon 13	AGTCATAAAATTCAGGAATT	40	6476	6495	516
588645	2073	2092	Exon 14	CGAGTTGTTCCCTCGGTGCA	57	6662	6681	517
588646	2085	2104	Exon 14	AGCCTCAAAGCTCGAGTTGT	48	6674	6693	518
588648	2091	2110	Exon 14	GGAGGAAGCCTCAAAGCTCG	40	6680	6699	519
588651	2097	2116	Exon 14	GTAGTTGGAGGAAGCCTCAA	43	6686	6705	520
588652	2103	2122	Exon 14	CAAGTGGTAGTTGGAGGAAG	13	6692	6711	521
588654	2166	2185	Exon 15	TCCTCAGACACAAACAGAGC	55	6954	6973	522
588656	2172	2191	Exon 15	TTCTCCTCCTCAGACACAAA	44	6960	6979	523
588658	2196	2215	Exon 15	TAGACCTCCTTCCGAGTCAG	50	6984	7003	524
588660	2202	2221	Exon 15	TTGATGTAGACCTCCTTCCG	27	6990	7009	525
588582	2219	2238	Exon 15-16 Junction	CTTTCTTATCCCCATTCTTG	49	n/a	n/a	526
588583	2221	2240	Exon 15-16 Junction	GCCTTTCTTATCCCCATTCT	41	n/a	n/a	527
532775	2223	2242	Exon 15-16 Junction	CTGCCTTTCTTATCCCCATT	41	n/a	n/a	203
588584	2225	2244	Exon 15-16 Junction	AGCTGCCTTTCTTATCCCCA	43	n/a	n/a	528
588662	2226	2245	Exon 15-16 Junction	CAGCTGCCTTTCTTATCCCC	52	n/a	n/a	529
588585	2227	2246	Exon 15-16 Junction	ACAGCTGCCTTTCTTATCCC	39	n/a	n/a	530
588664	2238	2257	Exon 16	GCATCTCTCTCACAGCTGCC	69	7122	7141	531
588666	2276	2295	Exon 16	AGATGTCCTTGACTTTGTCA	46	7160	7179	532
588668	2330	2349	Exon 16	CAGCATAGGGACTCACTCCT	47	7214	7233	533

TABLE 10-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588670	2361	2380	Exon 16-17 Junction	CCGCCAGAATCACCTCTGCA	58	n/a	n/a	534
588672	2397	2416	Exon 17	TGAATGAAACGACTTCTCTT	48	7362	7381	535
588674	2430	2449	Exon 18	ACATCCACTACTCCCCAGCT	29	7665	7684	536
588676	2448	2467	Exon 18	CGCTTCTGGTTTTTGCAGAC	58	7683	7702	537
588678	2454	2473	Exon 18	TTTTGCCGCTTCTGGTTTTT	45	7689	7708	538
588680	2466	2485	Exon 18	GCAGGTACCTGCTTTTGCCG	36	7701	7720	539
588682	2532	2551	Exon 18	TCTTGGAGTTTCTCCTTCAG	47	7767	7786	540
532811	2599	2618	Exon 18	AGCTGTTTTAATTCAATCCC	96	7834	7853	239
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	96	7839	7858	317

TABLE 11

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
598973	2552	2568	Exon 18	GAAAACCCAAATCCTCA	40	7787	7803	3-10-4	619
599036	2552	2568	Exon 18	GAAAACCCAAATCCTCA	18	7787	7803	5-7-5	619
598974	2553	2569	Exon 18	AGAAAACCCAAATCCTC	28	7788	7804	3-10-4	620
599037	2553	2569	Exon 18	AGAAAACCCAAATCCTC	19	7788	7804	5-7-5	620
598975	2554	2570	Exon 18	TAGAAAACCCAAATCCT	15	7789	7805	3-10-4	621
599038	2554	2570	Exon 18	TAGAAAACCCAAATCCT	32	7789	7805	5-7-5	621
598976	2555	2571	Exon 18	ATAGAAAACCCAAATCC	12	7790	7806	3-10-4	622
599039	2555	2571	Exon 18	ATAGAAAACCCAAATCC	7	7790	7806	5-7-5	622
598977	2557	2573	Exon 18	TTATAGAAAACCCAAAT	13	7792	7808	3-10-4	623
599040	2557	2573	Exon 18	TTATAGAAAACCCAAAT	13	7792	7808	5-7-5	623
598978	2558	2574	Exon 18	CTTATAGAAAACCCAAA	0	7793	7809	3-10-4	624
599041	2558	2574	Exon 18	CTTATAGAAAACCCAAA	0	7793	7809	5-7-5	624
598979	2559	2575	Exon 18	CCTTATAGAAAACCCAA	8	7794	7810	3-10-4	625
599042	2559	2575	Exon 18	CCTTATAGAAAACCCAA	19	7794	7810	5-7-5	625
598980	2560	2576	Exon 18	CCCTTATAGAAAACCCA	42	7795	7811	3-10-4	626
599043	2560	2576	Exon 18	CCCTTATAGAAAACCCA	10	7795	7811	5-7-5	626
598981	2561	2577	Exon 18	CCCCTTATAGAAAACCC	20	7796	7812	3-10-4	627

TABLE 11-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599044	2561	2577	Exon 18	CCCCTTATAGAAAACCC	12	7796	7812	5-7-5	627
598982	2562	2578	Exon 18	ACCCCTTATAGAAAACC	10	7797	7813	3-10-4	628
599045	2562	2578	Exon 18	ACCCCTTATAGAAAACC	3	7797	7813	5-7-5	628
598983	2563	2579	Exon 18	AACCCCTTATAGAAAAC	0	7798	7814	3-10-4	629
599046	2563	2579	Exon 18	AACCCCTTATAGAAAAC	18	7798	7814	5-7-5	629
598984	2564	2580	Exon 18	AAACCCCTTATAGAAAA	0	7799	7815	3-10-4	630
599047	2564	2580	Exon 18	AAACCCCTTATAGAAAA	7	7799	7815	5-7-5	630
598985	2565	2581	Exon 18	GAAACCCCTTATAGAAA	0	7800	7816	3-10-4	631
599048	2565	2581	Exon 18	GAAACCCCTTATAGAAA	9	7800	7816	5-7-5	631
598986	2566	2582	Exon 18	GGAAACCCCTTATAGAA	0	7801	7817	3-10-4	632
599049	2566	2582	Exon 18	GGAAACCCCTTATAGAA	18	7801	7817	5-7-5	632
598988	2567	2583	Exon 18	AGGAAACCCCTTATAGA	0	7802	7818	3-10-4	633
599050	2567	2583	Exon 18	AGGAAACCCCTTATAGA	8	7802	7818	5-7-5	633
598989	2568	2584	Exon 18	CAGGAAACCCCTTATAG	0	7803	7819	3-10-4	634
598990	2569	2585	Exon 18	GCAGGAAACCCCTTATA	8	7804	7820	3-10-4	635
598991	2570	2586	Exon 18	AGCAGGAAACCCCTTAT	25	7805	7821	3-10-4	636
598992	2571	2587	Exon 18	CAGCAGGAAACCCCTTA	12	7806	7822	3-10-4	637
598993	2572	2588	Exon 18	CCAGCAGGAAACCCCTT	37	7807	7823	3-10-4	638
598994	2573	2589	Exon 18	TCCAGCAGGAAACCCCT	29	7808	7824	3-10-4	639
598995	2574	2590	Exon 18	GTCCAGCAGGAAACCCC	42	7809	7825	3-10-4	640
598996	2575	2591	Exon 18	TGTCCAGCAGGAAACCC	36	7810	7826	3-10-4	641
598997	2576	2592	Exon 18	CTGTCCAGCAGGAAACC	18	7811	7827	3-10-4	642
598998	2577	2593	Exon 18	CCTGTCCAGCAGGAAAC	27	7812	7828	3-10-4	643
598999	2578	2594	Exon 18	CCCTGTCCAGCAGGAAA	61	7813	7829	3-10-4	644
599000	2580	2596	Exon 18	GCCCCTGTCCAGCAGGA	71	7815	7831	3-10-4	645
599001	2581	2597	Exon 18	CGCCCCTGTCCAGCAGG	80	7816	7832	3-10-4	646
599002	2582	2598	Exon 18	ACGCCCCTGTCCAGCAG	68	7817	7833	3-10-4	647
599003	2583	2599	Exon 18	CACGCCCCTGTCCAGCA	71	7818	7834	3-10-4	648
599004	2584	2600	Exon 18	CCACGCCCCTGTCCAGC	76	7819	7835	3-10-4	649
599005	2585	2601	Exon 18	CCCACGCCCCTGTCCAG	70	7820	7836	3-10-4	650
599006	2586	2602	Exon 18	TCCCACGCCCCTGTCCA	65	7821	7837	3-10-4	651
599007	2587	2603	Exon 18	ATCCCACGCCCCTGTCC	60	7822	7838	3-10-4	652
599008	2588	2604	Exon 18	AATCCCACGCCCCTGTC	72	7823	7839	3-10-4	653
599009	2589	2605	Exon 18	CAATCCCACGCCCCTGT	79	7824	7840	3-10-4	654

TABLE 11-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599010	2590	2606	Exon 18	TCAATCCCACGCCCCTG	73	7825	7841	3-10-4	655
599011	2591	2607	Exon 18	TTCAATCCCACGCCCCT	79	7826	7842	3-10-4	656
599012	2592	2608	Exon 18	ATTCAATCCCACGCCCC	67	7827	7843	3-10-4	657
599013	2593	2609	Exon 18	AATTCAATCCCACGCCC	65	7828	7844	3-10-4	658
599014	2594	2610	Exon 18	TAATTCAATCCCACGCC	74	7829	7845	3-10-4	659
599015	2595	2611	Exon 18	TTAATTCAATCCCACGC	71	7830	7846	3-10-4	660
599016	2596	2612	Exon 18	TTTAATTCAATCCCACG	48	7831	7847	3-10-4	661
599017	2597	2613	Exon 18	TTTTAATTCAATCCCAC	34	7832	7848	3-10-4	662
599018	2598	2614	Exon 18	GTTTTAATTCAATCCCA	56	7833	7849	3-10-4	663
599019	2599	2615	Exon 18	TGTTTTAATTCAATCCC	60	7834	7850	3-10-4	664
599020	2600	2616	Exon 18	CTGTTTTAATTCAATCC	0	7835	7851	3-10-4	665
599021	2601	2617	Exon 18	GCTGTTTTAATTCAATC	33	7836	7852	3-10-4	666
599022	2602	2618	Exon 18	AGCTGTTTTAATTCAAT	17	7837	7853	3-10-4	667
599023	2603	2619	Exon 18	CAGCTGTTTTAATTCAA	52	7838	7854	3-10-4	668
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	86	7839	7858	5-10-5	317
599024	2604	2620	Exon 18	GCAGCTGTTTTAATTCA	88	7839	7855	3-10-4	669
599025	2605	2621	Exon 18	CGCAGCTGTTTTAATTC	85	7840	7856	3-10-4	670
599026	2606	2622	Exon 18	TCGCAGCTGTTTTAATT	69	7841	7857	3-10-4	671
599027	2607	2623	Exon 18	GTCGCAGCTGTTTTAAT	77	7842	7858	3-10-4	672
599028	2608	2624	Exon 18	TGTCGCAGCTGTTTTAA	73	7843	7859	3-10-4	673
599029	2609	2625	Exon 18	TTGTCGCAGCTGTTTTA	78	7844	7860	3-10-4	674
599030	2610	2626	Exon 18	GTTGTCGCAGCTGTTTT	75	7845	7861	3-10-4	675
599031	2611	2627	Exon 18	TGTTGTCGCAGCTGTTT	77	7846	7862	3-10-4	676
599032	2612	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTT	79	n/a	n/a	3-10-4	677
599033	2613	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGT	80	n/a	n/a	3-10-4	678
599034	2614	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTG	78	n/a	n/a	3-10-4	679
599035	2615	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCT	63	n/a	n/a	3-10-4	680

TABLE 12

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599098	2552	2568	Exon 18	GAAAACCCAAATCCTCA	57	7787	7803	4-8-5	619
599099	2553	2569	Exon 18	AGAAAACCCAAATCCTC	33	7788	7804	4-8-5	620
599100	2554	2570	Exon 18	TAGAAAACCCAAATCCT	32	7789	7805	4-8-5	621
599101	2555	2571	Exon 18	ATAGAAAACCCAAATCC	47	7790	7806	4-8-5	622
599102	2557	2573	Exon 18	TTATAGAAAACCCAAAT	59	7792	7808	4-8-5	623
599103	2558	2574	Exon 18	CTTATAGAAAACCCAAA	10	7793	7809	4-8-5	624
599104	2559	2575	Exon 18	CCTTATAGAAAACCCAA	3	7794	7810	4-8-5	625
599105	2560	2576	Exon 18	CCCTTATAGAAAACCCA	45	7795	7811	4-8-5	626
599106	2561	2577	Exon 18	CCCCTTATAGAAAACCC	49	7796	7812	4-8-5	627
599107	2562	2578	Exon 18	ACCCCTTATAGAAAACC	35	7797	7813	4-8-5	628
599108	2563	2579	Exon 18	AACCCCTTATAGAAAAC	17	7798	7814	4-8-5	629
599109	2564	2580	Exon 18	AAACCCCTTATAGAAAA	36	7799	7815	4-8-5	630
599110	2565	2581	Exon 18	GAAACCCCTTATAGAAA	20	7800	7816	4-8-5	631
599111	2566	2582	Exon 18	GGAAACCCCTTATAGAA	20	7801	7817	4-8-5	632
599112	2567	2583	Exon 18	AGGAAACCCCTTATAGA	15	7802	7818	4-8-5	633
599113	2568	2584	Exon 18	CAGGAAACCCCTTATAG	19	7803	7819	4-8-5	634
599051	2568	2584	Exon 18	CAGGAAACCCCTTATAG	26	7803	7819	5-7-5	634
599114	2569	2585	Exon 18	GCAGGAAACCCCTTATA	18	7804	7820	4-8-5	635
599052	2569	2585	Exon 18	GCAGGAAACCCCTTATA	21	7804	7820	5-7-5	635
599115	2570	2586	Exon 18	AGCAGGAAACCCCTTAT	31	7805	7821	4-8-5	636
599053	2570	2586	Exon 18	AGCAGGAAACCCCTTAT	25	7805	7821	5-7-5	636
599116	2571	2587	Exon 18	CAGCAGGAAACCCCTTA	39	7806	7822	4-8-5	637
599054	2571	2587	Exon 18	CAGCAGGAAACCCCTTA	36	7806	7822	5-7-5	637
599117	2572	2588	Exon 18	CCAGCAGGAAACCCCTT	46	7807	7823	4-8-5	638
599055	2572	2588	Exon 18	CCAGCAGGAAACCCCTT	22	7807	7823	5-7-5	638
599118	2573	2589	Exon 18	TCCAGCAGGAAACCCCT	40	7808	7824	4-8-5	639
599056	2573	2589	Exon 18	TCCAGCAGGAAACCCCT	32	7808	7824	5-7-5	639
599119	2574	2590	Exon 18	GTCCAGCAGGAAACCCC	50	7809	7825	4-8-5	640
599057	2574	2590	Exon 18	GTCCAGCAGGAAACCCC	46	7809	7825	5-7-5	640
599120	2575	2591	Exon 18	TGTCCAGCAGGAAACCC	30	7810	7826	4-8-5	641
599058	2575	2591	Exon 18	TGTCCAGCAGGAAACCC	52	7810	7826	5-7-5	641
599121	2576	2592	Exon 18	CTGTCCAGCAGGAAACC	31	7811	7827	4-8-5	642
599059	2576	2592	Exon 18	CTGTCCAGCAGGAAACC	24	7811	7827	5-7-5	642
599122	2577	2593	Exon 18	CCTGTCCAGCAGGAAAC	23	7812	7828	4-8-5	643
599060	2577	2593	Exon 18	CCTGTCCAGCAGGAAAC	37	7812	7828	5-7-5	643

TABLE 12-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599123	2578	2594	Exon 18	CCCTGTCCAGCAGGAAA	51	7813	7829	4-8-5	644
599061	2578	2594	Exon 18	CCCTGTCCAGCAGGAAA	34	7813	7829	5-7-5	644
599124	2580	2596	Exon 18	GCCCCTGTCCAGCAGGA	56	7815	7831	4-8-5	645
599062	2580	2596	Exon 18	GCCCCTGTCCAGCAGGA	51	7815	7831	5-7-5	645
599125	2581	2597	Exon 18	CGCCCCTGTCCAGCAGG	70	7816	7832	4-8-5	646
599063	2581	2597	Exon 18	CGCCCCTGTCCAGCAGG	56	7816	7832	5-7-5	646
599126	2582	2598	Exon 18	ACGCCCCTGTCCAGCAG	76	7817	7833	4-8-5	647
599064	2582	2598	Exon 18	ACGCCCCTGTCCAGCAG	61	7817	7833	5-7-5	647
599127	2583	2599	Exon 18	CACGCCCCTGTCCAGCA	67	7818	7834	4-8-5	648
599065	2583	2599	Exon 18	CACGCCCCTGTCCAGCA	64	7818	7834	5-7-5	648
599066	2584	2600	Exon 18	CCACGCCCCTGTCCAGC	40	7819	7835	5-7-5	649
599067	2585	2601	Exon 18	CCCACGCCCCTGTCCAG	37	7820	7836	5-7-5	650
599068	2586	2602	Exon 18	TCCCACGCCCCTGTCCA	31	7821	7837	5-7-5	651
599069	2587	2603	Exon 18	ATCCCACGCCCCTGTCC	39	7822	7838	5-7-5	652
599070	2588	2604	Exon 18	AATCCCACGCCCCTGTC	59	7823	7839	5-7-5	653
599071	2589	2605	Exon 18	CAATCCCACGCCCCTGT	63	7824	7840	5-7-5	657
599072	2590	2606	Exon 18	TCAATCCCACGCCCCTG	74	7825	7841	5-7-5	655
599073	2591	2607	Exon 18	TTCAATCCCACGCCCCT	53	7826	7842	5-7-5	656
599074	2592	2608	Exon 18	ATTCAATCCCACGCCCC	56	7827	7843	5-7-5	657
599075	2593	2609	Exon 18	AATTCAATCCCACGCCC	49	7828	7844	5-7-5	658
599076	2594	2610	Exon 18	TAATTCAATCCCACGCC	54	7829	7845	5-7-5	659
599077	2595	2611	Exon 18	TTAATTCAATCCCACGC	79	7830	7846	5-7-5	660
599078	2596	2612	Exon 18	TTTAATTCAATCCCACG	67	7831	7847	5-7-5	661
599079	2597	2613	Exon 18	TTTTAATTCAATCCCAC	69	7832	7848	5-7-5	662
599080	2598	2614	Exon 18	GTTTTAATTCAATCCCA	79	7833	7849	5-7-5	663
599081	2599	2615	Exon 18	TGTTTTAATTCAATCCC	57	7834	7850	5-7-5	664
599082	2600	2616	Exon 18	CTGTTTTAATTCAATCC	50	7835	7851	5-7-5	665
599083	2601	2617	Exon 18	GCTGTTTTAATTCAATC	67	7836	7852	5-7-5	666
599084	2602	2618	Exon 18	AGCTGTTTTAATTCAAT	60	7837	7853	5-7-5	667
599085	2603	2619	Exon 18	CAGCTGTTTTAATTCAA	71	7838	7854	5-7-5	668
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	82	7839	7858	5-10-5	317
599086	2604	2620	Exon 18	GCAGCTGTTTTAATTCA	81	7839	7855	5-7-5	669
599087	2605	2621	Exon 18	CGCAGCTGTTTTAATTC	88	7840	7856	5-7-5	670
599088	2606	2622	Exon 18	TCGCAGCTGTTTTAATT	84	7841	7857	5-7-5	671

TABLE 12-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599089	2607	2623	Exon 18	GTCGCAGCTGTTTTAAT	81	7842	7858	5-7-5	672
599090	2608	2624	Exon 18	TGTCGCAGCTGTTTTAA	77	7843	7859	5-7-5	673
599091	2609	2625	Exon 18	TTGTCGCAGCTGTTTTA	74	7844	7860	5-7-5	674
599092	2610	2626	Exon 18	GTTGTCGCAGCTGTTTT	66	7845	7861	5-7-5	675
599093	2611	2627	Exon 18	TGTTGTCGCAGCTGTTT	89	7846	7862	5-7-5	676
599094	2612	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTT	82	n/a	n/a	5-7-5	677
599095	2613	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGT	87	n/a	n/a	5-7-5	678
599096	2614	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTG	85	n/a	n/a	5-7-5	679
599097	2615	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCT	78	n/a	n/a	5-7-5	680

TABLE 13

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599510	2552	2570	Exon 18	TAGAAAACCCAAATCCTCA	45	7787	7805	5-9-5	681
599331	2553	2571	Exon 18	ATAGAAAACCCAAATCCTC	46	7788	7806	5-9-5	682
599332	2554	2572	Exon 18	TATAGAAAACCCAAATCCT	38	7789	7807	5-9-5	683
599333	2556	2574	Exon 18	CTTATAGAAAACCCAAATC	1	7791	7809	5-9-5	684
599334	2557	2575	Exon 18	CCTTATAGAAAACCCAAAT	5	7792	7810	5-9-5	685
599335	2558	2576	Exon 18	CCCTTATAGAAAACCCAAA	34	7793	7811	5-9-5	686
599336	2559	2577	Exon 18	CCCCTTATAGAAAACCCAA	40	7794	7812	5-9-5	687
599337	2560	2578	Exon 18	ACCCCTTATAGAAAACCCA	39	7795	7813	5-9-5	688
599338	2561	2579	Exon 18	AACCCCTTATAGAAAACCC	57	7796	7814	5-9-5	689
599339	2562	2580	Exon 18	AAACCCCTTATAGAAAACC	26	7797	7815	5-9-5	690
599281	2562	2580	Exon 18	AAACCCCTTATAGAAAACC	15	7797	7815	6-7-6	690
599340	2563	2581	Exon 18	GAAACCCCTTATAGAAAAC	17	7798	7816	5-9-5	691
599282	2563	2581	Exon 18	GAAACCCCTTATAGAAAAC	12	7798	7816	6-7-6	691
599341	2564	2582	Exon 18	GGAAACCCCTTATAGAAAA	23	7799	7817	5-9-5	692
599283	2564	2582	Exon 18	GGAAACCCCTTATAGAAAA	18	7799	7817	6-7-6	692
599342	2565	2583	Exon 18	AGGAAACCCCTTATAGAAA	10	7800	7818	5-9-5	693
599284	2565	2583	Exon 18	AGGAAACCCCTTATAGAAA	14	7800	7818	6-7-6	693

TABLE 13-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599343	2566	2584	Exon 18	CAGGAAACCCCTTATAGAA	10	7801	7819	5-9-5	694
599285	2566	2584	Exon 18	CAGGAAACCCCTTATAGAA	13	7801	7819	6-7-6	694
599344	2567	2585	Exon 18	GCAGGAAACCCCTTATAGA	22	7802	7820	5-9-5	695
599286	2567	2585	Exon 18	GCAGGAAACCCCTTATAGA	31	7802	7820	6-7-6	695
599345	2568	2586	Exon 18	AGCAGGAAACCCCTTATAG	19	7803	7821	5-9-5	696
599287	2568	2586	Exon 18	AGCAGGAAACCCCTTATAG	12	7803	7821	6-7-6	696
599346	2569	2587	Exon 18	CAGCAGGAAACCCCTTATA	30	7804	7822	5-9-5	697
599288	2569	2587	Exon 18	CAGCAGGAAACCCCTTATA	28	7804	7822	6-7-6	697
599347	2570	2588	Exon 18	CCAGCAGGAAACCCCTTAT	46	7805	7823	5-9-5	698
599289	2570	2588	Exon 18	CCAGCAGGAAACCCCTTAT	32	7805	7823	6-7-6	698
599348	2571	2589	Exon 18	TCCAGCAGGAAACCCCTTA	44	7806	7824	5-9-5	699
599290	2571	2589	Exon 18	TCCAGCAGGAAACCCCTTA	24	7806	7824	6-7-6	699
599349	2572	2590	Exon 18	GTCCAGCAGGAAACCCCTT	60	7807	7825	5-9-5	700
599291	2572	2590	Exon 18	GTCCAGCAGGAAACCCCTT	38	7807	7825	6-7-6	700
599350	2573	2591	Exon 18	TGTCCAGCAGGAAACCCCT	49	7808	7826	5-9-5	701
599292	2573	2591	Exon 18	TGTCCAGCAGGAAACCCCT	35	7808	7826	6-7-6	701
599351	2575	2593	Exon 18	CCTGTCCAGCAGGAAACCC	46	7810	7828	5-9-5	702
599293	2575	2593	Exon 18	CCTGTCCAGCAGGAAACCC	12	7810	7828	6-7-6	702
599352	2576	2594	Exon 18	CCCTGTCCAGCAGGAAACC	49	7811	7829	5-9-5	703
599294	2576	2594	Exon 18	CCCTGTCCAGCAGGAAACC	38	7811	7829	6-7-6	703
599353	2577	2595	Exon 18	CCCCTGTCCAGCAGGAAAC	64	7812	7830	5-9-5	704
599295	2577	2595	Exon 18	CCCCTGTCCAGCAGGAAAC	33	7812	7830	6-7-6	704
599354	2578	2596	Exon 18	GCCCCTGTCCAGCAGGAAA	56	7813	7831	5-9-5	705
599296	2578	2596	Exon 18	GCCCCTGTCCAGCAGGAAA	13	7813	7831	6-7-6	705
599355	2580	2598	Exon 18	ACGCCCCTGTCCAGCAGGA	81	7815	7833	5-9-5	706
599297	2580	2598	Exon 18	ACGCCCCTGTCCAGCAGGA	57	7815	7833	6-7-6	706
599356	2581	2599	Exon 18	CACGCCCCTGTCCAGCAGG	64	7816	7834	5-9-5	707
599298	2581	2599	Exon 18	CACGCCCCTGTCCAGCAGG	39	7816	7834	6-7-6	707
599299	2582	2600	Exon 18	CCACGCCCCTGTCCAGCAG	55	7817	7835	6-7-6	708
599300	2583	2601	Exon 18	CCCACGCCCCTGTCCAGCA	45	7818	7836	6-7-6	709
599301	2584	2602	Exon 18	TCCCACGCCCCTGTCCAGC	39	7819	7837	6-7-6	710
599302	2585	2603	Exon 18	ATCCCACGCCCCTGTCCAG	27	7820	7838	6-7-6	711
599303	2586	2604	Exon 18	AATCCCACGCCCCTGTCCA	35	7821	7839	6-7-6	712
599304	2587	2605	Exon 18	CAATCCCACGCCCCTGTCC	16	7822	7840	6-7-6	713
599305	2588	2606	Exon 18	TCAATCCCACGCCCCTGTC	41	7823	7841	6-7-6	714

TABLE 13-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599306	2589	2607	Exon 18	TTCAATCCCACGCCCCTGT	70	7824	7842	6-7-6	715
599307	2590	2608	Exon 18	ATTCAATCCCACGCCCCTG	66	7825	7843	6-7-6	716
599308	2591	2609	Exon 18	AATTCAATCCCACGCCCCT	68	7826	7844	6-7-6	717
599309	2592	2610	Exon 18	TAATTCAATCCCACGCCCC	52	7827	7845	6-7-6	718
599310	2593	2611	Exon 18	TTAATTCAATCCCACGCCC	39	7828	7846	6-7-6	719
599311	2594	2612	Exon 18	TTTAATTCAATCCCACGCC	83	7829	7847	6-7-6	720
599312	2595	2613	Exon 18	TTTTAATTCAATCCCACGC	72	7830	7848	6-7-6	721
599313	2596	2614	Exon 18	GTTTTAATTCAATCCCACG	86	7831	7849	6-7-6	722
599314	2597	2615	Exon 18	TGTTTTAATTCAATCCCAC	91	7832	7850	6-7-6	723
599315	2598	2616	Exon 18	CTGTTTTAATTCAATCCCA	71	7833	7851	6-7-6	724
599316	2599	2617	Exon 18	GCTGTTTTAATTCAATCCC	89	7834	7852	6-7-6	725
599317	2600	2618	Exon 18	AGCTGTTTTAATTCAATCC	87	7835	7853	6-7-6	726
599318	2601	2619	Exon 18	CAGCTGTTTTAATTCAATC	81	7836	7854	6-7-6	727
599319	2602	2620	Exon 18	GCAGCTGTTTTAATTCAAT	75	7837	7855	6-7-6	728
599320	2603	2621	Exon 18	CGCAGCTGTTTTAATTCAA	84	7838	7856	6-7-6	729
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	92	7839	7858	5-10-5	317
599321	2604	2622	Exon 18	TCGCAGCTGTTTTAATTCA	90	7839	7857	6-7-6	730
599322	2605	2623	Exon 18	GTCGCAGCTGTTTTAATTC	89	7840	7858	6-7-6	731
599323	2606	2624	Exon 18	TGTCGCAGCTGTTTTAATT	81	7841	7859	6-7-6	732
599324	2607	2625	Exon 18	TTGTCGCAGCTGTTTTAAT	68	7842	7860	6-7-6	733
599325	2608	2626	Exon 18	GTTGTCGCAGCTGTTTTAA	71	7843	7861	6-7-6	734
599326	2609	2627	Exon 18	TGTTGTCGCAGCTGTTTTA	52	7844	7862	6-7-6	735
599327	2610	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTTTT	88	n/a	n/a	6-7-6	736
599328	2611	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGTTT	87	n/a	n/a	6-7-6	737
599329	2612	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTGTT	84	n/a	n/a	6-7-6	738
599330	2613	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCTGT	87	n/a	n/a	6-7-6	739

TABLE 14

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599512	2552	2571	Exon 18	ATAGAAAACCCAAATCCTCA	74	7787	7806	3-10-7	410
599449	2553	2572	Exon 18	TATAGAAAACCCAAATCCTC	43	7788	7807	3-10-7	411
599450	2554	2573	Exon 18	TTATAGAAAACCCAAATCCT	51	7789	7808	3-10-7	412
599451	2555	2574	Exon 18	CTTATAGAAAACCCAAATCC	35	7790	7809	3-10-7	413
599452	2556	2575	Exon 18	CCTTATAGAAAACCCAAATC	34	7791	7810	3-10-7	414
599453	2557	2576	Exon 18	CCCTTATAGAAAACCCAAAT	44	7792	7811	3-10-7	415
599454	2558	2577	Exon 18	CCCCTTATAGAAAACCCAAA	54	7793	7812	3-10-7	416
599455	2559	2578	Exon 18	ACCCCTTATAGAAAACCCAA	53	7794	7813	3-10-7	417
599456	2560	2579	Exon 18	AACCCCTTATAGAAAACCCA	69	7795	7814	3-10-7	418
599457	2561	2580	Exon 18	AAACCCCTTATAGAAAACCC	46	7796	7815	3-10-7	419
599458	2562	2581	Exon 18	GAAACCCCTTATAGAAAACC	0	7797	7816	3-10-7	420
599459	2563	2582	Exon 18	GGAAACCCCTTATAGAAAAC	12	7798	7817	3-10-7	421
599460	2564	2583	Exon 18	AGGAAACCCCTTATAGAAAA	17	7799	7818	3-10-7	422
599461	2565	2584	Exon 18	CAGGAAACCCCTTATAGAAA	24	7800	7819	3-10-7	423
599462	2566	2585	Exon 18	GCAGGAAACCCCTTATAGAA	33	7801	7820	3-10-7	424
599463	2567	2586	Exon 18	AGCAGGAAACCCCTTATAGA	38	7802	7821	3-10-7	425
599464	2568	2587	Exon 18	CAGCAGGAAACCCCTTATAG	33	7803	7822	3-10-7	426
599465	2569	2588	Exon 18	CCAGCAGGAAACCCCTTATA	49	7804	7823	3-10-7	427
599466	2570	2589	Exon 18	TCCAGCAGGAAACCCCTTAT	45	7805	7824	3-10-7	428
599467	2571	2590	Exon 18	GTCCAGCAGGAAACCCCTTA	60	7806	7825	3-10-7	237
599468	2572	2591	Exon 18	TGTCCAGCAGGAAACCCCTT	61	7807	7826	3-10-7	429
599469	2573	2592	Exon 18	CTGTCCAGCAGGAAACCCCT	52	7808	7827	3-10-7	430
599470	2574	2593	Exon 18	CCTGTCCAGCAGGAAACCCC	45	7809	7828	3-10-7	431
599471	2575	2594	Exon 18	CCCTGTCCAGCAGGAAACCC	67	7810	7829	3-10-7	432
599472	2576	2595	Exon 18	CCCCTGTCCAGCAGGAAACC	79	7811	7830	3-10-7	433
599473	2577	2596	Exon 18	GCCCCTGTCCAGCAGGAAAC	72	7812	7831	3-10-7	238
599474	2578	2597	Exon 18	CGCCCCTGTCCAGCAGGAAA	87	7813	7832	3-10-7	434
599475	2579	2598	Exon 18	ACGCCCCTGTCCAGCAGGAA	76	7814	7833	3-10-7	435
599476	2580	2599	Exon 18	CACGCCCCTGTCCAGCAGGA	81	7815	7834	3-10-7	436
599477	2581	2600	Exon 18	CCACGCCCCTGTCCAGCAGG	83	7816	7835	3-10-7	437
599478	2582	2601	Exon 18	CCCACGCCCCTGTCCAGCAG	72	7817	7836	3-10-7	438
599479	2583	2602	Exon 18	TCCCACGCCCCTGTCCAGCA	81	7818	7837	3-10-7	439
599480	2584	2603	Exon 18	ATCCCACGCCCCTGTCCAGC	77	7819	7838	3-10-7	440
599481	2585	2604	Exon 18	AATCCCACGCCCCTGTCCAG	83	7820	7839	3-10-7	441
599482	2586	2605	Exon 18	CAATCCCACGCCCCTGTCCA	87	7821	7840	3-10-7	442

TABLE 14-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599483	2587	2606	Exon 18	TCAATCCCACGCCCCTGTCC	90	7822	7841	3-10-7	443
599484	2588	2607	Exon 18	TTCAATCCCACGCCCCTGTC	72	7823	7842	3-10-7	444
599485	2589	2608	Exon 18	ATTCAATCCCACGCCCCTGT	82	7824	7843	3-10-7	445
599486	2590	2609	Exon 18	AATTCAATCCCACGCCCCTG	84	7825	7844	3-10-7	446
599487	2591	2610	Exon 18	TAATTCAATCCCACGCCCCT	84	7826	7845	3-10-7	447
599488	2592	2611	Exon 18	TTAATTCAATCCCACGCCCC	87	7827	7846	3-10-7	448
599489	2593	2612	Exon 18	TTTAATTCAATCCCACGCCC	87	7828	7847	3-10-7	449
599490	2594	2613	Exon 18	TTTTAATTCAATCCCACGCC	86	7829	7848	3-10-7	450
599491	2595	2614	Exon 18	GTTTTAATTCAATCCCACGC	87	7830	7849	3-10-7	451
599492	2596	2615	Exon 18	TGTTTTAATTCAATCCCACG	88	7831	7850	3-10-7	452
599493	2597	2616	Exon 18	CTGTTTTAATTCAATCCCAC	75	7832	7851	3-10-7	453
599433	2597	2616	Exon 18	CTGTTTTAATTCAATCCCAC	89	7832	7851	6-8-6	453
599494	2598	2617	Exon 18	GCTGTTTTAATTCAATCCCA	90	7833	7852	3-10-7	454
599434	2598	2617	Exon 18	GCTGTTTTAATTCAATCCCA	89	7833	7852	6-8-6	454
599495	2599	2618	Exon 18	AGCTGTTTTAATTCAATCCC	88	7834	7853	3-10-7	239
599435	2599	2618	Exon 18	AGCTGTTTTAATTCAATCCC	91	7834	7853	6-8-6	239
599496	2600	2619	Exon 18	CAGCTGTTTTAATTCAATCC	89	7835	7854	3-10-7	455
599436	2600	2619	Exon 18	CAGCTGTTTTAATTCAATCC	89	7835	7854	6-8-6	455
599497	2601	2620	Exon 18	GCAGCTGTTTTAATTCAATC	89	7836	7855	3-10-7	456
599437	2601	2620	Exon 18	GCAGCTGTTTTAATTCAATC	91	7836	7855	6-8-6	456
599498	2602	2621	Exon 18	CGCAGCTGTTTTAATTCAAT	88	7837	7856	3-10-7	457
599438	2602	2621	Exon 18	CGCAGCTGTTTTAATTCAAT	90	7837	7856	6-8-6	457
599499	2603	2622	Exon 18	TCGCAGCTGTTTTAATTCAA	81	7838	7857	3-10-7	458
599439	2603	2622	Exon 18	TCGCAGCTGTTTTAATTCAA	88	7838	7857	6-8-6	458
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	90	7839	7858	5-10-5	317
599500	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	88	7839	7858	3-10-7	317
599440	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	88	7839	7858	6-8-6	317
599501	2605	2624	Exon 18	TGTCGCAGCTGTTTTAATTC	78	7840	7859	3-10-7	459
599441	2605	2624	Exon 18	TGTCGCAGCTGTTTTAATTC	90	7840	7859	6-8-6	459
599502	2606	2625	Exon 18	TTGTCGCAGCTGTTTTAATT	87	7841	7860	3-10-7	460
599442	2606	2625	Exon 18	TTGTCGCAGCTGTTTTAATT	76	7841	7860	6-8-6	460
599503	2607	2626	Exon 18	GTTGTCGCAGCTGTTTTAAT	83	7842	7861	3-10-7	461
599443	2607	2626	Exon 18	GTTGTCGCAGCTGTTTTAAT	77	7842	7861	6-8-6	461
599504	2608	2627	Exon 18	TGTTGTCGCAGCTGTTTTAA	89	7843	7862	3-10-7	395

TABLE 14-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599444	2608	2627	Exon 18	TGTTGTCGCAGCTGTTTTAA	69	7843	7862	6-8-6	395
599505	2609	2628	Exon 19/ Repeat	TTGTTGTCGCAGCTGTTTTA	83	n/a	n/a	3-10-7	462
599445	2609	2628	Exon 19/ Repeat	TTGTTGTCGCAGCTGTTTTA	85	n/a	n/a	6-8-6	462
599506	2610	2629	Exon 19/ Repeat	TTTGTTGTCGCAGCTGTTTT	89	n/a	n/a	3-10-7	463
599446	2610	2629	Exon 19/ Repeat	TTTGTTGTCGCAGCTGTTTT	85	n/a	n/a	6-8-6	463
599507	2611	2630	Exon 19/ Repeat	TTTTGTTGTCGCAGCTGTTT	82	n/a	n/a	3-10-7	464
599447	2611	2630	Exon 19/ Repeat	TTTTGTTGTCGCAGCTGTTT	83	n/a	n/a	6-8-6	464
599508	2612	2631	Exon 19/ Repeat	TTTTTGTTGTCGCAGCTGTT	90	n/a	n/a	3-10-7	465
599448	2612	2631	Exon 19/ Repeat	TTTTTGTTGTCGCAGCTGTT	87	n/a	n/a	6-8-6	465

Example 5

Antisense Inhibition of Human Complement Factor B (CFB) in HepG2 Cells by MOE Gapmers

[0439] Additional antisense oligonucleotides were designed targeting human Complement Factor B (CFB) nucleic acid and were tested for their effects on CFB mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 20,000 cells per well were transfected using electroporation with 2,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0440] The newly designed chimeric antisense oligonucleotides in the Tables below were designed as 4-8-5 MOE, 5-8-5 MOE, 5-9-5 MOE, 5-10-5 MOE, 6-7-6-MOE, 3-10-5 MOE, or 6-8-6 MOE gapmers.

[0441] The 4-8-5 MOE gapmers are 17 nucleosides in length, wherein the central gap segment comprises of eight 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising four and five nucleosides respectively. The 5-8-5 MOE gapmers are 18 nucleosides in length, wherein the central gap segment comprises of eight 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 5-9-5 MOE gapmers are 19 nucleosides in length, wherein the central gap segment comprises of nine 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 5-10-5 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 3-10-5 MOE gapmers are 18 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising three and five nucleosides respectively. The 6-7-6 MOE gapmers are 19 nucleosides in length, wherein the central gap segment comprises of seven 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising six nucleosides each. The 6-8-6 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of eight 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising six nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines.

[0442] "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in the Tables below is targeted to either the human CFB mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_001710.5) or the human CFB genomic sequence, designated herein as SEQ ID NO: 2 (GENBANK Accession No. NT_007592.15 truncated from nucleotides 31852000 to 31861000), or both. 'n/a' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity.

TABLE 15

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599160	2560	2577	Exon 18	CCCCTTATAGAAAACCCA	26	7795	7812	5-8-5	740
599161	2561	2578	Exon 18	ACCCCTTATAGAAAACCC	20	7796	7813	5-8-5	741
599162	2562	2579	Exon 18	AACCCCTTATAGAAAACC	12	7797	7814	5-8-5	742
599163	2563	2580	Exon 18	AAACCCCTTATAGAAAAC	11	7798	7815	5-8-5	743
599164	2564	2581	Exon 18	GAAACCCCTTATAGAAAA	11	7799	7816	5-8-5	744
599165	2566	2583	Exon 18	AGGAAACCCCTTATAGAA	0	7801	7818	5-8-5	745
599166	2567	2584	Exon 18	CAGGAAACCCCTTATAGA	12	7802	7819	5-8-5	746
599167	2568	2585	Exon 18	GCAGGAAACCCCTTATAG	14	7803	7820	5-8-5	747
599168	2569	2586	Exon 18	AGCAGGAAACCCCTTATA	16	7804	7821	5-8-5	748
599169	2570	2587	Exon 18	CAGCAGGAAACCCCTTAT	24	7805	7822	5-8-5	749
599170	2571	2588	Exon 18	CCAGCAGGAAACCCCTTA	37	7806	7823	5-8-5	750
599171	2572	2589	Exon 18	TCCAGCAGGAAACCCCTT	30	7807	7824	5-8-5	751
599172	2573	2590	Exon 18	GTCCAGCAGGAAACCCCT	43	7808	7825	5-8-5	752
599173	2574	2591	Exon 18	TGTCCAGCAGGAAACCCC	47	7809	7826	5-8-5	753
599174	2575	2592	Exon 18	CTGTCCAGCAGGAAACCC	27	7810	7827	5-8-5	754
599175	2576	2593	Exon 18	CCTGTCCAGCAGGAAACC	30	7811	7828	5-8-5	755
599176	2577	2594	Exon 18	CCCTGTCCAGCAGGAAAC	34	7812	7829	5-8-5	756
599177	2578	2595	Exon 18	CCCCTGTCCAGCAGGAAA	41	7813	7830	5-8-5	757
599178	2580	2597	Exon 18	CGCCCCTGTCCAGCAGGA	67	7815	7832	5-8-5	758
599179	2581	2598	Exon 18	ACGCCCCTGTCCAGCAGG	61	7816	7833	5-8-5	759
599180	2582	2599	Exon 18	CACGCCCCTGTCCAGCAG	62	7817	7834	5-8-5	760
599181	2583	2600	Exon 18	CCACGCCCCTGTCCAGCA	63	7818	7835	5-8-5	761
599128	2584	2600	Exon 18	CCACGCCCCTGTCCAGC	55	7819	7835	4-8-5	649
599182	2584	2601	Exon 18	CCCACGCCCCTGTCCAGC	58	7819	7836	5-8-5	762
599129	2585	2601	Exon 18	CCCACGCCCCTGTCCAG	41	7820	7836	4-8-5	650
599183	2585	2602	Exon 18	TCCCACGCCCCTGTCCAG	43	7820	7837	5-8-5	763
599130	2586	2602	Exon 18	TCCCACGCCCCTGTCCA	46	7821	7837	4-8-5	651
599184	2586	2603	Exon 18	ATCCCACGCCCCTGTCCA	32	7821	7838	5-8-5	764
599131	2587	2603	Exon 18	ATCCCACGCCCCTGTCC	30	7822	7838	4-8-5	652
599185	2587	2604	Exon 18	AATCCCACGCCCCTGTCC	35	7822	7839	5-8-5	765
599132	2588	2604	Exon 18	AATCCCACGCCCCTGTC	52	7823	7839	4-8-5	653
599186	2588	2605	Exon 18	CAATCCCACGCCCCTGTC	55	7823	7840	5-8-5	766
599133	2589	2605	Exon 18	CAATCCCACGCCCCTGT	66	7824	7840	4-8-5	654
599187	2589	2606	Exon 18	TCAATCCCACGCCCCTGT	72	7824	7841	5-8-5	767
599134	2590	2606	Exon 18	TCAATCCCACGCCCCTG	80	7825	7841	4-8-5	655

TABLE 15-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599188	2590	2607	Exon 18	TTCAATCCCACGCCCCTG	92	7825	7842	5-8-5	768
599135	2591	2607	Exon 18	TTCAATCCCACGCCCCT	61	7826	7842	4-8-5	656
599189	2591	2608	Exon 18	ATTCAATCCCACGCCCCT	52	7826	7843	5-8-5	769
599136	2592	2608	Exon 18	ATTCAATCCCACGCCCC	68	7827	7843	4-8-5	657
599190	2592	2609	Exon 18	AATTCAATCCCACGCCCC	62	7827	7844	5-8-5	770
599137	2593	2609	Exon 18	AATTCAATCCCACGCCC	51	7828	7844	4-8-5	658
599191	2593	2610	Exon 18	TAATTCAATCCCACGCCC	54	7828	7845	5-8-5	771
599138	2594	2610	Exon 18	TAATTCAATCCCACGCC	71	7829	7845	4-8-5	659
599192	2594	2611	Exon 18	TTAATTCAATCCCACGCC	66	7829	7846	5-8-5	772
599139	2595	2611	Exon 18	TTAATTCAATCCCACGC	80	7830	7846	4-8-5	660
599193	2595	2612	Exon 18	TTTAATTCAATCCCACGC	74	7830	7847	5-8-5	773
599140	2596	2612	Exon 18	TTTAATTCAATCCCACG	66	7831	7847	4-8-5	786
599194	2596	2613	Exon 18	TTTTAATTCAATCCCACG	66	7831	7848	5-8-5	774
599141	2597	2613	Exon 18	TTTTAATTCAATCCCAC	63	7832	7848	4-8-5	662
599195	2597	2614	Exon 18	GTTTTAATTCAATCCCAC	86	7832	7849	5-8-5	775
599142	2598	2614	Exon 18	GTTTTAATTCAATCCCA	69	7833	7849	4-8-5	663
599196	2598	2615	Exon 18	TGTTTTAATTCAATCCCA	82	7833	7850	5-8-5	776
599143	2599	2615	Exon 18	TGTTTTAATTCAATCCC	59	7834	7850	4-8-5	664
599197	2599	2616	Exon 18	CTGTTTTAATTCAATCCC	79	7834	7851	5-8-5	777
599144	2600	2616	Exon 18	CTGTTTTAATTCAATCC	52	7835	7851	4-8-5	665
599198	2600	2617	Exon 18	GCTGTTTTAATTCAATCC	86	7835	7852	5-8-5	778
599145	2601	2617	Exon 18	GCTGTTTTAATTCAATC	53	7836	7852	4-8-5	666
599199	2601	2618	Exon 18	AGCTGTTTTAATTCAATC	72	7836	7853	5-8-5	779
599146	2602	2618	Exon 18	AGCTGTTTTAATTCAAT	42	7837	7853	4-8-5	667
599200	2602	2619	Exon 18	CAGCTGTTTTAATTCAAT	76	7837	7854	5-8-5	780
599147	2603	2619	Exon 18	CAGCTGTTTTAATTCAA	55	7838	7854	4-8-5	668
599201	2603	2620	Exon 18	GCAGCTGTTTTAATTCAA	87	7838	7855	5-8-5	781
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	93	7839	7858	5-10-5	317
599148	2604	2620	Exon 18	GCAGCTGTTTTAATTCA	84	7839	7855	4-8-5	669
599202	2604	2621	Exon 18	CGCAGCTGTTTTAATTCA	89	7839	7856	5-8-5	782
599149	2605	2621	Exon 18	CGCAGCTGTTTTAATTC	92	7840	7856	4-8-5	670
599203	2605	2622	Exon 18	TCGCAGCTGTTTTAATTC	90	7840	7857	5-8-5	783
599150	2606	2622	Exon 18	TCGCAGCTGTTTTAATT	75	7841	7857	4-8-5	671
599151	2607	2623	Exon 18	GTCGCAGCTGTTTTAAT	80	7842	7858	4-8-5	672

TABLE 15-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599152	2608	2624	Exon 18	TGTCGCAGCTGTTTTAA	76	7843	7859	4-8-5	673
599153	2609	2625	Exon 18	TTGTCGCAGCTGTTTTA	56	7844	7860	4-8-5	674
599154	2610	2626	Exon 18	GTTGTCGCAGCTGTTTT	85	7845	7861	4-8-5	675
599155	2611	2627	Exon 18	TGTTGTCGCAGCTGTTT	89	7846	7862	4-8-5	676
599156	2612	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTT	83	n/a	n/a	4-8-5	813
599157	2613	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGT	78	n/a	n/a	4-8-5	678
599158	2614	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTG	83	n/a	n/a	4-8-5	679
599159	2615	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCT	65	n/a	n/a	4-8-5	680
599204	2606	2623	Exon 18	GTCGCAGCTGTTTTAATT	83	7841	7858	5-8-5	784

TABLE 16

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599509	2552	2570	Exon 18	TAGAAAACCCAAATCCTCA	45	7787	7805	6-7-6	681
599213	2553	2570	Exon 18	TAGAAAACCCAAATCCTC	89	7788	7805	3-10-5	785
599273	2553	2571	Exon 18	ATAGAAAACCCAAATCCTC	85	7788	7806	6-7-6	682
599214	2554	2571	Exon 18	ATAGAAAACCCAAATCCT	79	7789	7806	3-10-5	786
599274	2554	2572	Exon 18	TATAGAAAACCCAAATCCT	75	7789	7807	6-7-6	683
599215	2555	2572	Exon 18	TATAGAAAACCCAAATCC	81	7790	7807	3-10-5	787
599216	2556	2573	Exon 18	TTATAGAAAACCCAAATC	87	7791	7808	3-10-5	788
599275	2556	2574	Exon 18	CTTATAGAAAACCCAAATC	84	7791	7809	6-7-6	684
599217	2557	2574	Exon 18	CTTATAGAAAACCCAAAT	84	7792	7809	3-10-5	789
599276	2557	2575	Exon 18	CCTTATAGAAAACCCAAAT	68	7792	7810	6-7-6	685
599218	2558	2575	Exon 18	CCTTATAGAAAACCCAAA	82	7793	7810	3-10-5	790
599277	2558	2576	Exon 18	CCCTTATAGAAAACCCAAA	82	7793	7811	6-7-6	686
599219	2559	2576	Exon 18	CCCTTATAGAAAACCCAA	81	7794	7811	3-10-5	791
599278	2559	2577	Exon 18	CCCCTTATAGAAAACCCAA	84	7794	7812	6-7-6	687
599220	2560	2577	Exon 18	CCCCTTATAGAAAACCCA	92	7795	7812	3-10-5	740
599279	2560	2578	Exon 18	ACCCCTTATAGAAAACCCA	92	7795	7813	6-7-6	688
599221	2561	2578	Exon 18	ACCCCTTATAGAAAACCC	93	7796	7813	3-10-5	741

TABLE 16-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599280	2561	2579	Exon 18	AACCCCTTATAGAAAACCC	90	7796	7814	6-7-6	689
599222	2562	2579	Exon 18	AACCCCTTATAGAAAACC	95	7797	7814	3-10-5	742
599223	2563	2580	Exon 18	AAACCCCTTATAGAAAAC	93	7798	7815	3-10-5	743
599224	2564	2581	Exon 18	GAAACCCCTTATAGAAAA	90	7799	7816	3-10-5	744
599225	2566	2583	Exon 18	AGGAAACCCCTTATAGAA	93	7801	7818	3-10-5	745
599226	2567	2584	Exon 18	CAGGAAACCCCTTATAGA	95	7802	7819	3-10-5	746
599227	2568	2585	Exon 18	GCAGGAAACCCCTTATAG	94	7803	7820	3-10-5	747
599228	2569	2586	Exon 18	AGCAGGAAACCCCTTATA	96	7804	7821	3-10-5	748
599229	2570	2587	Exon 18	CAGCAGGAAACCCCTTAT	92	7805	7822	3-10-5	749
599230	2571	2588	Exon 18	CCAGCAGGAAACCCCTTA	88	7806	7823	3-10-5	750
599231	2572	2589	Exon 18	TCCAGCAGGAAACCCCTT	83	7807	7824	3-10-5	751
599232	2573	2590	Exon 18	GTCCAGCAGGAAACCCCT	89	7808	7825	3-10-5	752
599233	2574	2591	Exon 18	TGTCCAGCAGGAAACCCC	83	7809	7826	3-10-5	753
599234	2575	2592	Exon 18	CTGTCCAGCAGGAAACCC	88	7810	7827	3-10-5	754
599235	2576	2593	Exon 18	CCTGTCCAGCAGGAAACC	91	7811	7828	3-10-5	755
599236	2577	2594	Exon 18	CCCTGTCCAGCAGGAAAC	90	7812	7829	3-10-5	756
599237	2578	2595	Exon 18	CCCCTGTCCAGCAGGAAA	34	7813	7830	3-10-5	757
599238	2580	2597	Exon 18	CGCCCCTGTCCAGCAGGA	14	7815	7832	3-10-5	758
599239	2581	2598	Exon 18	ACGCCCCTGTCCAGCAGG	10	7816	7833	3-10-5	759
599240	2582	2599	Exon 18	CACGCCCCTGTCCAGCAG	26	7817	7834	3-10-5	760
599241	2583	2600	Exon 18	CCACGCCCCTGTCCAGCA	11	7818	7835	3-10-5	761
599242	2584	2601	Exon 18	CCCACGCCCCTGTCCAGC	24	7819	7836	3-10-5	762
599243	2585	2602	Exon 18	TCCCACGCCCCTGTCCAG	23	7820	7837	3-10-5	763
599244	2586	2603	Exon 18	ATCCCACGCCCCTGTCCA	29	7821	7838	3-10-5	764
599245	2587	2604	Exon 18	AATCCCACGCCCCTGTCC	11	7822	7839	3-10-5	765
599246	2588	2605	Exon 18	CAATCCCACGCCCCTGTC	0	7823	7840	3-10-5	766
599247	2589	2606	Exon 18	TCAATCCCACGCCCCTGT	21	7824	7841	3-10-5	767
599248	2590	2607	Exon 18	TTCAATCCCACGCCCCTG	0	7825	7842	3-10-5	768
599249	2591	2608	Exon 18	ATTCAATCCCACGCCCCT	9	7826	7843	3-10-5	769
599250	2592	2609	Exon 18	AATTCAATCCCACGCCCC	4	7827	7844	3-10-5	770
599251	2593	2610	Exon 18	TAATTCAATCCCACGCCC	12	7828	7845	3-10-5	771
599252	2594	2611	Exon 18	TTAATTCAATCCCACGCC	2	7829	7846	3-10-5	772
599253	2595	2612	Exon 18	TTTAATTCAATCCCACGC	28	7830	7847	3-10-5	773
599254	2596	2613	Exon 18	TTTTAATTCAATCCCACG	27	7831	7848	3-10-5	774
599255	2597	2614	Exon 18	GTTTTAATTCAATCCCAC	38	7832	7849	3-10-5	775

TABLE 16-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599256	2598	2615	Exon 18	TGTTTTAATTCAATCCCA	36	7833	7850	3-10-5	776
599257	2599	2616	Exon 18	CTGTTTTAATTCAATCCC	48	7834	7851	3-10-5	777
599258	2600	2617	Exon 18	GCTGTTTTAATTCAATCC	19	7835	7852	3-10-5	778
599259	2601	2618	Exon 18	AGCTGTTTTAATTCAATC	36	7836	7853	3-10-5	779
599260	2602	2619	Exon 18	CAGCTGTTTTAATTCAAT	58	7837	7854	3-10-5	780
599261	2603	2620	Exon 18	GCAGCTGTTTTAATTCAA	35	7838	7855	3-10-5	781
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	96	7839	7858	5-10-5	317
599262	2604	2621	Exon 18	CGCAGCTGTTTTAATTCA	52	7839	7856	3-10-5	782
599263	2605	2622	Exon 18	TCGCAGCTGTTTTAATTC	66	7840	7857	3-10-5	783
599264	2606	2623	Exon 18	GTCGCAGCTGTTTTAATT	48	7841	7858	3-10-5	784
599265	2607	2624	Exon 18	TGTCGCAGCTGTTTTAAT	46	7842	7859	3-10-5	792
599205	2607	2624	Exon 18	TGTCGCAGCTGTTTTAAT	83	7842	7859	5-8-5	792
599266	2608	2625	Exon 18	TTGTCGCAGCTGTTTTAA	76	7843	7860	3-10-5	793
599206	2608	2625	Exon 18	TTGTCGCAGCTGTTTTAA	90	7843	7860	5-8-5	793
599267	2609	2626	Exon 18	GTTGTCGCAGCTGTTTTA	53	7844	7861	3-10-5	794
599207	2609	2626	Exon 18	GTTGTCGCAGCTGTTTTA	82	7844	7861	5-8-5	794
599268	2610	2627	Exon 18	TGTTGTCGCAGCTGTTTT	58	7845	7862	3-10-5	795
599208	2610	2627	Exon 18	TGTTGTCGCAGCTGTTTT	70	7845	7862	5-8-5	795
599269	2611	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTTT	38	n/a	n/a	3-10-5	796
599209	2611	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTTT	50	n/a	n/a	5-8-5	796
599270	2612	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGTT	46	n/a	n/a	3-10-5	797
599210	2612	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGTT	76	n/a	n/a	5-8-5	797
599271	2613	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTGT	64	n/a	n/a	3-10-5	798
599211	2613	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTGT	78	n/a	n/a	5-8-5	798
599272	2614	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCTG	89	n/a	n/a	3-10-5	799
599212	2614	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCTG	84	n/a	n/a	5-8-5	799

TABLE 17

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599511	2552	2571	Exon 18	ATAGAAAACCCAAATCCTCA	38	7787	7806	6-8-6	410
599389	2553	2572	Exon 18	TATAGAAAACCCAAATCCTC	80	7788	7807	6-8-6	411
599390	2554	2573	Exon 18	TTATAGAAAACCCAAATCCT	92	7789	7808	6-8-6	412
599391	2555	2574	Exon 18	CTTATAGAAAACCCAAATCC	90	7790	7809	6-8-6	413
599392	2556	2575	Exon 18	CCTTATAGAAAACCCAAATC	87	7791	7810	6-8-6	414
599393	2557	2576	Exon 18	CCCTTATAGAAAACCCAAAT	87	7792	7811	6-8-6	415
599394	2558	2577	Exon 18	CCCCTTATAGAAAACCCAAA	74	7793	7812	6-8-6	416
599395	2559	2578	Exon 18	ACCCCTTATAGAAAACCCAA	78	7794	7813	6-8-6	417
599396	2560	2579	Exon 18	AACCCCTTATAGAAAACCCA	77	7795	7814	6-8-6	418
599397	2561	2580	Exon 18	AAACCCCTTATAGAAAACCC	89	7796	7815	6-8-6	419
599398	2562	2581	Exon 18	GAAACCCCTTATAGAAAACC	90	7797	7816	6-8-6	420
599399	2563	2582	Exon 18	GGAAACCCCTTATAGAAAAC	91	7798	7817	6-8-6	421
599400	2564	2583	Exon 18	AGGAAACCCCTTATAGAAAA	88	7799	7818	6-8-6	422
599401	2565	2584	Exon 18	CAGGAAACCCCTTATAGAAA	85	7800	7819	6-8-6	423
599402	2566	2585	Exon 18	GCAGGAAACCCCTTATAGAA	77	7801	7820	6-8-6	424
599403	2567	2586	Exon 18	AGCAGGAAACCCCTTATAGA	85	7802	7821	6-8-6	425
599404	2568	2587	Exon 18	CAGCAGGAAACCCCTTATAG	90	7803	7822	6-8-6	426
599405	2569	2588	Exon 18	CCAGCAGGAAACCCCTTATA	89	7804	7823	6-8-6	427
599406	2570	2589	Exon 18	TCCAGCAGGAAACCCCTTAT	72	7805	7824	6-8-6	428
599407	2571	2590	Exon 18	GTCCAGCAGGAAACCCCTTA	87	7806	7825	6-8-6	237
599408	2572	2591	Exon 18	TGTCCAGCAGGAAACCCCTT	87	7807	7826	6-8-6	429
599409	2573	2592	Exon 18	CTGTCCAGCAGGAAACCCCT	83	7808	7827	6-8-6	430
599410	2574	2593	Exon 18	CCTGTCCAGCAGGAAACCCC	88	7809	7828	6-8-6	431
599411	2575	2594	Exon 18	CCCTGTCCAGCAGGAAACCC	45	7810	7829	6-8-6	432
599412	2576	2595	Exon 18	CCCCTGTCCAGCAGGAAACC	66	7811	7830	6-8-6	433
599413	2577	2596	Exon 18	GCCCCTGTCCAGCAGGAAAC	92	7812	7831	6-8-6	238
599414	2578	2597	Exon 18	CGCCCCTGTCCAGCAGGAAA	92	7813	7832	6-8-6	434
599415	2579	2598	Exon 18	ACGCCCCTGTCCAGCAGGAA	87	7814	7833	6-8-6	435
599416	2580	2599	Exon 18	CACGCCCCTGTCCAGCAGGA	91	7815	7834	6-8-6	436
599417	2581	2600	Exon 18	CCACGCCCCTGTCCAGCAGG	84	7816	7835	6-8-6	437
599357	2582	2600	Exon 18	CCACGCCCCTGTCCAGCAG	88	7817	7835	5-9-5	708
599418	2582	2601	Exon 18	CCCACGCCCCTGTCCAGCAG	85	7817	7836	6-8-6	438
599358	2583	2601	Exon 18	CCCACGCCCCTGTCCAGCA	86	7818	7836	5-9-5	709
599419	2583	2602	Exon 18	TCCCACGCCCCTGTCCAGCA	91	7818	7837	6-8-6	833
599359	2584	2602	Exon 18	TCCCACGCCCCTGTCCAGC	85	7819	7837	5-9-5	834

TABLE 17-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599420	2584	2603	Exon 18	ATCCCACGCCCCTGTCCAGC	91	7819	7838	6-8-6	440
599360	2585	2603	Exon 18	ATCCCACGCCCCTGTCCAG	89	7820	7838	5-9-5	711
599421	2585	2604	Exon 18	AATCCCACGCCCCTGTCCAG	87	7820	7839	6-8-6	441
599361	2586	2604	Exon 18	AATCCCACGCCCCTGTCCA	89	7821	7839	5-9-5	712
599422	2586	2605	Exon 18	CAATCCCACGCCCCTGTCCA	90	7821	7840	6-8-6	442
599362	2587	2605	Exon 18	CAATCCCACGCCCCTGTCC	94	7822	7840	5-9-5	713
599423	2587	2606	Exon 18	TCAATCCCACGCCCCTGTCC	85	7822	7841	6-8-6	841
599363	2588	2606	Exon 18	TCAATCCCACGCCCCTGTC	88	7823	7841	5-9-5	714
599424	2588	2607	Exon 18	TTCAATCCCACGCCCCTGTC	88	7823	7842	6-8-6	444
599364	2589	2607	Exon 18	TTCAATCCCACGCCCCTGT	88	7824	7842	5-9-5	715
599425	2589	2608	Exon 18	ATTCAATCCCACGCCCCTGT	68	7824	7843	6-8-6	445
599365	2590	2608	Exon 18	ATTCAATCCCACGCCCCTG	48	7825	7843	5-9-5	716
599426	2590	2609	Exon 18	AATTCAATCCCACGCCCCTG	55	7825	7844	6-8-6	446
599366	2591	2609	Exon 18	AATTCAATCCCACGCCCCT	28	7826	7844	5-9-5	717
599427	2591	2610	Exon 18	TAATTCAATCCCACGCCCCT	13	7826	7845	6-8-6	849
599367	2592	2610	Exon 18	TAATTCAATCCCACGCCCC	21	7827	7845	5-9-5	718
599428	2592	2611	Exon 18	TTAATTCAATCCCACGCCCC	39	7827	7846	6-8-6	448
599368	2593	2611	Exon 18	TTAATTCAATCCCACGCCC	20	7828	7846	5-9-5	719
599429	2593	2612	Exon 18	TTTAATTCAATCCCACGCCC	18	7828	7847	6-8-6	449
599369	2594	2612	Exon 18	TTTAATTCAATCCCACGCC	78	7829	7847	5-9-5	720
599430	2594	2613	Exon 18	TTTTAATTCAATCCCACGCC	24	7829	7848	6-8-6	450
599370	2595	2613	Exon 18	TTTTAATTCAATCCCACGC	25	7830	7848	5-9-5	721
599431	2595	2614	Exon 18	GTTTTAATTCAATCCCACGC	30	7830	7849	6-8-6	451
599371	2596	2614	Exon 18	GTTTTAATTCAATCCCACG	84	7831	7849	5-9-5	722
599432	2596	2615	Exon 18	TGTTTTAATTCAATCCCACG	29	7831	7850	6-8-6	452
599372	2597	2615	Exon 18	TGTTTTAATTCAATCCCAC	83	7832	7850	5-9-5	723
599373	2598	2616	Exon 18	CTGTTTTAATTCAATCCCA	81	7833	7851	5-9-5	724
599374	2599	2617	Exon 18	GCTGTTTTAATTCAATCCC	26	7834	7852	5-9-5	725
599375	2600	2618	Exon 18	AGCTGTTTTAATTCAATCC	26	7835	7853	5-9-5	726
599376	2601	2619	Exon 18	CAGCTGTTTTAATTCAATC	62	7836	7854	5-9-5	727
599377	2602	2620	Exon 18	GCAGCTGTTTTAATTCAAT	21	7837	7855	5-9-5	728
599378	2603	2621	Exon 18	CGCAGCTGTTTTAATTCAA	90	7838	7856	5-9-5	729
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	95	7839	7858	5-10-5	867
599379	2604	2622	Exon 18	TCGCAGCTGTTTTAATTCA	88	7839	7857	5-9-5	730

TABLE 17-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599380	2605	2623	Exon 18	GTCGCAGCTGTTTTAATTC	37	7840	7858	5-9-5	869
599381	2606	2624	Exon 18	TGTCGCAGCTGTTTTAATT	33	7841	7859	5-9-5	732
599382	2607	2625	Exon 18	TTGTCGCAGCTGTTTTAAT	81	7842	7860	5-9-5	733
599383	2608	2626	Exon 18	GTTGTCGCAGCTGTTTTAA	54	7843	7861	5-9-5	734
599384	2609	2627	Exon 18	TGTTGTCGCAGCTGTTTTA	85	7844	7862	5-9-5	873
599385	2610	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTTTT	59	n/a	n/a	5-9-5	736
599386	2611	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGTTT	81	n/a	n/a	5-9-5	737
599387	2612	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTGTT	80	n/a	n/a	5-9-5	738
599388	2613	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCTGT	84	n/a	n/a	5-9-5	739

Example 6

Antisense Inhibition of Human Complement Factor B (CFB) in HepG2 Cells

[0443] Additional antisense oligonucleotides were designed targeting human Complement Factor B (CFB) nucleic acid and were tested for their effects on CFB mRNA in vitro. Cultured HepG2 cells at a density of 20,000 cells per well were transfected using electroporation with 1,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0444] The newly designed chimeric antisense oligonucleotides in the Tables below were designed as deoxy, MOE and cEt oligonucleotides. The deoxy, MOE and cEt oligonucleotides are 16 nucleosides in length wherein the nucleoside have either a MOE sugar modification, an cEt sugar modification, or a deoxy modification. The 'Chemistry' column describes the sugar modifications of each oligonucleotide. 'k' indicates an cEt sugar modification; 'd' indicates deoxyribose; and 'e' indicates a MOE modification.

[0445] "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in the Tables below is targeted to either the human CFB mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_001710.5) or the human CFB genomic sequence, designated herein as SEQ ID NO: 2 (GENBANK Accession No. NT_007592.15 truncated from nucleotides 31852000 to 31861000), or both. 'n/a' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity.

TABLE 18

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599513	2551	2566	Exon 18	AAACCCAAATCCTCAT	11	7786	7801	ekkeekkddddddkk	557
599514	2553	2568	Exon 18	GAAAACCCAAATCCTC	13	7788	7803	ekkeekkddddddkk	801
599515	2555	2570	Exon 18	TAGAAAACCCAAATCC	54	7790	7805	ekkeekkddddddkk	559
599516	2559	2574	Exon 18	CTTATAGAAAACCCAA	16	7794	7809	ekkeekkddddddkk	561
599517	2560	2575	Exon 18	CCTTATAGAAAACCCA	29	7795	7810	ekkeekkddddddkk	562

TABLE 18-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599518	2561	2576	Exon 18	CCCTTATAGAAAACCC	55	7796	7811	ekkeekkddddddddk	563
599519	2562	2577	Exon 18	CCCCTTATAGAAAACC	31	7797	7812	ekkeekkddddddddk	564
599520	2563	2578	Exon 18	ACCCCTTATAGAAAAC	14	7798	7813	ekkeekkddddddddk	565
599521	2564	2579	Exon 18	AACCCCTTATAGAAAA	9	7799	7814	ekkeekkddddddddk	566
599522	2565	2580	Exon 18	AAACCCCTTATAGAAA	8	7800	7815	ekkeekkddddddddk	567
599523	2566	2581	Exon 18	GAAACCCCTTATAGAA	6	7801	7816	ekkeekkddddddddk	568
599524	2567	2582	Exon 18	GGAAACCCCTTATAGA	14	7802	7817	ekkeekkddddddddk	569
599525	2568	2583	Exon 18	AGGAAACCCCTTATAG	6	7803	7818	ekkeekkddddddddk	570
599526	2569	2584	Exon 18	CAGGAAACCCCTTATA	16	7804	7819	ekkeekkddddddddk	571
599527	2570	2585	Exon 18	GCAGGAAACCCCTTAT	0	7805	7820	ekkeekkddddddddk	572
599528	2571	2586	Exon 18	AGCAGGAAACCCCTTA	6	7806	7821	ekkeekkddddddddk	573
599529	2572	2587	Exon 18	CAGCAGGAAACCCCTT	6	7807	7822	ekkeekkddddddddk	574
599530	2574	2589	Exon 18	TCCAGCAGGAAACCCC	29	7809	7824	ekkeekkddddddddk	576
599531	2575	2590	Exon 18	GTCCAGCAGGAAACCC	64	7810	7825	ekkeekkddddddddk	577
599532	2576	2591	Exon 18	TGTCCAGCAGGAAACC	43	7811	7826	ekkeekkddddddddk	578
599533	2577	2592	Exon 18	CTGTCCAGCAGGAAAC	25	7812	7827	ekkeekkddddddddk	820
599534	2578	2593	Exon 18	CCTGTCCAGCAGGAAA	12	7813	7828	ekkeekkddddddddk	580
599535	2580	2595	Exon 18	CCCCTGTCCAGCAGGA	16	7815	7830	ekkeekkddddddddk	582
599536	2582	2597	Exon 18	CGCCCCTGTCCAGCAG	27	7817	7832	ekkeekkddddddddk	584
599537	2583	2598	Exon 18	ACGCCCCTGTCCAGCA	35	7818	7833	ekkeekkddddddddk	585
599538	2584	2599	Exon 18	CACGCCCCTGTCCAGC	26	7819	7834	ekkeekkddddddddk	586
599539	2585	2600	Exon 18	CCACGCCCCTGTCCAG	33	7820	7835	ekkeekkddddddddk	587
599540	2586	2601	Exon 18	CCCACGCCCCTGTCCA	27	7821	7836	ekkeekkddddddddk	588
599541	2587	2602	Exon 18	TCCCACGCCCCTGTCC	52	7822	7837	ekkeekkddddddddk	589
599542	2588	2603	Exon 18	ATCCCACGCCCCTGTC	16	7823	7838	ekkeekkddddddddk	590
599543	2589	2604	Exon 18	AATCCCACGCCCCTGT	19	7824	7839	ekkeekkddddddddk	591
599544	2590	2605	Exon 18	CAATCCCACGCCCCTG	33	7825	7840	ekkeekkddddddddk	831
599545	2591	2606	Exon 18	TCAATCCCACGCCCCT	24	7826	7841	ekkeekkddddddddk	593
599546	2592	2607	Exon 18	TTCAATCCCACGCCCC	54	7827	7842	ekkeekkddddddddk	594
599547	2593	2608	Exon 18	ATTCAATCCCACGCCC	87	7828	7843	ekkeekkddddddddk	595
599548	2594	2609	Exon 18	AATTCAATCCCACGCC	79	7829	7844	ekkeekkddddddddk	596
599549	2595	2610	Exon 18	TAATTCAATCCCACGC	62	7830	7845	ekkeekkddddddddk	597
599550	2596	2611	Exon 18	TTAATTCAATCCCACG	52	7831	7846	ekkeekkddddddddk	598
599551	2597	2612	Exon 18	TTTAATTCAATCCCAC	27	7832	7847	ekkeekkddddddddk	599

TABLE 18-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599577	2597	2613	Exon 18	TTTTAATTCAATCCCAC	90	7832	7848	eeekkddddddddkkeee	662
599552	2598	2613	Exon 18	TTTTAATTCAATCCCA	92	7833	7848	ekkeekkddddddddk	600
599578	2598	2614	Exon 18	GTTTTAATTCAATCCCA	88	7833	7849	eeekkddddddddkkeee	663
599553	2599	2614	Exon 18	GTTTTAATTCAATCCC	91	7834	7849	ekkeekkddddddddk	601
599579	2599	2615	Exon 18	TGTTTTAATTCAATCCC	79	7834	7850	eeekkddddddddkkeee	664
599554	2600	2615	Exon 18	TGTTTTAATTCAATCC	90	7835	7850	ekkeekkddddddddk	602
599580	2600	2616	Exon 18	CTGTTTTAATTCAATCC	79	7835	7851	eeekkddddddddkkeee	665
599555	2601	2616	Exon 18	CTGTTTTAATTCAATC	79	7836	7851	ekkeekkddddddddk	846
599581	2601	2617	Exon 18	GCTGTTTTAATTCAATC	90	7836	7852	eeekkddddddddkkeee	666
599556	2602	2617	Exon 18	GCTGTTTTAATTCAAT	47	7837	7852	ekkeekkddddddddk	604
599582	2602	2618	Exon 18	AGCTGTTTTAATTCAAT	89	7837	7853	eeekkddddddddkkeee	849
599557	2603	2618	Exon 18	AGCTGTTTTAATTCAA	67	7838	7853	ekkeekkddddddddk	850
599583	2603	2619	Exon 18	CAGCTGTTTTAATTCAA	49	7838	7854	eeekkddddddddkkeee	668
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	78	7839	7858	eeeeeddddddddddeeeee	317
599558	2604	2619	Exon 18	CAGCTGTTTTAATTCA	80	7839	7854	ekkeekkddddddddk	606
599584	2604	2620	Exon 18	GCAGCTGTTTTAATTCA	66	7839	7855	eeekkddddddddkkeee	669
599559	2605	2620	Exon 18	GCAGCTGTTTTAATTC	38	7840	7855	ekkeekkddddddddk	607
599585	2605	2621	Exon 18	CGCAGCTGTTTTAATTC	80	7840	7856	eeekkddddddddkkeee	670
599560	2606	2621	Exon 18	CGCAGCTGTTTTAATT	16	7841	7856	ekkeekkddddddddk	608
599586	2606	2622	Exon 18	TCGCAGCTGTTTTAATT	78	7841	7857	eeekkddddddddkkeee	671
599561	2607	2622	Exon 18	TCGCAGCTGTTTTAAT	58	7842	7857	ekkeekkddddddddk	609
599587	2607	2623	Exon 18	GTCGCAGCTGTTTTAAT	81	7842	7858	eeekkddddddddkkeee	672
588860	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	92	7843	7858	eekddddddddddkke	610
599562	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	78	7843	7858	ekkeekkddddddddk	610
599588	2608	2624	Exon 18	TGTCGCAGCTGTTTTAA	81	7843	7859	eeekkddddddddkkeee	673
599563	2609	2624	Exon 18	TGTCGCAGCTGTTTTA	86	7844	7859	ekkeekkddddddddk	611
599589	2609	2625	Exon 18	TTGTCGCAGCTGTTTTA	75	7844	7860	eeekkddddddddkkeee	674
599564	2610	2625	Exon 18	TTGTCGCAGCTGTTTT	75	7845	7860	ekkeekkddddddddk	612
599590	2610	2626	Exon 18	GTTGTCGCAGCTGTTTT	88	7845	7861	eeekkddddddddkkeee	675
599565	2611	2626	Exon 18	GTTGTCGCAGCTGTTT	65	7846	7861	ekkeekkddddddddk	613
599591	2611	2627	Exon 18	TGTTGTCGCAGCTGTTT	94	7846	7862	eeekkddddddddkkeee	676
599566	2612	2627	Exon 18	TGTTGTCGCAGCTGTT	72	7847	7862	ekkeekkddddddddk	614
599592	2612	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTT	90	n/a	n/a	eeekkddddddddkkeee	677

TABLE 18-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599567	2613	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGT	82	n/a	n/a	ekkeekkddddddkk	615
599593	2613	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGT	95	n/a	n/a	eeekkddddddkkeee	678
599568	2614	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTG	92	n/a	n/a	ekkeekkddddddkk	616
599594	2614	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTG	86	n/a	n/a	eeekkddddddkkeee	679
599569	2615	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCT	89	n/a	n/a	ekkeekkddddddkk	617
599595	2615	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCT	76	n/a	n/a	eeekkddddddkkeee	680
599570	2616	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGC	95	n/a	n/a	ekkeekkddddddkk	618

Example 7

Antisense Inhibition of Human Complement Factor B (CFB) in HepG2 Cells

[0446] Additional antisense oligonucleotides were designed targeting human Complement Factor B (CFB) nucleic acid and were tested for their effects on CFB mRNA in vitro. The antisense oligonucleotides were tested in a series of experiments that had similar culture conditions. The results for each experiment are presented in separate tables shown below. Cultured HepG2 cells at a density of 20,000 cells per well were transfected using electroporation with 500 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0447] The newly designed chimeric antisense oligonucleotides in the Tables below were designed as deoxy, MOE and cEt oligonucleotides, or as 5-8-5 MOE, 5-9-5 MOE, 5-10-5 MOE, 6-7-6-MOE, 3-10-5 MOE, or 6-8-6 MOE gapmers.

[0448] The deoxy, MOE and cEt oligonucleotides are 16 nucleosides in length wherein the nucleoside have either a MOE sugar modification, an cEt sugar modification, or a deoxy modification. The 'Chemistry' column describes the sugar modifications of each oligonucleotide. 'k' indicates an cEt sugar modification; 'd' indicates deoxyribose; and 'e' indicates a MOE modification.

[0449] The 5-8-5 MOE gapmers are 18 nucleosides in length, wherein the central gap segment comprises of eight 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 5-9-5 MOE gapmers are 19 nucleosides in length, wherein the central gap segment comprises of nine 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 5-10-5 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising five nucleosides each. The 3-10-5 MOE gapmers are 18 nucleosides in length, wherein the central gap segment comprises of ten 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising three and five nucleosides respectively. The 6-7-6 MOE gapmers are 19 nucleosides in length, wherein the central gap segment comprises of seven 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising six nucleosides each. The 6-8-6 MOE gapmers are 20 nucleosides in length, wherein the central gap segment comprises of eight 2'-deoxynucleosides and is flanked by wing segments on the 5' direction and the 3' direction comprising six nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P═S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines.

[0450] "Start site" indicates the 5'-most nucleoside to which the gapmer is targeted in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the gapmer is targeted human gene sequence. Each gapmer listed in the Tables below is targeted to either the human CFB mRNA, designated herein as SEQ ID NO: 1 (GENBANK Accession No. NM_001710.5) or the human CFB genomic sequence, designated herein as SEQ ID NO: 2 (GENBANK Accession No. NT_007592.15 truncated from nucleotides 31852000 to 31861000), or both. 'n/a' indicates that the antisense oligonucleotide does not target that particular gene sequence with 100% complementarity.

TABLE 19

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
601152	2551	2566	Exon 18	AAACCCAAATCCTCAT	22	7786	7801	eekkddddddddkkee	557
601218	2551	2566	Exon 18	AAACCCAAATCCTCAT	21	7786	7801	ekkkddddddddkeee	557
601153	2552	2567	Exon 18	AAAACCCAAATCCTCA	27	7787	7802	eekkddddddddkkee	800
601219	2552	2567	Exon 18	AAAACCCAAATCCTCA	19	7787	7802	ekkkddddddddkeee	800
601154	2553	2568	Exon 18	GAAAACCCAAATCCTC	23	7788	7803	eekkddddddddkkee	558
601220	2553	2568	Exon 18	GAAAACCCAAATCCTC	24	7788	7803	ekkkddddddddkeee	558
601155	2554	2569	Exon 18	AGAAAACCCAAATCCT	20	7789	7804	eekkddddddddkkee	801
601221	2554	2569	Exon 18	AGAAAACCCAAATCCT	0	7789	7804	ekkkddddddddkeee	801
601156	2555	2570	Exon 18	TAGAAAACCCAAATCC	11	7790	7805	eekkddddddddkkee	559
601222	2555	2570	Exon 18	TAGAAAACCCAAATCC	23	7790	7805	ekkkddddddddkeee	559
601157	2556	2571	Exon 18	ATAGAAAACCCAAATC	9	7791	7806	eekkddddddddkkee	560
601223	2556	2571	Exon 18	ATAGAAAACCCAAATC	0	7791	7806	ekkkddddddddkeee	560
601158	2557	2572	Exon 18	TATAGAAAACCCAAAT	0	7792	7807	eekkddddddddkkee	802
601224	2557	2572	Exon 18	TATAGAAAACCCAAAT	0	7792	7807	ekkkddddddddkeee	802
601159	2558	2573	Exon 18	TTATAGAAAACCCAAA	2	7793	7808	eekkddddddddkkee	803
601225	2558	2573	Exon 18	TTATAGAAAACCCAAA	0	7793	7808	ekkkddddddddkeee	803
601160	2559	2574	Exon 18	CTTATAGAAAACCCAA	0	7794	7809	eekkddddddddkkee	561
601226	2559	2574	Exon 18	CTTATAGAAAACCCAA	0	7794	7809	ekkkddddddddkeee	561
601161	2560	2575	Exon 18	CCTTATAGAAAACCCA	1	7795	7810	eekkddddddddkkee	562
601227	2560	2575	Exon 18	CCTTATAGAAAACCCA	14	7795	7810	ekkkddddddddkeee	562
601162	2561	2576	Exon 18	CCCTTATAGAAAACCC	9	7796	7811	eekkddddddddkkee	563
601228	2561	2576	Exon 18	CCCTTATAGAAAACCC	9	7796	7811	ekkkddddddddkeee	563
601163	2562	2577	Exon 18	CCCCTTATAGAAAACC	0	7797	7812	eekkddddddddkkee	564
601164	2563	2578	Exon 18	ACCCCTTATAGAAAAC	3	7798	7813	eekkddddddddkkee	565
601165	2564	2579	Exon 18	AACCCCTTATAGAAAA	0	7799	7814	eekkddddddddkkee	566
601166	2565	2580	Exon 18	AAACCCCTTATAGAAA	0	7800	7815	eekkddddddddkkee	567
601167	2566	2581	Exon 18	GAAACCCCTTATAGAA	0	7801	7816	eekkddddddddkkee	568
601168	2567	2582	Exon 18	GGAAACCCCTTATAGA	0	7802	7817	eekkddddddddkkee	569
601169	2568	2583	Exon 18	AGGAAACCCCTTATAG	0	7803	7818	eekkddddddddkkee	570
601170	2569	2584	Exon 18	CAGGAAACCCCTTATA	10	7804	7819	eekkddddddddkkee	571
601171	2570	2585	Exon 18	GCAGGAAACCCCTTAT	9	7805	7820	eekkddddddddkkee	572
601172	2571	2586	Exon 18	AGCAGGAAACCCCTTA	15	7806	7821	eekkddddddddkkee	573
601173	2572	2587	Exon 18	CAGCAGGAAACCCCTT	29	7807	7822	eekkddddddddkkee	574
601174	2573	2588	Exon 18	CCAGCAGGAAACCCCT	25	7808	7823	eekkddddddddkkee	575

TABLE 19-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
601175	2574	2589	Exon 18	TCCAGCAGGAAACCCC	15	7809	7824	eekkddddddddkkee	576
601176	2575	2590	Exon 18	GTCCAGCAGGAAACCC	18	7810	7825	eekkddddddddkkee	577
601177	2576	2591	Exon 18	TGTCCAGCAGGAAACC	10	7811	7826	eekkddddddddkkee	578
601178	2577	2592	Exon 18	CTGTCCAGCAGGAAAC	11	7812	7827	eekkddddddddkkee	579
601179	2578	2593	Exon 18	CCTGTCCAGCAGGAAA	19	7813	7828	eekkddddddddkkee	580
601180	2579	2594	Exon 18	CCCTGTCCAGCAGGAA	7	7814	7829	eekkddddddddkkee	581
601181	2580	2595	Exon 18	CCCCTGTCCAGCAGGA	3	7815	7830	eekkddddddddkkee	582
601182	2581	2596	Exon 18	GCCCCTGTCCAGCAGG	0	7816	7831	eekkddddddddkkee	583
601183	2582	2597	Exon 18	CGCCCCTGTCCAGCAG	4	7817	7832	eekkddddddddkkee	584
601184	2583	2598	Exon 18	ACGCCCCTGTCCAGCA	14	7818	7833	eekkddddddddkkee	585
601185	2584	2599	Exon 18	CACGCCCCTGTCCAGC	26	7819	7834	eekkddddddddkkee	586
601186	2585	2600	Exon 18	CCACGCCCCTGTCCAG	8	7820	7835	eekkddddddddkkee	587
601187	2586	2601	Exon 18	CCCACGCCCCTGTCCA	18	7821	7836	eekkddddddddkkee	588
601188	2587	2602	Exon 18	TCCCACGCCCCTGTCC	20	7822	7837	eekkddddddddkkee	589
601189	2588	2603	Exon 18	ATCCCACGCCCCTGTC	12	7823	7838	eekkddddddddkkee	590
601190	2589	2604	Exon 18	AATCCCACGCCCCTGT	33	7824	7839	eekkddddddddkkee	591
601191	2590	2605	Exon 18	CAATCCCACGCCCCTG	52	7825	7840	eekkddddddddkkee	592
601192	2591	2606	Exon 18	TCAATCCCACGCCCCT	46	7826	7841	eekkddddddddkkee	593
601193	2592	2607	Exon 18	TTCAATCCCACGCCCC	30	7827	7842	eekkddddddddkkee	594
601194	2593	2608	Exon 18	ATTCAATCCCACGCCC	41	7828	7843	eekkddddddddkkee	595
601195	2594	2609	Exon 18	AATTCAATCCCACGCC	40	7829	7844	eekkddddddddkkee	596
601196	2595	2610	Exon 18	TAATTCAATCCCACGC	71	7830	7845	eekkddddddddkkee	597
601197	2596	2611	Exon 18	TTAATTCAATCCCACG	42	7831	7846	eekkddddddddkkee	598
601198	2597	2612	Exon 18	TTTAATTCAATCCCAC	63	7832	7847	eekkddddddddkkee	599
601199	2598	2613	Exon 18	TTTTAATTCAATCCCA	51	7833	7848	eekkddddddddkkee	600
601200	2599	2614	Exon 18	GTTTTAATTCAATCCC	65	7834	7849	eekkddddddddkkee	601
601201	2600	2615	Exon 18	TGTTTTAATTCAATCC	49	7835	7850	eekkddddddddkkee	602
601202	2601	2616	Exon 18	CTGTTTTAATTCAATC	33	7836	7851	eekkddddddddkkee	603
601203	2602	2617	Exon 18	GCTGTTTTAATTCAAT	63	7837	7852	eekkddddddddkkee	604
601204	2603	2618	Exon 18	AGCTGTTTTAATTCAA	69	7838	7853	eekkddddddddkkee	605
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	73	7839	7858	eeeeeddddddddddeeeee	317
601205	2604	2619	Exon 18	CAGCTGTTTTAATTCA	51	7839	7854	eekkddddddddkkee	606
601206	2605	2620	Exon 18	GCAGCTGTTTTAATTC	43	7840	7855	eekkddddddddkkee	607
601207	2606	2621	Exon 18	CGCAGCTGTTTTAATT	52	7841	7856	eekkddddddddkkee	608

TABLE 19-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
601208	2607	2622	Exon 18	TCGCAGCTGTTTTAAT	61	7842	7857	eekkddddddddkkee	609
588860	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	75	7843	7858	eekddddddddddkke	610
601209	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	73	7843	7858	eekkddddddddkkee	610
601210	2609	2624	Exon 18	TGTCGCAGCTGTTTTA	80	7844	7859	eekkddddddddkkee	611
601211	2610	2625	Exon 18	TTGTCGCAGCTGTTTT	64	7845	7860	eekkddddddddkkee	612
601212	2611	2626	Exon 18	GTTGTCGCAGCTGTTT	86	7846	7861	eekkddddddddkkee	613
601213	2612	2627	Exon 18	TGTTGTCGCAGCTGTT	87	7847	7862	eekkddddddddkkee	614
601214	2613	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGT	84	n/a	n/a	eekkddddddddkkee	615
601215	2614	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTG	78	n/a	n/a	eekkddddddddkkee	616
601216	2615	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCT	73	n/a	n/a	eekkddddddddkkee	617
601217	2616	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGC	66	n/a	n/a	eekkddddddddkkee	618

TABLE 20

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
601284	2551	2566	Exon 18	AAACCCAAATCCTCAT	8	7786	7801	ekkddddddddkkeee	557
601285	2552	2567	Exon 18	AAAACCCAAATCCTCA	15	7787	7802	ekkddddddddkkeee	800
601286	2553	2568	Exon 18	GAAAACCCAAATCCTC	21	7788	7803	ekkddddddddkkeee	558
601287	2554	2569	Exon 18	AGAAAACCCAAATCCT	9	7789	7804	ekkddddddddkkeee	801
601288	2555	2570	Exon 18	TAGAAAACCCAAATCC	0	7790	7805	ekkddddddddkkeee	559
601289	2556	2571	Exon 18	ATAGAAAACCCAAATC	40	7791	7806	ekkddddddddkkeee	560
601290	2557	2572	Exon 18	TATAGAAAACCCAAAT	16	7792	7807	ekkddddddddkkeee	802
601291	2558	2573	Exon 18	TTATAGAAAACCCAAA	15	7793	7808	ekkddddddddkkeee	803
601292	2559	2574	Exon 18	CTTATAGAAAACCCAA	5	7794	7809	ekkddddddddkkeee	561
601293	2560	2575	Exon 18	CCTTATAGAAAACCCA	15	7795	7810	ekkddddddddkkeee	562
601294	2561	2576	Exon 18	CCCTTATAGAAAACCC	3	7796	7811	ekkddddddddkkeee	563
601229	2562	2577	Exon 18	CCCCTTATAGAAAACC	15	7797	7812	ekkkddddddddkeee	564
601295	2562	2577	Exon 18	CCCCTTATAGAAAACC	5	7797	7812	ekkddddddddkkeee	564
601230	2563	2578	Exon 18	ACCCCTTATAGAAAAC	14	7798	7813	ekkkddddddddkeee	565

TABLE 20-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
601296	2563	2578	Exon 18	ACCCCTTATAGAAAAC	0	7798	7813	ekkddddddddkkeee	565
601231	2564	2579	Exon 18	AACCCCTTATAGAAAA	14	7799	7814	ekkddddddddkeee	566
601297	2564	2579	Exon 18	AACCCCTTATAGAAAA	14	7799	7814	ekkddddddddkkeee	566
601232	2565	2580	Exon 18	AAACCCCTTATAGAAA	15	7800	7815	ekkddddddddkeee	567
601298	2565	2580	Exon 18	AAACCCCTTATAGAAA	7	7800	7815	ekkddddddddkkeee	567
601233	2566	2581	Exon 18	GAAACCCCTTATAGAA	0	7801	7816	ekkddddddddkeee	568
601299	2566	2581	Exon 18	GAAACCCCTTATAGAA	0	7801	7816	ekkddddddddkkeee	568
601234	2567	2582	Exon 18	GGAAACCCCTTATAGA	0	7802	7817	ekkddddddddkeee	569
601300	2567	2582	Exon 18	GGAAACCCCTTATAGA	9	7802	7817	ekkddddddddkkeee	569
601235	2568	2583	Exon 18	AGGAAACCCCTTATAG	3	7803	7818	ekkddddddddkeee	570
601301	2568	2583	Exon 18	AGGAAACCCCTTATAG	14	7803	7818	ekkddddddddkkeee	570
601236	2569	2584	Exon 18	CAGGAAACCCCTTATA	0	7804	7819	ekkddddddddkeee	571
601302	2569	2584	Exon 18	CAGGAAACCCCTTATA	0	7804	7819	ekkddddddddkkeee	571
601237	2570	2585	Exon 18	GCAGGAAACCCCTTAT	16	7805	7820	ekkddddddddkeee	572
601303	2570	2585	Exon 18	GCAGGAAACCCCTTAT	16	7805	7820	ekkddddddddkkeee	572
601238	2571	2586	Exon 18	AGCAGGAAACCCCTTA	11	7806	7821	ekkddddddddkeee	573
601304	2571	2586	Exon 18	AGCAGGAAACCCCTTA	10	7806	7821	ekkddddddddkkeee	573
601239	2572	2587	Exon 18	CAGCAGGAAACCCCTT	21	7807	7822	ekkddddddddkeee	574
601305	2572	2587	Exon 18	CAGCAGGAAACCCCTT	7	7807	7822	ekkddddddddkkeee	574
601240	2573	2588	Exon 18	CCAGCAGGAAACCCCT	6	7808	7823	ekkddddddddkeee	575
601241	2574	2589	Exon 18	TCCAGCAGGAAACCCC	10	7809	7824	ekkddddddddkeee	576
601242	2575	2590	Exon 18	GTCCAGCAGGAAACCC	19	7810	7825	ekkddddddddkeee	577
601243	2576	2591	Exon 18	TGTCCAGCAGGAAACC	10	7811	7826	ekkddddddddkeee	578
601244	2577	2592	Exon 18	CTGTCCAGCAGGAAAC	28	7812	7827	ekkddddddddkeee	579
601245	2578	2593	Exon 18	CCTGTCCAGCAGGAAA	5	7813	7828	ekkddddddddkeee	580
601246	2579	2594	Exon 18	CCCTGTCCAGCAGGAA	18	7814	7829	ekkddddddddkeee	581
601247	2580	2595	Exon 18	CCCCTGTCCAGCAGGA	4	7815	7830	ekkddddddddkeee	582
601248	2581	2596	Exon 18	GCCCCTGTCCAGCAGG	6	7816	7831	ekkddddddddkeee	583
601249	2582	2597	Exon 18	CGCCCCTGTCCAGCAG	18	7817	7832	ekkddddddddkeee	584
601250	2583	2598	Exon 18	ACGCCCCTGTCCAGCA	26	7818	7833	ekkddddddddkeee	585
601251	2584	2599	Exon 18	CACGCCCCTGTCCAGC	27	7819	7834	ekkddddddddkeee	586
601252	2585	2600	Exon 18	CCACGCCCCTGTCCAG	21	7820	7835	ekkddddddddkeee	587
601253	2586	2601	Exon 18	CCCACGCCCCTGTCCA	0	7821	7836	ekkddddddddkeee	588
601254	2587	2602	Exon 18	TCCCACGCCCCTGTCC	31	7822	7837	ekkddddddddkeee	589

TABLE 20-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
601255	2588	2603	Exon 18	ATCCCACGCCCCTGTC	3	7823	7838	ekkkddddddddkeee	590
601256	2589	2604	Exon 18	AATCCCACGCCCCTGT	21	7824	7839	ekkkddddddddkeee	591
601257	2590	2605	Exon 18	CAATCCCACGCCCCTG	47	7825	7840	ekkkddddddddkeee	592
601258	2591	2606	Exon 18	TCAATCCCACGCCCCT	48	7826	7841	ekkkddddddddkeee	593
601259	2592	2607	Exon 18	TTCAATCCCACGCCCC	38	7827	7842	ekkkddddddddkeee	594
601260	2593	2608	Exon 18	ATTCAATCCCACGCCC	33	7828	7843	ekkkddddddddkeee	595
601261	2594	2609	Exon 18	AATTCAATCCCACGCC	17	7829	7844	ekkkddddddddkeee	596
601262	2595	2610	Exon 18	TAATTCAATCCCACGC	40	7830	7845	ekkkddddddddkeee	597
601263	2596	2611	Exon 18	TTAATTCAATCCCACG	31	7831	7846	ekkkddddddddkeee	598
601264	2597	2612	Exon 18	TTTAATTCAATCCCAC	72	7832	7847	ekkkddddddddkeee	599
601265	2598	2613	Exon 18	TTTTAATTCAATCCCA	48	7833	7848	ekkkddddddddkeee	600
601266	2599	2614	Exon 18	GTTTTAATTCAATCCC	64	7834	7849	ekkkddddddddkeee	601
601267	2600	2615	Exon 18	TGTTTTAATTCAATCC	43	7835	7850	ekkkddddddddkeee	602
601268	2601	2616	Exon 18	CTGTTTTAATTCAATC	44	7836	7851	ekkkddddddddkeee	603
601269	2602	2617	Exon 18	GCTGTTTTAATTCAAT	66	7837	7852	ekkkddddddddkeee	604
601270	2603	2618	Exon 18	AGCTGTTTTAATTCAA	47	7838	7853	ekkkddddddddkeee	605
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	3	7839	7858	eeeeeddddddddddeeeee	317
601271	2604	2619	Exon 18	CAGCTGTTTTAATTCA	26	7839	7854	ekkkddddddddkeee	606
601272	2605	2620	Exon 18	GCAGCTGTTTTAATTC	33	7840	7855	ekkkddddddddkeee	607
601273	2606	2621	Exon 18	CGCAGCTGTTTTAATT	34	7841	7856	ekkkddddddddkeee	608
601274	2607	2622	Exon 18	TCGCAGCTGTTTTAAT	39	7842	7857	ekkkddddddddkeee	609
588860	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	72	7843	7858	eekddddddddddkke	610
601275	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	65	7843	7858	ekkkddddddddkeee	610
601276	2609	2624	Exon 18	TGTCGCAGCTGTTTTA	65	7844	7859	ekkkddddddddkeee	611
601277	2610	2625	Exon 18	TTGTCGCAGCTGTTTT	51	7845	7860	ekkkddddddddkeee	612
601278	2611	2626	Exon 18	GTTGTCGCAGCTGTTT	78	7846	7861	ekkkddddddddkeee	613
601279	2612	2627	Exon 18	TGTTGTCGCAGCTGTT	79	7847	7862	ekkkddddddddkeee	614
601280	2613	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGT	70	n/a	n/a	ekkkddddddddkeee	615
601281	2614	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTG	78	n/a	n/a	ekkkddddddddkeee	616
601282	2615	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCT	68	n/a	n/a	ekkkddddddddkeee	617
601283	2616	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGC	61	n/a	n/a	ekkkddddddddkeee	618

TABLE 21

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
601306	2573	2588	Exon 18	CCAGCAGGAAACCCCT	22	7808	7823	ekkddddddddkkeee	575
601307	2574	2589	Exon 18	TCCAGCAGGAAACCCC	22	7809	7824	ekkddddddddkkeee	576
601308	2575	2590	Exon 18	GTCCAGCAGGAAACCC	33	7810	7825	ekkddddddddkkeee	577
601309	2576	2591	Exon 18	TGTCCAGCAGGAAACC	33	7811	7826	ekkddddddddkkeee	578
601310	2577	2592	Exon 18	CTGTCCAGCAGGAAAC	28	7812	7827	ekkddddddddkkeee	579
601311	2578	2593	Exon 18	CCTGTCCAGCAGGAAA	33	7813	7828	ekkddddddddkkeee	580
601312	2579	2594	Exon 18	CCCTGTCCAGCAGGAA	13	7814	7829	ekkddddddddkkeee	581
601313	2580	2595	Exon 18	CCCCTGTCCAGCAGGA	32	7815	7830	ekkddddddddkkeee	582
601314	2581	2596	Exon 18	GCCCCTGTCCAGCAGG	0	7816	7831	ekkddddddddkkeee	583
601315	2582	2597	Exon 18	CGCCCCTGTCCAGCAG	36	7817	7832	ekkddddddddkkeee	584
601316	2583	2598	Exon 18	ACGCCCCTGTCCAGCA	39	7818	7833	ekkddddddddkkeee	585
601317	2584	2599	Exon 18	CACGCCCCTGTCCAGC	33	7819	7834	ekkddddddddkkeee	586
601356	2584	2599	Exon 18	CACGCCCCTGTCCAGC	27	7819	7834	kkkddddddddkeeee	586
601318	2585	2600	Exon 18	CCACGCCCCTGTCCAG	35	7820	7835	ekkddddddddkkeee	587
601357	2585	2600	Exon 18	CCACGCCCCTGTCCAG	26	7820	7835	kkkddddddddkeeee	587
601319	2586	2601	Exon 18	CCCACGCCCCTGTCCA	33	7821	7836	ekkddddddddkkeee	588
601358	2586	2601	Exon 18	CCCACGCCCCTGTCCA	26	7821	7836	kkkddddddddkeeee	588
601320	2587	2602	Exon 18	TCCCACGCCCCTGTCC	25	7822	7837	ekkddddddddkkeee	589
601359	2587	2602	Exon 18	TCCCACGCCCCTGTCC	23	7822	7837	kkkddddddddkeeee	589
601321	2588	2603	Exon 18	ATCCCACGCCCCTGTC	50	7823	7838	ekkddddddddkkeee	590
601360	2588	2603	Exon 18	ATCCCACGCCCCTGTC	33	7823	7838	kkkddddddddkeeee	590
601322	2589	2604	Exon 18	AATCCCACGCCCCTGT	52	7824	7839	ekkddddddddkkeee	591
601361	2589	2604	Exon 18	AATCCCACGCCCCTGT	48	7824	7839	kkkddddddddkeeee	591
601323	2590	2605	Exon 18	CAATCCCACGCCCCTG	67	7825	7840	ekkddddddddkkeee	592
601362	2590	2605	Exon 18	CAATCCCACGCCCCTG	51	7825	7840	kkkddddddddkeeee	592
601324	2591	2606	Exon 18	TCAATCCCACGCCCCT	42	7826	7841	ekkddddddddkkeee	593
601363	2591	2606	Exon 18	TCAATCCCACGCCCCT	42	7826	7841	kkkddddddddkeeee	593
601325	2592	2607	Exon 18	TTCAATCCCACGCCCC	52	7827	7842	ekkddddddddkkeee	594
601364	2592	2607	Exon 18	TTCAATCCCACGCCCC	48	7827	7842	kkkddddddddkeeee	594
601326	2593	2608	Exon 18	ATTCAATCCCACGCCC	27	7828	7843	ekkddddddddkkeee	595
601365	2593	2608	Exon 18	ATTCAATCCCACGCCC	36	7828	7843	kkkddddddddkeeee	595
601327	2594	2609	Exon 18	AATTCAATCCCACGCC	66	7829	7844	ekkddddddddkkeee	596
601366	2594	2609	Exon 18	AATTCAATCCCACGCC	49	7829	7844	kkkddddddddkeeee	596
601328	2595	2610	Exon 18	TAATTCAATCCCACGC	55	7830	7845	ekkddddddddkkeee	597

TABLE 21-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
601367	2595	2610	Exon 18	TAATTCAATCCCACGC	57	7830	7845	kkkddddddddkeeee	597
601329	2596	2611	Exon 18	TTAATTCAATCCCACG	69	7831	7846	ekkddddddddkkeee	598
601368	2596	2611	Exon 18	TTAATTCAATCCCACG	68	7831	7846	kkkddddddddkeeee	598
601330	2597	2612	Exon 18	TTTAATTCAATCCCAC	58	7832	7847	ekkddddddddkkeee	599
601369	2597	2612	Exon 18	TTTAATTCAATCCCAC	65	7832	7847	kkkddddddddkeeee	599
601331	2598	2613	Exon 18	TTTTAATTCAATCCCA	45	7833	7848	ekkddddddddkkeee	600
601370	2598	2613	Exon 18	TTTTAATTCAATCCCA	42	7833	7848	kkkddddddddkeeee	600
601332	2599	2614	Exon 18	GTTTTAATTCAATCCC	84	7834	7849	ekkddddddddkkeee	601
601371	2599	2614	Exon 18	GTTTTAATTCAATCCC	79	7834	7849	kkkddddddddkeeee	601
601333	2600	2615	Exon 18	TGTTTTAATTCAATCC	61	7835	7850	ekkddddddddkkeee	602
601372	2600	2615	Exon 18	TGTTTTAATTCAATCC	71	7835	7850	kkkddddddddkeeee	602
601334	2601	2616	Exon 18	CTGTTTTAATTCAATC	61	7836	7851	ekkddddddddkkeee	603
601373	2601	2616	Exon 18	CTGTTTTAATTCAATC	57	7836	7851	kkkddddddddkeeee	603
601335	2602	2617	Exon 18	GCTGTTTTAATTCAAT	73	7837	7852	ekkddddddddkkeee	604
601374	2602	2617	Exon 18	GCTGTTTTAATTCAAT	66	7837	7852	kkkddddddddkeeee	604
601336	2603	2618	Exon 18	AGCTGTTTTAATTCAA	64	7838	7853	ekkddddddddkkeee	605
601375	2603	2618	Exon 18	AGCTGTTTTAATTCAA	61	7838	7853	kkkddddddddkeeee	605
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	66	7839	7858	eeeeeddddddddde eeee	317
601337	2604	2619	Exon 18	CAGCTGTTTTAATTCA	53	7839	7854	ekkddddddddkkeee	606
601376	2604	2619	Exon 18	CAGCTGTTTTAATTCA	39	7839	7854	kkkddddddddkeeee	606
601338	2605	2620	Exon 18	GCAGCTGTTTTAATTC	67	7840	7855	ekkddddddddkkeee	607
601377	2605	2620	Exon 18	GCAGCTGTTTTAATTC	67	7840	7855	kkkddddddddkeeee	607
601339	2606	2621	Exon 18	CGCAGCTGTTTTAATT	63	7841	7856	ekkddddddddkkeee	608
601378	2606	2621	Exon 18	CGCAGCTGTTTTAATT	60	7841	7856	kkkddddddddkeeee	608
601340	2607	2622	Exon 18	TCGCAGCTGTTTTAAT	40	7842	7857	ekkddddddddkkeee	609
601379	2607	2622	Exon 18	TCGCAGCTGTTTTAAT	36	7842	7857	kkkddddddddkeeee	609
588860	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	84	7843	7858	eekddddddddddkke	610
601341	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	74	7843	7858	ekkddddddddkkeee	610
601380	2608	2623	Exon 18	GTCGCAGCTGTTTTAA	78	7843	7858	kkkddddddddkeeee	610
601342	2609	2624	Exon 18	TGTCGCAGCTGTTTTA	68	7844	7859	ekkddddddddkkeee	611
601381	2609	2624	Exon 18	TGTCGCAGCTGTTTTA	66	7844	7859	kkkddddddddkeeee	611
601343	2610	2625	Exon 18	TTGTCGCAGCTGTTTT	71	7845	7860	ekkddddddddkkeee	612
601382	2610	2625	Exon 18	TTGTCGCAGCTGTTTT	84	7845	7860	kkkddddddddkeeee	612
601344	2611	2626	Exon 18	GTTGTCGCAGCTGTTT	87	7846	7861	ekkddddddddkkeee	613

TABLE 21-continued

Inhibition of CFB mRNA by deoxy, MOE and cEt oligonucleotides targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
601383	2611	2626	Exon 18	GTTGTCGCAGCTGTTT	85	7846	7861	kkkddddddddkeeee	613
601345	2612	2627	Exon 18	TGTTGTCGCAGCTGTT	82	7847	7862	ekkddddddddkkeee	614
601384	2612	2627	Exon 18	TGTTGTCGCAGCTGTT	79	7847	7862	kkkddddddddkeeee	614
601346	2613	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGT	73	n/a	n/a	ekkddddddddkkeee	615
601385	2613	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGT	84	n/a	n/a	kkkddddddddkeeee	615
601347	2614	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTG	70	n/a	n/a	ekkddddddddkkeee	616
601386	2614	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTG	71	n/a	n/a	kkkddddddddkeeee	616
601348	2615	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCT	71	n/a	n/a	ekkddddddddkkeee	617
601387	2615	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCT	76	n/a	n/a	kkkddddddddkeeee	617
601349	2616	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGC	71	n/a	n/a	ekkddddddddkkeee	618
601388	2616	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGC	67	n/a	n/a	kkkddddddddkeeee	618

TABLE 22

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599357	2582	2600	Exon 18	CCACGCCCCTGTCCAGCAG	26	7817	7835	5-9-5	708
599358	2583	2601	Exon 18	CCCACGCCCCTGTCCAGCA	22	7818	7836	5-9-5	709
599359	2584	2602	Exon 18	TCCCACGCCCCTGTCCAGC	13	7819	7837	5-9-5	710
599360	2585	2603	Exon 18	ATCCCACGCCCCTGTCCAG	7	7820	7838	5-9-5	711
599361	2586	2604	Exon 18	AATCCCACGCCCCTGTCCA	11	7821	7839	5-9-5	712
599362	2587	2605	Exon 18	CAATCCCACGCCCCTGTCC	14	7822	7840	5-9-5	713
599363	2588	2606	Exon 18	TCAATCCCACGCCCCTGTC	17	7823	7841	5-9-5	714
599364	2589	2607	Exon 18	TTCAATCCCACGCCCCTGT	20	7824	7842	5-9-5	715
599365	2590	2608	Exon 18	ATTCAATCCCACGCCCCTG	22	7825	7843	5-9-5	716
599366	2591	2609	Exon 18	AATTCAATCCCACGCCCCT	13	7826	7844	5-9-5	717
599367	2592	2610	Exon 18	TAATTCAATCCCACGCCCC	11	7827	7845	5-9-5	718
599368	2593	2611	Exon 18	TTAATTCAATCCCACGCCC	10	7828	7846	5-9-5	719

TABLE 22-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599369	2594	2612	Exon 18	TTTAATTCAATCCCACGCC	19	7829	7847	5-9-5	720
599370	2595	2613	Exon 18	TTTTAATTCAATCCCACGC	23	7830	7848	5-9-5	721
599371	2596	2614	Exon 18	GTTTTAATTCAATCCCACG	4	7831	7849	5-9-5	722
599372	2597	2615	Exon 18	TGTTTTAATTCAATCCCAC	16	7832	7850	5-9-5	723
599373	2598	2616	Exon 18	CTGTTTTAATTCAATCCCA	3	7833	7851	5-9-5	724
599374	2599	2617	Exon 18	GCTGTTTTAATTCAATCCC	10	7834	7852	5-9-5	725
599375	2600	2618	Exon 18	AGCTGTTTTAATTCAATCC	17	7835	7853	5-9-5	726
599376	2601	2619	Exon 18	CAGCTGTTTTAATTCAATC	18	7836	7854	5-9-5	727
599377	2602	2620	Exon 18	GCAGCTGTTTTAATTCAAT	22	7837	7855	5-9-5	728
599378	2603	2621	Exon 18	CGCAGCTGTTTTAATTCAA	11	7838	7856	5-9-5	729
599511	2552	2571	Exon 18	ATAGAAAACCCAAATCCTCA	7	7787	7806	6-8-6	410
599389	2553	2572	Exon 18	TATAGAAAACCCAAATCCTC	22	7788	7807	6-8-6	411
599390	2554	2573	Exon 18	TTATAGAAAACCCAAATCCT	21	7789	7808	6-8-6	412
599391	2555	2574	Exon 18	CTTATAGAAAACCCAAATCC	27	7790	7809	6-8-6	413
599392	2556	2575	Exon 18	CCTTATAGAAAACCCAAATC	30	7791	7810	6-8-6	414
599393	2557	2576	Exon 18	CCCTTATAGAAAACCCAAAT	30	7792	7811	6-8-6	415
599394	2558	2577	Exon 18	CCCCTTATAGAAAACCCAAA	28	7793	7812	6-8-6	416
599395	2559	2578	Exon 18	ACCCCTTATAGAAAACCCAA	23	7794	7813	6-8-6	417
599396	2560	2579	Exon 18	AACCCCTTATAGAAAACCCA	53	7795	7814	6-8-6	418
599397	2561	2580	Exon 18	AAACCCCTTATAGAAAACCC	33	7796	7815	6-8-6	419
599398	2562	2581	Exon 18	GAAACCCCTTATAGAAAACC	58	7797	7816	6-8-6	420
599399	2563	2582	Exon 18	GGAAACCCCTTATAGAAAAC	23	7798	7817	6-8-6	421
599400	2564	2583	Exon 18	AGGAAACCCCTTATAGAAAA	54	7799	7818	6-8-6	422
599401	2565	2584	Exon 18	CAGGAAACCCCTTATAGAAA	30	7800	7819	6-8-6	423
599402	2566	2585	Exon 18	GCAGGAAACCCCTTATAGAA	25	7801	7820	6-8-6	424
599403	2567	2586	Exon 18	AGCAGGAAACCCCTTATAGA	17	7802	7821	6-8-6	425
599404	2568	2587	Exon 18	CAGCAGGAAACCCCTTATAG	20	7803	7822	6-8-6	426
599405	2569	2588	Exon 18	CCAGCAGGAAACCCCTTATA	12	7804	7823	6-8-6	427
599406	2570	2589	Exon 18	TCCAGCAGGAAACCCCTTAT	51	7805	7824	6-8-6	428
599407	2571	2590	Exon 18	GTCCAGCAGGAAACCCCTTA	39	7806	7825	6-8-6	237
599408	2572	2591	Exon 18	TGTCCAGCAGGAAACCCCTT	53	7807	7826	6-8-6	429
599409	2573	2592	Exon 18	CTGTCCAGCAGGAAACCCCT	65	7808	7827	6-8-6	430
599410	2574	2593	Exon 18	CCTGTCCAGCAGGAAACCCC	56	7809	7828	6-8-6	431
599411	2575	2594	Exon 18	CCCTGTCCAGCAGGAAACCC	60	7810	7829	6-8-6	432
599412	2576	2595	Exon 18	CCCCTGTCCAGCAGGAAACC	61	7811	7830	6-8-6	433

TABLE 22-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599413	2577	2596	Exon 18	GCCCCTGTCCAGCAGGAAAC	40	7812	7831	6-8-6	238
599414	2578	2597	Exon 18	CGCCCCTGTCCAGCAGGAAA	41	7813	7832	6-8-6	434
599415	2579	2598	Exon 18	ACGCCCCTGTCCAGCAGGAA	37	7814	7833	6-8-6	435
599416	2580	2599	Exon 18	CACGCCCCTGTCCAGCAGGA	54	7815	7834	6-8-6	436
599417	2581	2600	Exon 18	CCACGCCCCTGTCCAGCAGG	36	7816	7835	6-8-6	437
599418	2582	2601	Exon 18	CCCACGCCCCTGTCCAGCAG	53	7817	7836	6-8-6	438
599419	2583	2602	Exon 18	TCCCACGCCCCTGTCCAGCA	54	7818	7837	6-8-6	439
599420	2584	2603	Exon 18	ATCCCACGCCCCTGTCCAGC	50	7819	7838	6-8-6	440
599421	2585	2604	Exon 18	AATCCCACGCCCCTGTCCAG	48	7820	7839	6-8-6	441
599422	2586	2605	Exon 18	CAATCCCACGCCCCTGTCCA	55	7821	7840	6-8-6	442
599423	2587	2606	Exon 18	TCAATCCCACGCCCCTGTCC	75	7822	7841	6-8-6	443
599424	2588	2607	Exon 18	TTCAATCCCACGCCCCTGTC	69	7823	7842	6-8-6	444
599425	2589	2608	Exon 18	ATTCAATCCCACGCCCCTGT	77	7824	7843	6-8-6	445
599426	2590	2609	Exon 18	AATTCAATCCCACGCCCCTG	60	7825	7844	6-8-6	446
599427	2591	2610	Exon 18	TAATTCAATCCCACGCCCCT	72	7826	7845	6-8-6	447
599428	2592	2611	Exon 18	TTAATTCAATCCCACGCCCC	81	7827	7846	6-8-6	448
599429	2593	2612	Exon 18	TTTAATTCAATCCCACGCCC	68	7828	7847	6-8-6	449
599430	2594	2613	Exon 18	TTTTAATTCAATCCCACGCC	58	7829	7848	6-8-6	450
599431	2595	2614	Exon 18	GTTTTAATTCAATCCCACGC	70	7830	7849	6-8-6	451
599432	2596	2615	Exon 18	TGTTTTAATTCAATCCCACG	85	7831	7850	6-8-6	452
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	85	7839	7858	5-10-5	317
599379	2604	2622	Exon 18	TCGCAGCTGTTTTAATTCA	73	7839	7857	5-9-5	730
599380	2605	2623	Exon 18	GTCGCAGCTGTTTTAATTC	77	7840	7858	5-9-5	731
599381	2606	2624	Exon 18	TGTCGCAGCTGTTTTAATT	69	7841	7859	5-9-5	732
599382	2607	2625	Exon 18	TTGTCGCAGCTGTTTTAAT	58	7842	7860	5-9-5	733
599383	2608	2626	Exon 18	GTTGTCGCAGCTGTTTTAA	52	7843	7861	5-9-5	734
599384	2609	2627	Exon 18	TGTTGTCGCAGCTGTTTTA	63	7844	7862	5-9-5	735
599385	2610	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTTTT	53	n/a	n/a	5-9-5	736
599386	2611	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGTTT	63	n/a	n/a	5-9-5	737
599387	2612	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTGTT	64	n/a	n/a	5-9-5	438
599388	2613	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCTGT	66	n/a	n/a	5-9-5	739

TABLE 23

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599213	2553	2570	Exon 18	TAGAAAACCCAAATCCTC	0	7788	7805	3-10-5	785
599214	2554	2571	Exon 18	ATAGAAAACCCAAATCCT	0	7789	7806	3-10-5	786
599215	2555	2572	Exon 18	TATAGAAAACCCAAATCC	36	7790	7807	3-10-5	787
599216	2556	2573	Exon 18	TTATAGAAAACCCAAATC	8	7791	7808	3-10-5	788
599217	2557	2574	Exon 18	CTTATAGAAAACCCAAAT	5	7792	7809	3-10-5	789
599218	2558	2575	Exon 18	CCTTATAGAAAACCCAAA	0	7793	7810	3-10-5	790
599219	2559	2576	Exon 18	CCCTTATAGAAAACCCAA	8	7794	7811	3-10-5	791
599220	2560	2577	Exon 18	CCCCTTATAGAAAACCCA	0	7795	7812	3-10-5	740
599221	2561	2578	Exon 18	ACCCCTTATAGAAAACCC	54	7796	7813	3-10-5	741
599222	2562	2579	Exon 18	AACCCCTTATAGAAAACC	3	7797	7814	3-10-5	742
599223	2563	2580	Exon 18	AAACCCCTTATAGAAAAC	0	7798	7815	3-10-5	743
599224	2564	2581	Exon 18	GAAACCCCTTATAGAAAA	0	7799	7816	3-10-5	744
599225	2566	2583	Exon 18	AGGAAACCCCTTATAGAA	60	7801	7818	3-10-5	745
599226	2567	2584	Exon 18	CAGGAAACCCCTTATAGA	0	7802	7819	3-10-5	746
599227	2568	2585	Exon 18	GCAGGAAACCCCTTATAG	37	7803	7820	3-10-5	747
599228	2569	2586	Exon 18	AGCAGGAAACCCCTTATA	0	7804	7821	3-10-5	748
599229	2570	2587	Exon 18	CAGCAGGAAACCCCTTAT	39	7805	7822	3-10-5	749
599230	2571	2588	Exon 18	CCAGCAGGAAACCCCTTA	10	7806	7823	3-10-5	750
599231	2572	2589	Exon 18	TCCAGCAGGAAACCCCTT	16	7807	7824	3-10-5	751
599232	2573	2590	Exon 18	GTCCAGCAGGAAACCCCT	9	7808	7825	3-10-5	752
599233	2574	2591	Exon 18	TGTCCAGCAGGAAACCCC	44	7809	7826	3-10-5	753
599234	2575	2592	Exon 18	CTGTCCAGCAGGAAACCC	14	7810	7827	3-10-5	754
599235	2576	2593	Exon 18	CCTGTCCAGCAGGAAACC	0	7811	7828	3-10-5	755
599236	2577	2594	Exon 18	CCCTGTCCAGCAGGAAAC	43	7812	7829	3-10-5	756
599237	2578	2595	Exon 18	CCCCTGTCCAGCAGGAAA	0	7813	7830	3-10-5	757
599238	2580	2597	Exon 18	CGCCCCTGTCCAGCAGGA	9	7815	7832	3-10-5	758
599239	2581	2598	Exon 18	ACGCCCCTGTCCAGCAGG	36	7816	7833	3-10-5	759
599240	2582	2599	Exon 18	CACGCCCCTGTCCAGCAG	11	7817	7834	3-10-5	760
599241	2583	2600	Exon 18	CCACGCCCCTGTCCAGCA	51	7818	7835	3-10-5	761
599242	2584	2601	Exon 18	CCCACGCCCCTGTCCAGC	7	7819	7836	3-10-5	762
599243	2585	2602	Exon 18	TCCCACGCCCCTGTCCAG	47	7820	7837	3-10-5	763
599244	2586	2603	Exon 18	ATCCCACGCCCCTGTCCA	37	7821	7838	3-10-5	764
599245	2587	2604	Exon 18	AATCCCACGCCCCTGTCC	35	7822	7839	3-10-5	765
599246	2588	2605	Exon 18	CAATCCCACGCCCCTGTC	21	7823	7840	3-10-5	766
599247	2589	2606	Exon 18	TCAATCCCACGCCCCTGT	61	7824	7841	3-10-5	767

TABLE 23-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599248	2590	2607	Exon 18	TTCAATCCCACGCCCCTG	51	7825	7842	3-10-5	768
599249	2591	2608	Exon 18	ATTCAATCCCACGCCCCT	58	7826	7843	3-10-5	769
599250	2592	2609	Exon 18	AATTCAATCCCACGCCCC	49	7827	7844	3-10-5	770
599251	2593	2610	Exon 18	TAATTCAATCCCACGCCC	46	7828	7845	3-10-5	771
599252	2594	2611	Exon 18	TTAATTCAATCCCACGCC	32	7829	7846	3-10-5	772
599253	2595	2612	Exon 18	TTTAATTCAATCCCACGC	23	7830	7847	3-10-5	773
599254	2596	2613	Exon 18	TTTTAATTCAATCCCACG	0	7831	7848	3-10-5	774
599255	2597	2614	Exon 18	GTTTTAATTCAATCCCAC	61	7832	7849	3-10-5	775
599256	2598	2615	Exon 18	TGTTTTAATTCAATCCCA	64	7833	7850	3-10-5	776
599257	2599	2616	Exon 18	CTGTTTTAATTCAATCCC	66	7834	7851	3-10-5	777
599258	2600	2617	Exon 18	GCTGTTTTAATTCAATCC	59	7835	7852	3-10-5	778
599259	2601	2618	Exon 18	AGCTGTTTTAATTCAATC	40	7836	7853	3-10-5	779
599260	2602	2619	Exon 18	CAGCTGTTTTAATTCAAT	38	7837	7854	3-10-5	780
599261	2603	2620	Exon 18	GCAGCTGTTTTAATTCAA	54	7838	7855	3-10-5	781
599509	2552	2570	Exon 18	TAGAAAACCCAAATCCTCA	54	7787	7805	6-7-6	681
599273	2553	2571	Exon 18	ATAGAAAACCCAAATCCTC	0	7788	7806	6-7-6	682
599274	2554	2572	Exon 18	TATAGAAAACCCAAATCCT	57	7789	7807	6-7-6	683
599275	2556	2574	Exon 18	CTTATAGAAAACCCAAATC	0	7791	7809	6-7-6	684
599276	2557	2575	Exon 18	CCTTATAGAAAACCCAAAT	44	7792	7810	6-7-6	685
599277	2558	2576	Exon 18	CCCTTATAGAAAACCCAAA	0	7793	7811	6-7-6	686
599278	2559	2577	Exon 18	CCCCTTATAGAAAACCCAA	0	7794	7812	6-7-6	687
599279	2560	2578	Exon 18	ACCCCTTATAGAAAACCCA	20	7795	7813	6-7-6	688
599280	2561	2579	Exon 18	AACCCCTTATAGAAAACCC	70	7796	7814	6-7-6	689
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	85	7839	7858	5-10-5	317
599262	2604	2621	Exon 18	CGCAGCTGTTTTAATTCA	49	7839	7856	3-10-5	782
599263	2605	2622	Exon 18	TCGCAGCTGTTTTAATTC	49	7840	7857	3-10-5	783
599264	2606	2623	Exon 18	GTCGCAGCTGTTTTAATT	62	7841	7858	3-10-5	784
599265	2607	2624	Exon 18	TGTCGCAGCTGTTTTAAT	63	7842	7859	3-10-5	792
599266	2608	2625	Exon 18	TTGTCGCAGCTGTTTTAA	41	7843	7860	3-10-5	793
599267	2609	2626	Exon 18	GTTGTCGCAGCTGTTTTA	52	7844	7861	3-10-5	794
599268	2610	2627	Exon 18	TGTTGTCGCAGCTGTTTT	51	7845	7862	3-10-5	795
599269	2611	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTTT	58	n/a	n/a	3-10-5	796
599270	2612	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGTT	69	n/a	n/a	3-10-5	797

TABLE 23-continued

Inhibition of CFB mRNA by MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	Motif	SEQ ID NO:
599271	2613	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTGT	69	n/a	n/a	3-10-5	798
599272	2614	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCTG	72	n/a	n/a	3-10-5	799
599205	2607	2624	Exon 18	TGTCGCAGCTGTTTTAAT	54	7842	7859	5-8-5	792
599206	2608	2625	Exon 18	TTGTCGCAGCTGTTTTAA	62	7843	7860	5-8-5	793
599207	2609	2626	Exon 18	GTTGTCGCAGCTGTTTTA	62	7844	7861	5-8-5	794
599208	2610	2627	Exon 18	TGTTGTCGCAGCTGTTTT	66	7845	7862	5-8-5	795
599209	2611	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTTT	60	n/a	n/a	5-8-5	796
599210	2612	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGTT	62	n/a	n/a	5-8-5	797
599211	2613	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTGT	65	n/a	n/a	5-8-5	798
599212	2614	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCTG	67	n/a	n/a	5-8-5	799

TABLE 24

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588570	150	169	Exon 1	TGGTCACATTCCCTTCCCCT	72	1871	1890	396
588571	152	171	Exon 1	CCTGGTCACATTCCCTTCCC	80	1873	1892	397
532614	154	173	Exon 1	GACCTGGTCACATTCCCTTC	65	1875	1894	12
588572	156	175	Exon 1	TAGACCTGGTCACATTCCCT	74	1877	1896	398
588573	158	177	Exon 1	CCTAGACCTGGTCACATTCC	72	1879	1898	399
588566	2189	2208	Exon 15	CCTTCCGAGTCAGCTTTTTC	66	6977	6996	400
588567	2191	2210	Exon 15	CTCCTTCCGAGTCAGCTTTT	66	6979	6998	401
532770	2193	2212	Exon 15	ACCTCCTTCCGAGTCAGCTT	64	6981	7000	198
588568	2195	2214	Exon 15	AGACCTCCTTCCGAGTCAGC	78	6983	7002	402
588569	2197	2216	Exon 15	GTAGACCTCCTTCCGAGTCA	74	6985	7004	403
588574	2453	2472	Exon 18	TTTGCCGCTTCTGGTTTTTG	71	7688	7707	404
588575	2455	2474	Exon 18	CTTTTGCCGCTTCTGGTTTT	72	7690	7709	405
532800	2457	2476	Exon 18	TGCTTTTGCCGCTTCTGGTT	71	7692	7711	228
588576	2459	2478	Exon 18	CCTGCTTTTGCCGCTTCTGG	59	7694	7713	406
588577	2461	2480	Exon 18	TACCTGCTTTTGCCGCTTCT	76	7696	7715	407

TABLE 24-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
516350	2550	2569	Exon 18	AGAAAACCCAAATCCTCATC	58	7785	7804	408
588509	2551	2570	Exon 18	TAGAAAACCCAAATCCTCAT	6	7786	7805	409
588510	2552	2571	Exon 18	ATAGAAAACCCAAATCCTCA	10	7787	7806	410
588511	2553	2572	Exon 18	TATAGAAAACCCAAATCCTC	9	7788	7807	411
588512	2554	2573	Exon 18	TTATAGAAAACCCAAATCCT	80	7789	7808	412
588513	2555	2574	Exon 18	CTTATAGAAAACCCAAATCC	70	7790	7809	413
588514	2556	2575	Exon 18	CCTTATAGAAAACCCAAATC	71	7791	7810	414
588515	2557	2576	Exon 18	CCCTTATAGAAAACCCAAAT	78	7792	7811	415
588516	2558	2577	Exon 18	CCCCTTATAGAAAACCCAAA	72	7793	7812	416
588517	2559	2578	Exon 18	ACCCCTTATAGAAAACCCAA	80	7794	7813	417
588518	2560	2579	Exon 18	AACCCCTTATAGAAAACCCA	80	7795	7814	418
588519	2561	2580	Exon 18	AAACCCCTTATAGAAAACCC	62	7796	7815	419
588520	2562	2581	Exon 18	GAAACCCCTTATAGAAAACC	59	7797	7816	420
588521	2563	2582	Exon 18	GGAAACCCCTTATAGAAAAC	40	7798	7817	421
588522	2564	2583	Exon 18	AGGAAACCCCTTATAGAAAA	66	7799	7818	422
588523	2565	2584	Exon 18	CAGGAAACCCCTTATAGAAA	63	7800	7819	423
588524	2566	2585	Exon 18	GCAGGAAACCCCTTATAGAA	70	7801	7820	424
588525	2567	2586	Exon 18	AGCAGGAAACCCCTTATAGA	67	7802	7821	425
588526	2568	2587	Exon 18	CAGCAGGAAACCCCTTATAG	0	7803	7822	426
588527	2569	2588	Exon 18	CCAGCAGGAAACCCCTTATA	11	7804	7823	427
588528	2570	2589	Exon 18	TCCAGCAGGAAACCCCTTAT	15	7805	7824	428
532809	2571	2590	Exon 18	GTCCAGCAGGAAACCCCTTA	75	7806	7825	237
588529	2572	2591	Exon 18	TGTCCAGCAGGAAACCCCTT	16	7807	7826	429
588530	2573	2592	Exon 18	CTGTCCAGCAGGAAACCCCT	16	7808	7827	430
588531	2574	2593	Exon 18	CCTGTCCAGCAGGAAACCCC	19	7809	7828	431
588532	2575	2594	Exon 18	CCCTGTCCAGCAGGAAACCC	15	7810	7829	432
588533	2576	2595	Exon 18	CCCCTGTCCAGCAGGAAACC	29	7811	7830	433
532810	2577	2596	Exon 18	GCCCCTGTCCAGCAGGAAAC	74	7812	7831	238
588534	2578	2597	Exon 18	CGCCCCTGTCCAGCAGGAAA	21	7813	7832	434
588535	2579	2598	Exon 18	ACGCCCCTGTCCAGCAGGAA	16	7814	7833	435
588536	2580	2599	Exon 18	CACGCCCCTGTCCAGCAGGA	0	7815	7834	436
588537	2581	2600	Exon 18	CCACGCCCCTGTCCAGCAGG	8	7816	7835	437
588538	2582	2601	Exon 18	CCCACGCCCCTGTCCAGCAG	10	7817	7836	438
588539	2583	2602	Exon 18	TCCCACGCCCCTGTCCAGCA	23	7818	7837	439

TABLE 24-continued

Inhibition of CFB mRNA by 5-10-5 MOE gapmers targeting SEQ ID NO: 1 or SEQ ID NO: 2

ISIS NO	SEQ ID NO: 1 start site	SEQ ID NO: 1 stop site	Target region	Sequence	% inhibition	SEQ ID NO: 2 start site	SEQ ID NO: 2 stop site	SEQ ID NO:
588540	2584	2603	Exon 18	ATCCCACGCCCCTGTCCAGC	16	7819	7838	440
588541	2585	2604	Exon 18	AATCCCACGCCCCTGTCCAG	16	7820	7839	441
588542	2586	2605	Exon 18	CAATCCCACGCCCCTGTCCA	12	7821	7840	442
588543	2587	2606	Exon 18	TCAATCCCACGCCCCTGTCC	26	7822	7841	443
588544	2588	2607	Exon 18	TTCAATCCCACGCCCCTGTC	26	7823	7842	444
588545	2589	2608	Exon 18	ATTCAATCCCACGCCCCTGT	31	7824	7843	445
588546	2590	2609	Exon 18	AATTCAATCCCACGCCCCTG	22	7825	7844	446
588547	2591	2610	Exon 18	TAATTCAATCCCACGCCCCT	12	7826	7845	447
588548	2592	2611	Exon 18	TTAATTCAATCCCACGCCCC	20	7827	7846	448
588549	2593	2612	Exon 18	TTTAATTCAATCCCACGCCC	26	7828	7847	449
588550	2594	2613	Exon 18	TTTTAATTCAATCCCACGCC	32	7829	7848	450
588551	2595	2614	Exon 18	GTTTTAATTCAATCCCACGC	48	7830	7849	451
588552	2596	2615	Exon 18	TGTTTTAATTCAATCCCACG	57	7831	7850	452
588553	2597	2616	Exon 18	CTGTTTTAATTCAATCCCAC	49	7832	7851	453
588554	2598	2617	Exon 18	GCTGTTTTAATTCAATCCCA	64	7833	7852	454
532811	2599	2618	Exon 18	AGCTGTTTTAATTCAATCCC	78	7834	7853	239
588555	2600	2619	Exon 18	CAGCTGTTTTAATTCAATCC	48	7835	7854	455
588556	2601	2620	Exon 18	GCAGCTGTTTTAATTCAATC	55	7836	7855	456
588557	2602	2621	Exon 18	CGCAGCTGTTTTAATTCAAT	51	7837	7856	457
588558	2603	2622	Exon 18	TCGCAGCTGTTTTAATTCAA	51	7838	7857	458
532917	2604	2623	Exon 18	GTCGCAGCTGTTTTAATTCA	82	7839	7858	317
588559	2605	2624	Exon 18	TGTCGCAGCTGTTTTAATTC	58	7840	7859	459
588560	2606	2625	Exon 18	TTGTCGCAGCTGTTTTAATT	72	7841	7860	460
588561	2607	2626	Exon 18	GTTGTCGCAGCTGTTTTAAT	75	7842	7861	461
532952	2608	2627	Exon 18	TGTTGTCGCAGCTGTTTTAA	39	7843	7862	395
588562	2609	2628	Exon 18/ Repeat	TTGTTGTCGCAGCTGTTTTA	53	n/a	n/a	462
588563	2610	2629	Exon 18/ Repeat	TTTGTTGTCGCAGCTGTTTT	62	n/a	n/a	463
588564	2611	2630	Exon 18/ Repeat	TTTTGTTGTCGCAGCTGTTT	63	n/a	n/a	464
588565	2612	2631	Exon 18/ Repeat	TTTTTGTTGTCGCAGCTGTT	64	n/a	n/a	465

Example 8

Dose-Dependent Antisense Inhibition of Human CFB in HepG2 Cells by 5-10-5 MOE Gapmers

[0451] Gapmers from studies described above exhibiting in vitro inhibition of CFB mRNA were selected and tested at various doses in HepG2 cells. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 0.313 μM, 0.625 μM, 1.25 μM, 2.50 μM, 5.00 μM, or 10.00 μM concentrations of antisense oligonucleotide, as specified in the Table below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0452] The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. CFB mRNA levels were reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

TABLE 25

ISIS No	0.313 μM	0.625 μM	1.25 μM	2.50 μM	5.00 μM	10.00 μM	IC_{50} (μM)
532614	7	13	43	72	65	71	2.2
532635	12	0	3	28	0	0	>10
532692	26	0	12	52	55	74	3.7
532770	21	18	32	73	64	88	1.8
532775	8	0	26	35	47	59	6.2
532800	0	5	30	65	50	75	3.1
532809	12	30	28	40	46	66	4.6
532810	28	44	32	69	84	95	1.2
532811	66	83	90	94	97	99	<0.3
532917	64	85	88	96	97	99	<0.3
532952	50	53	68	80	91	94	0.4

Example 9

Dose-Dependent Antisense Inhibition of Human CFB in HepG2 Cells

[0453] Gapmers from studies described above exhibiting in vitro inhibition of CFB mRNA were selected and tested at various doses in HepG2 cells. The antisense oligonucleotides were tested in a number of experiments with similar culture conditions. The results for each experiment are presented in separate tables shown below. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 0.08 μM, 0.25 μM, 0.74 μM, 2.22 μM, 6.67 μM, and 20.00 μM concentrations of antisense oligonucleotide, as specified in the Table below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0454] The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. CFB mRNA levels were reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

TABLE 26

ISIS No	0.08 μM	0.25 μM	0.74 μM	2.22 μM	6.67 μM	20.00 μM	IC_{50} (μM)
532811	19	53	81	87	96	97	0.2
588834	7	42	64	92	98	98	0.5
588835	11	30	66	89	97	97	0.5
588836	14	40	61	91	97	97	0.5
588837	6	39	67	89	96	97	0.5
588838	0	27	41	81	87	97	1.0
588842	17	51	68	86	93	95	0.3
588843	21	38	72	90	95	96	0.4
588870	9	31	56	88	95	97	0.6
588871	14	25	47	79	93	97	0.7
588872	18	28	59	84	92	97	0.6

TABLE 27

ISIS No	0.08 μM	0.25 μM	0.74 μM	2.22 μM	6.67 μM	20.00 μM	IC_{50} μM
532811	31	70	89	94	97	97	0.1
588844	31	60	77	91	95	96	0.1
588846	32	52	78	89	95	97	0.2
588847	22	52	77	91	95	97	0.2
588848	20	40	73	91	96	98	0.3
588851	40	52	82	94	97	97	0.1
588854	17	55	59	84	94	96	0.4
588855	10	32	56	82	93	96	0.6
588856	13	46	75	90	96	97	0.3
588857	11	52	73	94	96	97	0.3
588858	19	48	75	94	97	98	0.3

TABLE 28

ISIS No	0.08 μM	0.25 μM	0.74 μM	2.22 μM	6.67 μM	20.00 μM	IC_{50} μM
532811	42	66	88	96	97	98	0.1
588859	18	46	66	90	96	97	0.4
588860	55	80	94	97	97	97	<0.1
588861	24	61	86	93	96	97	0.2
588862	25	64	85	94	96	98	0.1
588863	50	73	89	96	96	98	<0.1
588864	52	80	92	96	98	98	<0.1
588865	46	72	91	96	96	99	<0.1
588866	47	76	88	96	97	98	<0.1
588867	43	69	83	92	96	99	0.1
588868	43	56	65	84	93	97	0.1

TABLE 29

ISIS No	0.08 μM	0.25 μM	0.74 μM	2.22 μM	6.67 μM	20.00 μM	IC_{50} μM
532810	0	14	38	72	89	96	1.2
532811	18	54	79	93	96	97	0.3
532952	19	34	73	87	94	96	0.4
588534	17	13	44	77	93	97	0.9
588544	12	43	69	86	89	93	0.4
588545	17	55	67	86	91	93	0.3
588546	10	32	67	85	91	93	0.6
588552	27	54	76	90	94	97	0.2
588553	32	68	87	93	95	97	0.1
588560	16	54	76	90	94	96	0.3
588561	18	45	68	85	93	96	0.4

TABLE 30

ISIS No	0.08 μM	0.25 μM	0.74 μM	2.22 μM	6.67 μM	20.00 μM	IC_{50} μM
532811	22	60	82	94	97	98	0.2
588536	2	38	65	90	96	97	0.6
588537	12	38	63	87	94	97	0.5
588547	19	35	61	86	93	97	0.5
588548	19	36	75	88	95	96	0.4
588554	0	76	92	95	97	97	<0.1
588555	31	61	89	96	97	98	0.1
588556	33	56	82	95	94	97	0.1
588562	12	39	71	87	94	97	0.4
588563	25	48	72	86	94	96	0.3
588564	15	33	63	89	91	97	0.5

TABLE 31

ISIS No	0.08 μM	0.25 μM	0.74 μM	2.22 μM	6.67 μM	20.00 μM	IC_{50} μM
532811	39	68	86	96	98	98	0.1
588538	0	40	82	94	97	98	0.3
588539	34	65	88	95	98	98	0.1
588540	30	51	81	91	97	98	0.2
588549	31	57	82	95	96	98	0.1
588550	34	65	88	96	98	98	0.1
588551	47	66	87	96	98	99	<0.1
588557	40	84	95	98	98	98	<0.1
588558	45	73	93	97	98	99	<0.1
588559	51	69	83	96	98	99	<0.1
588565	19	56	81	92	96	98	0.2

Example 10

Dose-Dependent Antisense Inhibition of Human CFB in HepG2 Cells

[0455] Gapmers from studies described above exhibiting in vitro inhibition of CFB mRNA were selected and tested at various doses in HepG2 cells. The antisense oligonucleotides were tested in a number of experiments with similar culture conditions. The results for each experiment are presented in separate tables shown below. Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 0.06 μM, 0.25 μM, 1.00 μM, and 4.00 μM concentrations of antisense oligonucleotide, as specified in the Table below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0456] The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. CFB mRNA levels were reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

TABLE 32

ISIS No	0.06 μM	0.25 μM	1.00 μM	4.00 μM	IC_{50} (μM)
532917	31	58	87	92	0.2
588860	18	50	79	93	0.3
599001	16	28	69	90	0.5
599024	14	32	74	90	0.4

TABLE 32-continued

ISIS No	0.06 μM	0.25 μM	1.00 μM	4.00 μM	IC_{50} (μM)
599025	0	31	56	92	0.7
599032	28	44	62	88	0.3
599033	28	46	80	92	0.2
599077	8	20	59	80	0.8
599080	9	33	48	76	0.9
599086	7	22	53	83	0.8
599087	21	31	74	87	0.4
599088	13	37	69	82	0.5
599089	3	36	55	79	0.7
599093	25	59	79	88	0.2
599094	19	29	75	89	0.4
599095	29	43	67	87	0.3
599096	23	51	70	88	0.3
599149	20	53	82	92	0.3
599188	0	21	62	85	0.8

TABLE 33

ISIS No	0.06 μM	0.25 μM	1.00 μM	4.00 μM	IC_{50} (μM)
532917	0	42	81	91	0.4
588860	17	49	74	92	0.3
599155	29	52	67	87	0.3
599198	3	25	64	89	0.6
599201	13	26	67	91	0.5
599202	0	44	72	87	0.5
599203	22	41	75	88	0.3
599314	12	34	71	84	0.5
599316	7	37	66	88	0.5
599317	8	1	54	83	1.0
599321	8	33	70	85	0.5
599322	24	38	66	87	0.4
599327	22	32	66	89	0.4
599328	0	31	59	88	0.7
599330	5	43	67	84	0.5
599374	23	42	80	91	0.3
599378	21	57	80	93	0.2
599380	23	56	82	93	0.2
599432	17	37	73	93	0.4

TABLE 34

ISIS No	0.06 μM	0.25 μM	1.00 μM	4.00 μM	IC_{50} (μM)
532917	23	65	76	93	0.2
588860	17	60	76	90	0.3
601282	48	68	81	88	0.1
601269	18	59	80	94	0.2
601276	34	64	81	91	0.1
601275	14	39	78	90	0.4
601344	52	84	92	94	<0.06
601383	53	81	86	94	<0.06
601382	41	76	88	94	0.1
601385	52	74	89	91	<0.06
601332	41	69	86	94	0.1
601345	36	75	86	95	0.1
601371	34	72	91	93	0.1
601384	50	78	91	95	<0.06
601380	28	57	83	92	0.2
601387	48	61	82	88	0.1
601341	28	65	83	91	0.2
601346	31	69	82	93	0.1
601335	24	56	85	92	0.2

TABLE 35

ISIS No	0.06 μM	0.25 μM	1.00 μM	4.00 μM	IC_{50} (μM)
532917	31	66	86	93	0.1
588860	28	62	85	94	0.2
599208	24	50	71	89	0.3
599261	31	49	81	94	0.2
599267	41	48	80	88	0.2
599268	28	56	75	92	0.2
599313	14	24	71	92	0.5
599441	24	57	80	87	0.2
599494	13	55	86	94	0.3
599552	30	69	93	95	0.1
599553	34	71	93	96	0.1
599554	30	74	93	96	0.1
599568	40	77	90	97	0.1
599570	61	82	93	96	<0.06
599577	18	62	81	93	0.2
599581	27	60	80	94	0.2
599591	49	74	93	96	<0.06
599592	46	76	90	94	0.1
599593	44	72	91	95	0.1

TABLE 36

ISIS No	0.06 μM	0.25 μM	1.00 μM	4.00 μM	IC_{50} (μM)
532917	25	56	84	92	0.2
588860	11	51	80	92	0.3
599547	23	60	82	90	0.2
599569	42	73	85	88	0.1
599578	29	49	82	89	0.2
599582	21	56	78	91	0.2
599590	24	62	80	90	0.2
601209	21	49	85	88	0.3
601210	34	64	86	92	0.1
601212	46	68	88	90	0.1
601213	54	80	90	92	<0.06
601214	38	77	88	95	0.1
601215	42	64	85	92	0.1
601216	45	57	76	89	0.1
601264	29	58	86	95	0.2
601278	51	82	83	93	<0.06
601279	44	80	92	96	0.1
601280	44	73	87	94	0.1
601281	51	80	91	94	<0.06

Example 11

Dose-Dependent Antisense Inhibition of Human CFB in HepG2 Cells

[0457] Gapmers from studies described above exhibiting in vitro inhibition of CFB mRNA were selected and tested at various doses in HepG2 cells. Additionally, a deoxy, MOE and cEt oligonucleotide, ISIS 594430, was designed with the same sequence (CTCCTTCCGAGTCAGC, SEQ ID NO: 549) and target region (target start site 2195 of SEQ ID NO: 1 and target start site 6983 of SED ID NO: 2) as ISIS 588870, another deoxy, MOE, and cEt oligonucleotide. ISIS 594430 is a 3-10-3 cEt gapmer.

[0458] Cells were plated at a density of 20,000 cells per well and transfected using electroporation with 0.01 μM, 0.04 μM, 0.12 μM, 0.37 μM, 1.11 μM, 3.33 μM, and 10.00 μM concentrations of antisense oligonucleotide, as specified in the Table below. After a treatment period of approximately 16 hours, RNA was isolated from the cells and CFB mRNA levels were measured by quantitative real-time PCR. Human primer probe set RTS3459 was used to measure mRNA levels. CFB mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented as percent inhibition of CFB, relative to untreated control cells.

[0459] The half maximal inhibitory concentration (IC_{50}) of each oligonucleotide is also presented. CFB mRNA levels were reduced in a dose-dependent manner in antisense oligonucleotide treated cells.

TABLE 37

ISIS No	0.01 μM	0.04 μM	0.12 μM	0.37 μM	1.11 μM	3.33 μM	10.00 μM	IC_{50} μM
588536	0	0	0	5	45	73	94	1.4
588548	0	0	0	19	52	78	90	1.2
588553	0	0	9	42	76	85	94	0.6
588555	0	52	23	58	78	83	95	0.3
588847	4	1	18	45	67	84	96	0.5
588848	0	3	13	38	67	83	95	0.6
594430	0	0	10	34	50	55	84	1.4

Example 12

Tolerability of MOE Gapmers Targeting Human CFB in CD1 Mice

[0460] CD1® mice (Charles River, Mass.) are a multipurpose mouse model, frequently utilized for safety and efficacy testing. The mice were treated with ISIS antisense oligonucleotides selected from studies described above and evaluated for changes in the levels of various plasma chemistry markers.

Study 1 (with 5-10-5 MOE gapmers)

[0461] Groups of seven-week old male CD1 mice were injected subcutaneously once a week for 6 weeks with 100 mg/kg of ISIS oligonucleotide. A group of male CD1 mice was injected subcutaneously once a week for 6 weeks with PBS. One group of mice was injected with subcutaneously once a week for 6 weeks with 100 mg/kg of control oligonucleotide ISIS 141923 (CCTTCCCTGAAGGTTCCTCC, designated herein as SEQ ID NO: 809, 5-10-5 MOE gapmer with no known murine target). Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma Chemistry Markers

[0462] To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, and BUN were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). The results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any of the liver or kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 38

Plasma chemistry markers in CD1 mice plasma on day 40

	ALT (IU/L)	AST (IU/L)	BUN (mg/dL)
PBS	25	46	20
ISIS 532614	513	407	22

TABLE 38-continued

Plasma chemistry markers in CD1 mice plasma on day 40

	ALT (IU/L)	AST (IU/L)	BUN (mg/dL)
ISIS 532692	131	130	24
ISIS 532770	36	53	25
ISIS 532775	193	158	23
ISIS 532800	127	110	25
ISIS 532809	36	42	22
ISIS 532810	229	286	26
ISIS 532811	197	183	21
ISIS 532917	207	204	27
ISIS 532952	246	207	25
ISIS 141923	39	67	23

Weights

[0463] Body weights of the mice were measured on day 40 before sacrificing the mice. Weights of organs, liver, kidney, and spleen were also measured after the mice were sacrificed. The results are presented in the Table below. ISIS oligonucleotides that caused changes in the weights outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 39

Weights (g) of CD1 mice on day 40

	Body	Kidney	Liver	Spleen
PBS	44	0.8	2.0	0.1
ISIS 532614	43	0.7	4.3	0.2
ISIS 532692	42	0.7	2.6	0.2
ISIS 532770	42	0.6	2.3	0.2
ISIS 532775	42	0.7	2.5	0.2
ISIS 532800	43	0.6	2.8	0.3
ISIS 532809	42	0.6	2.2	0.1
ISIS 532810	43	0.6	2.3	0.2
ISIS 532811	41	0.7	2.4	0.2
ISIS 532917	42	0.7	3.0	0.2
ISIS 532952	44	0.8	2.5	0.3
ISIS 141923	41	0.6	2.0	0.1

Study 2 (with 5-10-5 MOE Gapmers)

[0464] Groups of six- to eight-week old male CD1 mice were injected subcutaneously once a week for 6 weeks with 100 mg/kg of ISIS oligonucleotide. Two groups of male CD1 mice were injected subcutaneously once a week for 6 weeks with PBS. One group of mice was injected with subcutaneously once a week for 6 weeks with 100 mg/kg of control oligonucleotide ISIS 141923. Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma Chemistry Markers

[0465] To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, albumin, and BUN were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). The results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any of the liver or kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 40

Plasma chemistry markers in CD1 mice plasma on day 45

	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)	BUN (mg/dL)
PBS	39	53	2.9	29
PBS	50	97	2.9	30
ISIS 141923	163	174	4.1	25
ISIS 532810	321	297	2.5	26
ISIS 532952	182	199	2.7	27
ISIS 588534	276	248	2.6	29
ISIS 588536	48	60	2.9	31
ISIS 588537	72	79	4.0	25
ISIS 588538	63	67	4.5	29
ISIS 588539	238	177	3.9	28
ISIS 588545	496	256	4.4	24
ISIS 588547	323	210	4.4	25
ISIS 588548	61	63	4.2	27
ISIS 588549	127	132	4.1	23
ISIS 588551	302	282	4.2	22
ISIS 588552	76	98	4.0	30
ISIS 588558	1066	521	3.9	27
ISIS 588559	76	94	4.1	26
ISIS 588561	502	500	4.4	26
ISIS 588563	50	99	4.4	28

Weights

[0466] Body weights of the mice were measured on day 42. Weights of organs, liver, kidney, and spleen were also measured after the mice were sacrificed on day 45. The results are presented in the Table below. ISIS oligonucleotides that caused changes in the weights outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 41

Weights (g) of CD1 mice on day 40

	Body	Kidney	Liver	Spleen
PBS	44	0.7	2.4	0.1
PBS	43	0.7	2.4	0.2
ISIS 141923	43	0.6	2.4	0.2
ISIS 532810	41	0.6	1.9	0.1
ISIS 532952	43	0.6	2.4	0.2
ISIS 588534	44	0.7	2.8	0.2
ISIS 588536	43	0.7	2.7	0.2
ISIS 588537	43	0.7	2.4	0.2
ISIS 588538	44	0.7	2.8	0.2
ISIS 588539	44	0.6	2.7	0.2
ISIS 588545	44	0.8	3.3	0.3
ISIS 588547	42	0.6	3.3	0.3
ISIS 588548	43	0.6	2.8	0.2
ISIS 588549	42	0.6	2.8	0.3
ISIS 588551	39	0.6	2.2	0.2
ISIS 588552	41	0.6	2.2	0.2
ISIS 588558	44	0.7	3.3	0.3
ISIS 588559	43	0.6	2.7	0.3
ISIS 588561	40	0.7	2.4	0.3
ISIS 588563	41	0.7	2.4	0.2

Study 3 (with 5-10-5 MOE Gapmers)

[0467] Groups of six- to eight-week old male CD1 mice were injected subcutaneously once a week for 6 weeks with 100 mg/kg of ISIS oligonucleotide. Two groups of male CD1 mice were injected subcutaneously once a week for 6 weeks with PBS. Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma Chemistry Markers

[0468] To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, albumin, and BUN were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). The results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any of the liver or kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 42

Plasma chemistry markers in CD1 mice plasma on day 42

	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)	BUN (mg/dL)
PBS	37	108	3.1	30
PBS	45	51	3.0	27
ISIS 588544	209	168	2.9	26
ISIS 588546	526	279	3.0	22
ISIS 588550	82	136	2.7	25
ISIS 588553	79	105	3.0	24
ISIS 588554	112	220	3.2	19
ISIS 588555	95	162	2.8	25
ISIS 588556	345	236	3.0	26
ISIS 588557	393	420	2.8	24
ISIS 588560	109	148	2.7	27
ISIS 588562	279	284	2.8	22
ISIS 588564	152	188	3.0	23
ISIS 588565	247	271	2.8	28

Weights

[0469] Body weights of the mice were measured on day 42. Weights of organs, liver, kidney, and spleen were also measured after the mice were sacrificed on day 42. The results are presented in the Table below. ISIS oligonucleotides that caused changes in the weights outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 43

Weights (g) of CD1 mice on day 40

	Body	Kidney	Liver	Spleen
PBS	42	0.7	2.4	0.1
PBS	41	0.7	2.4	0.2
ISIS 588544	44	0.6	1.9	0.1

TABLE 43-continued

Weights (g) of CD1 mice on day 40

	Body	Kidney	Liver	Spleen
ISIS 588546	43	0.6	2.4	0.2
ISIS 588550	41	0.7	2.8	0.2
ISIS 588553	44	0.7	2.7	0.2
ISIS 588554	40	0.7	2.4	0.2
ISIS 588555	44	0.7	2.8	0.2
ISIS 588556	39	0.6	2.7	0.2
ISIS 588557	41	0.8	3.3	0.3
ISIS 588560	38	0.6	3.2	0.3
ISIS 588562	41	0.6	2.8	0.2
ISIS 588564	40	0.6	2.8	0.3
ISIS 588565	39	0.6	2.2	0.2

Study 4 (with (S) cEt Gapmers and Deoxy, MOE and cEt Oligonucleotides)

[0470] Groups of ten-week old male CD1 mice were injected subcutaneously once a week for 6 weeks with 50 mg/kg of ISIS oligonucleotide from the studies described above. In addition, two oligonucleotides, ISIS 594431 and ISIS 594432, were designed as 3-10-3 cEt gapmers and were also tested in this study. ISIS 594431 (ACCTCCTTC-CGAGTCA, SEQ ID NO: 550) targets the same region as ISIS 588871, a deoxy, MOE and cEt gapmer (target start site 2197 of SEQ ID NO: 1 and target start site 6985 of SEQ ID NO: 2). ISIS 594432 (TGGTCACATTCCCTTC, SEQ ID NO: 542) targets the same region as ISIS 588872 a deoxy, MOE and cEt gapmer (target start site 154 of SEQ ID NO: 1 and target start site 1875 of SEQ ID NO: 2).

[0471] Two groups of male CD1 mice were injected subcutaneously once a week for 6 weeks with PBS. Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma Chemistry Markers

[0472] To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, albumin, creatinine, and BUN were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). The results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any of the liver or kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 44

Plasma chemistry markers in CD1 mice plasma on day 42

	Chemistry	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)	Creatinine (mg/dL)	BUN (mg/dL)
PBS	—	71	77	2.7	0.2	29
PBS	—	30	36	2.7	0.2	26
ISIS 588834	Deoxy, MOE and cEt	436	510	2.8	0.2	25
ISIS 588835	Deoxy, MOE and cEt	70	98	3.0	0.2	27
ISIS 588836	Deoxy, MOE and cEt	442	312	2.7	0.2	27
ISIS 588846	Deoxy, MOE and cEt	50	75	2.5	0.1	28
ISIS 588847	Deoxy, MOE and cEt	44	71	2.6	0.1	24
ISIS 588848	Deoxy, MOE and cEt	47	70	2.4	0.1	27
ISIS 588857	Deoxy, MOE and cEt	1287	655	2.7	0.2	26
ISIS 588858	Deoxy, MOE and cEt	1169	676	2.5	0.2	26
ISIS 588859	Deoxy, MOE and cEt	1036	1300	3.2	0.2	25

TABLE 44-continued

Plasma chemistry markers in CD1 mice plasma on day 42

	Chemistry	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)	Creatinine (mg/dL)	BUN (mg/dL)
ISIS 588861	Deoxy, MOE and cEt	749	466	3.1	0.1	24
ISIS 588862	Deoxy, MOE and cEt	1564	1283	2.9	0.2	22
ISIS 588863	Deoxy, MOE and cEt	477	362	2.8	0.1	23
ISIS 588864	Deoxy, MOE and cEt	118	165	2.9	0.2	27
ISIS 588866	Deoxy, MOE and cEt	843	784	3.2	0.2	25
ISIS 594430	3-10-3 cEt	89	99	2.4	0.1	28
ISIS 594431	3-10-3 cEt	590	433	3.0	0.2	24
ISIS 594432	3-10-3 cEt	2595	2865	2.4	0.1	25

Weights

[0473] Body weights of the mice were measured on day 39. Weights of organs, liver, kidney, and spleen were also measured after the mice were sacrificed on day 42. The results are presented in the Table below. ISIS oligonucleotides that caused changes in the weights outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 45

Weights (g) of CD1 mice

	Chemistry	Body	Kidney	Liver	Spleen
PBS	—	37	0.6	2.1	0.1
PBS	—	45	0.7	2.5	0.2
ISIS 588834	Deoxy, MOE and cEt	40	0.6	3.2	0.2
ISIS 588835	Deoxy, MOE and cEt	38	0.7	2.8	0.3
ISIS 588836	Deoxy, MOE and cEt	41	0.7	2.3	0.2
ISIS 588837	Deoxy, MOE and cEt	38	0.6	2.4	0.3
ISIS 588846	Deoxy, MOE and cEt	39	0.6	2.3	0.2
ISIS 588847	Deoxy, MOE and cEt	40	0.7	2.5	0.2
ISIS 588848	Deoxy, MOE and cEt	43	0.7	2.6	0.3
ISIS 588857	Deoxy, MOE and cEt	39	0.6	3.3	0.2
ISIS 588858	Deoxy, MOE and cEt	37	0.6	3.4	0.2
ISIS 588859	Deoxy, MOE and cEt	41	0.7	2.5	0.3
ISIS 588861	Deoxy, MOE and cEt	39	0.6	2.6	0.4
ISIS 588862	Deoxy, MOE and cEt	34	0.6	2.5	0.4
ISIS 588863	Deoxy, MOE and cEt	40	0.6	2.7	0.3
ISIS 588864	Deoxy, MOE and cEt	40	0.7	2.3	0.2

TABLE 45-continued

Weights (g) of CD1 mice

	Chemistry	Body	Kidney	Liver	Spleen
ISIS 588866	Deoxy, MOE and cEt	45	0.7	3.0	0.2
ISIS 594430	3-10-3 cEt	39	0.6	2.2	0.2
ISIS 594431	3-10-3 cEt	36	0.6	3.2	0.2
ISIS 594432	3-10-3 cEt	31	0.4	1.9	0.1

Study 5 (with MOE Gapmers, (S) cEt Gapmers and Deoxy, MOE and cEt Oligonucleotides)

[0474] Groups of eight- to nine-week old male CD1 mice were injected subcutaneously once a week for 6 weeks with 50 mg/kg of ISIS oligonucleotide. Two groups of male CD1 mice were injected subcutaneously once a week for 6 weeks with PBS. Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma Chemistry Markers

[0475] To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, albumin, creatinine, and BUN were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). The results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any of the liver or kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 46

Plasma chemistry markers in CD1 mice plasma on day 42

	Chemistry	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)	Creatinine (mg/dL)	BUN (mg/dL)
PBS	—	33	84	2.9	0.2	28
PBS	—	32	65	2.5	0.1	27
ISIS 532692	5-10-5 MOE	363	281	3.0	0.2	30
ISIS 532770	5-10-5 MOE	69	100	2.9	0.1	28
ISIS 532775	5-10-5 MOE	371	333	2.6	0.1	29
ISIS 532800	5-10-5 MOE	104	106	2.7	0.1	31
ISIS 532809	5-10-5 MOE	69	127	2.8	0.1	26
ISIS 588540	5-10-5 MOE	66	110	2.8	0.1	26
ISIS 588838	3-10-3 cEt	391	330	2.9	0.1	25
ISIS 588842	Deoxy, MOE and cEt	224	264	2.6	0.1	26
ISIS 588843	3-10-3 cEt	185	160	2.8	0.1	24
ISIS 588844	Deoxy, MOE and cEt	304	204	2.7	0.1	25
ISIS 588851	Deoxy, MOE and cEt	186	123	2.7	0.1	31
ISIS 588854	Deoxy, MOE and cEt	1232	925	2.7	0.1	25
ISIS 588855	Deoxy, MOE and cEt	425	321	2.7	0.1	28
ISIS 588856	Deoxy, MOE and cEt	78	101	2.4	0.1	31
ISIS 588865	Deoxy, MOE and cEt	126	145	2.5	0.1	23
ISIS 588867	Deoxy, MOE and cEt	108	112	2.5	0.1	32

TABLE 46-continued

Plasma chemistry markers in CD1 mice plasma on day 42

	Chemistry	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)	Creatinine (mg/dL)	BUN (mg/dL)
ISIS 588868	Deoxy, MOE and cEt	61	124	2.5	0.1	28
ISIS 588870	Deoxy, MOE and cEt	48	69	2.4	0.1	31
ISIS 588871	Deoxy, MOE and cEt	723	881	2.5	0.1	24
ISIS 588872	Deoxy, MOE and cEt	649	654	2.7	0.1	26

Weights

[0476] Body weights of the mice were measured on day 40. Weights of organs, liver, kidney, and spleen were also measured after the mice were sacrificed on day 42. The results are presented in the Table below. ISIS oligonucleotides that caused changes in the weights outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 47

Weights (g) of CD1 mice

	Chemistry	Body	Kidney	Liver	Spleen
PBS	—	46	0.7	2.3	0.2
PBS	—	44	0.7	2.3	0.2
ISIS 532692	5-10-5 MOE	44	0.6	2.8	0.2
ISIS 532770	5-10-5 MOE	43	0.6	2.2	0.2
ISIS 532775	5-10-5 MOE	43	0.6	2.8	0.2
ISIS 532800	5-10-5 MOE	47	0.7	2.9	0.2
ISIS 532809	5-10-5 MOE	44	0.7	2.6	0.2
ISIS 588540	5-10-5 MOE	44	0.7	2.5	0.2
ISIS 588838	3-10-3 cEt	45	0.7	3.1	0.2
ISIS 588842	Deoxy, MOE and cEt	41	0.6	2.6	0.2
ISIS 588843	3-10-3 cEt	43	0.7	2.9	0.2
ISIS 588844	Deoxy, MOE and cEt	43	0.7	2.8	0.2
ISIS 588851	Deoxy, MOE and cEt	46	0.6	2.6	0.2
ISIS 588854	Deoxy, MOE and cEt	45	0.7	4.1	0.2
ISIS 588855	Deoxy, MOE and cEt	44	0.7	2.9	0.3
ISIS 588856	Deoxy, MOE and cEt	44	0.7	3.2	0.2
ISIS 588865	Deoxy, MOE and cEt	45	0.7	2.6	0.3
ISIS 588867	Deoxy, MOE and cEt	46	0.7	3.2	0.3
ISIS 588868	Deoxy, MOE and cEt	42	0.7	2.9	0.3
ISIS 588870	Deoxy, MOE and cEt	43	0.6	2.2	0.2
ISIS 588871	Deoxy, MOE and cEt	41	0.7	3.1	0.2
ISIS 588872	Deoxy, MOE and cEt	39	0.6	3.2	0.3

Study 6 (with Deoxy, MOE and cEt Oligonucleotides)

[0477] Groups of eight- to nine-week old male CD1 mice were injected subcutaneously once a week for 6 weeks with 50 mg/kg of deoxy, MOE, and cEt oligonucleotides. Two groups of male CD1 mice were injected subcutaneously once a week for 6 weeks with PBS. Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma Chemistry Markers

[0478] To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, albumin, creatinine, bilirubin, and BUN were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). The results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any of the liver or kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 48

Plasma chemistry markers in CD1 mice plasma on day 45

	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)	Creatinine (mg/dL)	Bilirubin (mg/dL)	BUN (mg/dL)
PBS	39	78	3.4	0.2	0.2	31
PBS	37	59	2.9	0.1	0.2	27
ISIS 599552	167	208	3.0	0.1	0.2	32
ISIS 599553	43	86	2.9	0.1	0.2	28
ISIS 599554	57	101	2.2	0.2	0.2	31
ISIS 599569	469	530	3.5	0.2	0.3	27
ISIS 599577	37	84	2.9	0.1	0.1	31
ISIS 599578	45	104	2.8	0.1	0.2	30
ISIS 599581	54	88	3.1	0.1	0.2	31
ISIS 599590	1741	1466	3.1	0.1	0.3	25
ISIS 599591	2230	1183	3.2	0.1	0.3	27
ISIS 601209	68	104	2.9	0.1	0.2	30
ISIS 601212	1795	968	3.2	0.1	0.3	22
ISIS 601215	424	385	3.1	0.1	0.4	25
ISIS 601216	90	125	2.9	0.1	0.2	29
ISIS 601276	946	366	2.9	0.1	0.5	31
ISIS 601282	831	540	3.3	0.2	0.2	32

Weights

[0479] Body weights of the mice were measured on day 40. Weights of organs, liver, kidney, and spleen were also measured after the mice were sacrificed on day 45. The results are presented in the Table below. ISIS oligonucleotides that caused changes in the weights outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 49

Weights (g) of CD1 mice

	Body	Kidney	Liver	Spleen
PBS	40	0.7	2.1	0.2
PBS	42	0.8	2.3	0.2
ISIS 599552	38	0.6	2.3	0.2
ISIS 599553	39	0.7	2.2	0.2
ISIS 599554	39	0.7	2.4	0.2
ISIS 599569	39	0.7	2.2	0.2
ISIS 599577	41	0.7	2.5	0.2
ISIS 599578	37	0.6	2.0	0.2
ISIS 599581	40	0.6	2.5	0.2
ISIS 599590	34	0.6	3.5	0.2
ISIS 599591	38	0.8	2.7	0.2
ISIS 601209	42	0.7	2.6	0.3
ISIS 601212	38	0.6	2.9	0.2
ISIS 601215	36	0.7	2.6	0.2
ISIS 601216	42	0.6	2.7	0.2
ISIS 601276	42	0.7	3.2	0.2
ISIS 601282	38	0.7	3.2	0.2

Study 7 (with MOE Gapmers and Deoxy, MOE and cEt Oligonucleotides)

[0480] Groups of eight- to nine-week old male CD1 mice were injected subcutaneously once a week for 6 weeks with 100 mg/kg of ISIS oligonucleotides. One group of male CD1 mice was injected subcutaneously once a week for 6 weeks with PBS. Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma Chemistry Markers

[0481] To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, albumin, creatinine, and BUN were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). The results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any of the liver or kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 50

Plasma chemistry markers in CD1 mice plasma on day 45

	Chemistry	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)	Creatinine (mg/dL)	BUN (mg/dL)
PBS	—	120	102	2.7	0.2	26
ISIS 588842	Deoxy, MOE and cEt	177	164	2.7	0.1	23
ISIS 588843	Deoxy, MOE and cEt	98	194	2.7	0.1	24
ISIS 588851	Deoxy, MOE and cEt	91	142	2.6	0.1	23
ISIS 588856	Deoxy, MOE and cEt	78	110	2.7	0.1	23
ISIS 599024	3-10-4 MOE	91	108	2.7	0.1	23
ISIS 599087	5-7-5 MOE	198	183	2.6	0.2	28
ISIS 599093	5-7-5 MOE	3285	2518	2.6	0.2	24
ISIS 599149	4-8-5 MOE	30	64	2.9	0.2	25
ISIS 599155	4-8-5 MOE	145	189	2.6	0.2	25
ISIS 599202	5-8-5 MOE	150	128	2.8	0.2	23
ISIS 599203	5-8-5 MOE	111	127	2.8	0.2	24
ISIS 599208	5-8-5 MOE	146	178	2.9	0.2	22
ISIS 599261	3-10-5 MOE	144	165	2.8	0.2	26
ISIS 599267	3-10-5 MOE	96	132	2.6	0.2	27
ISIS 599268	3-10-5 MOE	87	115	2.6	0.1	23
ISIS 599322	6-7-6 MOE	115	138	2.7	0.1	22
ISIS 599374	5-9-5 MOE	375	271	2.6	0.1	21
ISIS 599378	5-9-5 MOE	77	99	2.7	0.1	23
ISIS 599441	6-8-6 MOE	150	250	2.9	0.1	23

Weights

[0482] Body weights of the mice were measured on day 44. Weights of organs, liver, kidney, and spleen were also measured after the mice were sacrificed on day 49. The results are presented in the Table below. ISIS oligonucleotides that caused changes in the weights outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 51

Weights (g) of CD1 mice

	Chemistry	Body	Kidney	Liver	Spleen
PBS	—	39	0.6	1.9	0.1
ISIS 588842	Deoxy, MOE and cEt	38	0.5	2.1	0.1
ISIS 588843	Deoxy, MOE and cEt	41	0.6	2.4	0.2
ISIS 588851	Deoxy, MOE and cEt	42	0.6	2.2	0.2
ISIS 588856	Deoxy, MOE and cEt	42	0.7	2.6	0.2
ISIS 599024	3-10-4 MOE	41	0.6	4.0	0.2
ISIS 599087	5-7-5 MOE	44	0.8	2.6	0.3

TABLE 51-continued

Weights (g) of CD1 mice

	Chemistry	Body	Kidney	Liver	Spleen
ISIS 599093	5-7-5 MOE	39	0.6	2.3	0.2
ISIS 599149	4-8-5 MOE	42	0.7	2.8	0.2
ISIS 599155	4-8-5 MOE	41	0.7	2.1	0.2
ISIS 599202	5-8-5 MOE	43	0.6	2.6	0.2
ISIS 599203	5-8-5 MOE	42	0.6	2.6	0.2
ISIS 599208	5-8-5 MOE	40	0.6	2.1	0.2
ISIS 599261	3-10-5 MOE	39	0.7	3.4	0.3
ISIS 599267	3-10-5 MOE	42	0.8	2.5	0.3
ISIS 599268	3-10-5 MOE	41	0.7	2.1	0.2
ISIS 599322	6-7-6 MOE	43	0.6	2.2	0.2
ISIS 599374	5-9-5 MOE	37	0.6	2.2	0.2
ISIS 599378	5-9-5 MOE	43	0.7	2.7	0.2
ISIS 599441	6-8-6 MOE	42	0.6	2.5	0.3

Study 8 (with MOE Gapmers, Deoxy, MOE and cEt Oligonucleotides, and cEt Gapmers)

[0483] Groups of eight- to nine-week old male CD1 mice were injected subcutaneously once a week for 6 weeks with 100 mg/kg of MOE gapmers, or 50 mg/kg of deoxy, MOE and cEt oligonucleotides or cEt gapmers. One group of male CD1 mice was injected subcutaneously once a week for 6 weeks with PBS. Mice were euthanized 48 hours after the last dose, and organs and plasma were harvested for further analysis.

Plasma Chemistry Markers

[0484] To evaluate the effect of ISIS oligonucleotides on liver and kidney function, plasma levels of transaminases, albumin, creatinine, and BUN were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). The results are presented in the Table below.

TABLE 52

Plasma chemistry markers in CD1 mice plasma on day 43

	Chemistry	Dose (mg/kg/wk)	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)	Creatinine (mg/dL)	BUN (mg/dL)
PBS	—	—	37	57	2.5	0.08	26
ISIS 532770	5-10-5 MOE	100	57	73	2.5	0.07	24
ISIS 532800	5-10-5 MOE	100	74	126	2.8	0.10	26
ISIS 532809	5-10-5 MOE	100	83	73	2.5	0.07	23
ISIS 588540	5-10-5 MOE	100	106	102	2.7	0.09	27
ISIS 588544	5-10-5 MOE	100	66	62	2.6	0.10	24
ISIS 588548	5-10-5 MOE	100	48	67	2.6	0.08	23
ISIS 588550	5-10-5 MOE	100	65	106	2.5	0.10	25
ISIS 588553	5-10-5 MOE	100	78	90	2.6	0.09	25
ISIS 588555	5-10-5 MOE	100	94	89	2.5	0.08	23
ISIS 588848	Deoxy, MOE and cEt	50	38	54	2.3	0.07	25
ISIS 594430	3-10-3 cEt	50	63	72	2.5	0.10	27

Weights

[0485] Body weights of the mice were measured on day 36. Weights of organs, liver, kidney, and spleen were also measured after the mice were sacrificed on day 43. The results for the organ weights were expressed as a ratio to the body weights and normalized to the PBS control ratio.

TABLE 53

Organ Weights/Body weight (BW) of CD1 mice

	Chemistry	Dose (mg/kg/wk)	Kidney/ BW	Liver/ BW	Spleen/ BW
PBS	—	—	1.0	1.0	1.0
ISIS 532770	5-10-5 MOE	100	1.4	1.1	1.0
ISIS 532800	5-10-5 MOE	100	1.5	1.1	0.9
ISIS 532809	5-10-5 MOE	100	1.3	1.2	0.9
ISIS 588540	5-10-5 MOE	100	1.3	1.2	1.0
ISIS 588544	5-10-5 MOE	100	1.6	1.1	1.0

TABLE 53-continued

Organ Weights/Body weight (BW) of CD1 mice

	Chemistry	Dose (mg/kg/wk)	Kidney/ BW	Liver/ BW	Spleen/ BW
ISIS 588548	5-10-5 MOE	100	1.7	1.2	1.0
ISIS 588550	5-10-5 MOE	100	1.5	1.2	1.0
ISIS 588553	5-10-5 MOE	100	1.5	1.0	0.8
ISIS 588555	5-10-5 MOE	100	1.8	1.2	1.0
ISIS 588848	Deoxy, MOE and cEt	50	1.3	1.0	0.9
ISIS 594430	3-10-3 cEt	50	1.4	1.1	0.9

Cytokine Assays

[0486] Blood obtained from all mice groups were sent to Antech Diagnostics for measurements of the various cytokine levels, such as IL-6, MDC, MIP1β, IP-10, MCP1, MIP-1α, and RANTES. The results are presented in Table 54.

TABLE 54

Cytokine levels (pg/mL) in CD1 mice plasma

	Chemistry	IL-6	MDC	MIP1β	IP-10	MCP1	MIP-1α	RANTES
PBS	—	70	16	23	20	17	6	2
ISIS 532770	5-10-5 MOE	101	18	146	116	101	24	6
ISIS 532800	5-10-5 MOE	78	17	83	53	105	1	3
ISIS 532809	5-10-5 MOE	66	19	60	32	55	20	4
ISIS 588540	5-10-5 MOE	51	18	126	70	75	4	3
ISIS 588544	5-10-5 MOE	157	14	94	34	102	1	3
ISIS 588548	5-10-5 MOE	164	12	90	66	84	10	4
ISIS 588550	5-10-5 MOE	58	21	222	124	157	3	5
ISIS 588553	5-10-5 MOE	62	14	183	60	103	9	4
ISIS 588555	5-10-5 MOE	70	19	172	171	178	16	9
ISIS 588848	Deoxy, MOE and cEt	59	13	61	27	63	12	4
ISIS 594430	3-10-3 cEt	48	14	56	38	85	10	3

Hematology Assays

[0487] Blood obtained from all mice groups were sent to Antech Diagnostics for measurements of hematocrit (HCT), as well as of the various blood cells, such as WBC, RBC, and platelets, and total hemoglobin (Hb) content. The results are presented in Table 55.

TABLE 55

Hematology markers in CD1 mice plasma

	Chemistry	HCT (%)	Hb (g/dL)	WBC (10^3/μL)	RBC (10^6/μL)	Platelets (10^3/μL)
PBS	—	46	15	7	9	960
ISIS 532770	5-10-5 MOE	45	14	5	9	879
ISIS 532800	5-10-5 MOE	45	14	5	9	690
ISIS 532809	5-10-5 MOE	46	14	6	9	1005
ISIS 588540	5-10-5 MOE	49	15	6	10	790
ISIS 588544	5-10-5 MOE	36	11	7	7	899
ISIS 588548	5-10-5 MOE	46	14	6	9	883
ISIS 588550	5-10-5 MOE	42	13	8	8	721
ISIS 588553	5-10-5 MOE	45	14	6	9	719
ISIS 588555	5-10-5 MOE	43	13	8	9	838
ISIS 588848	Deoxy, MOE and cEt	40	15	8	10	840
ISIS 594430	3-10-3 cEt	45	14	8	9	993

Example 13

Tolerability of Antisense Oligonucleotides Targeting Human CFB in Sprague-Dawley Rats

[0488] Sprague-Dawley rats are a multipurpose model used for safety and efficacy evaluations. The rats were treated with ISIS antisense oligonucleotides from the studies described in the Examples above and evaluated for changes in the levels of various plasma chemistry markers.

Study 1 (with 5-10-5 MOE Gapmers)

[0489] Male Sprague-Dawley rats, seven- to eight-week old, were maintained on a 12-hour light/dark cycle and fed ad libitum with Purina normal rat chow, diet 5001. Groups of 4 Sprague-Dawley rats each were injected subcutaneously once a week for 6 weeks with 100 mg/kg of 5-10-5 MOE gapmers. One control group of 6 rats was injected subcutaneously once a week for 6 weeks with PBS. Forty eight hours after the last dose, rats were euthanized and organs and plasma were harvested for further analysis.

Liver Function

[0490] To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma levels of transaminases were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Plasma levels of ALT (alanine transaminase) and AST (aspartate transaminase) were measured and the results are presented in the Table below expressed in IU/L. ISIS oligonucleotides that caused changes in the levels of any markers of liver function outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 56

Liver function markers in Sprague-Dawley rats

	ALT (IU/L)	AST (IU/L)
PBS	66	134
ISIS 588544	101	329
ISIS 588550	69	157
ISIS 588553	88	304
ISIS 588554	202	243
ISIS 588555	94	113
ISIS 588556	102	117
ISIS 588560	206	317
ISIS 588564	292	594

Kidney Function

[0491] To evaluate the effect of ISIS oligonucleotides on kidney function, plasma levels of blood urea nitrogen (BUN) and creatinine were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Results are presented in the Table below, expressed in mg/dL. ISIS oligonucleotides that caused changes in the levels of any of the kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 57

Kidney function markers (mg/dL) in Sprague-Dawley rats

	BUN	Creatinine
PBS	18	3.5
ISIS 588544	21	3.1
ISIS 588550	21	3.0
ISIS 588553	22	2.8
ISIS 588554	23	3.0
ISIS 588555	22	3.5
ISIS 588556	21	3.2
ISIS 588560	26	2.4
ISIS 588564	24	2.7

Weights

[0492] Body weight measurements were taken on day 39. Liver, heart, spleen and kidney weights were measured at the end of the study on day 42, and are presented in the Table below. ISIS oligonucleotides that caused any changes in organ weights outside the expected range for antisense oligonucleotides were excluded from further studies.

TABLE 58

Weights (g)

	Body	Liver	Spleen	Kidney
PBS	422	16	1.2	3.9
ISIS 588544	353	15	1.7	2.9
ISIS 588550	321	14	2.1	3.2
ISIS 588553	313	15	2.3	3.2
ISIS 588554	265	11	1.6	2.7
ISIS 588555	345	14	1.4	3.3

TABLE 58-continued

	Weights (g)			
	Body	Liver	Spleen	Kidney
ISIS 588556	328	13	1.7	3.1
ISIS 588560	270	13	2.4	3.0
ISIS 588564	253	12	2.9	3.0

Study 2 (with Deoxy, MOE and cEt Oligonucleotides)

[0493] Male Sprague-Dawley rats, nine- to ten-week old, were maintained on a 12-hour light/dark cycle and fed ad libitum with Purina normal rat chow, diet 5001. Groups of 4 Sprague-Dawley rats each were injected subcutaneously once a week for 6 weeks with 100 mg/kg of deoxy, MOE, and cEt oligonucleotides. Two control groups of 3 rats each were injected subcutaneously once a week for 6 weeks with PBS. Forty eight hours after the last dose, rats were euthanized and organs and plasma were harvested for further analysis.

Liver Function

[0494] To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma levels of transaminases were measured on day 42 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Plasma levels of ALT (alanine transaminase) and AST (aspartate transaminase), and albumin were measured and the results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any markers of liver function outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 59

Liver function markers in Sprague-Dawley rats			
	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)
PBS	55	150	3.4
PBS	64	91	3.5
ISIS 588554	52	92	3.2
ISIS 588835	971	844	4.1
ISIS 588842	317	359	3.8
ISIS 588843	327	753	2.9
ISIS 588846	70	111	3.2
ISIS 588847	65	100	3.0
ISIS 588864	91	109	3.0
ISIS 594430	85	106	3.7

Kidney Function

[0495] To evaluate the effect of ISIS oligonucleotides on kidney function, plasma levels of blood urea nitrogen (BUN) and creatinine were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Results are presented in the Table below, expressed in mg/dL. ISIS oligonucleotides that caused changes in the levels of any of the kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 60

Kidney function markers (mg/dL) in Sprague-Dawley rats		
	BUN	Creatinine
PBS	17	0.4
PBS	21	0.4
ISIS 588554	20	0.4
ISIS 588835	23	0.5
ISIS 588842	22	0.4
ISIS 588843	51	0.4
ISIS 588846	25	0.5
ISIS 588847	23	0.5
ISIS 588864	23	0.4
ISIS 594430	22	0.5

Weights

[0496] Body weight measurements were taken on day 39. Liver, heart, spleen and kidney weights were measured at the end of the study on day 42, and are presented in the Table below. ISIS oligonucleotides that caused any changes in organ weights outside the expected range for antisense oligonucleotides were excluded from further studies.

TABLE 61

Weights (g)				
	Body	Liver	Spleen	Kidney
PBS	466	16	0.9	3.8
PBS	485	16	0.9	3.6
ISIS 588554	393	15	2.3	2.6
ISIS 588835	387	16	1.0	3.3
ISIS 588842	414	22	1.5	3.7
ISIS 588843	427	20	2.5	4.2
ISIS 588846	366	16	2.1	3.3
ISIS 588847	402	15	1.6	3.1
ISIS 588864	364	15	2.1	3.8
ISIS 594430	420	16	1.2	3.6

Study 3 (with MOE Gapmers)

[0497] Male Sprague-Dawley rats, nine- to ten-week old, were maintained on a 12-hour light/dark cycle and fed ad libitum with Purina normal rat chow, diet 5001. Groups of 4 Sprague-Dawley rats each were injected subcutaneously once a week for 6 weeks with 100 mg/kg of MOE gapmers. One control group of 6 rats was injected subcutaneously once a week for 6 weeks with PBS. Forty eight hours after the last dose, rats were euthanized and organs and plasma were harvested for further analysis.

Liver Function

[0498] To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma levels of transaminases were measured on day 43 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Plasma levels of ALT (alanine transaminase) and AST (aspartate transaminase) were measured and the results are presented in the Table below expressed in IU/L. ISIS oligonucleotides that caused changes in the levels of any markers of liver function outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 62

Liver function markers in Sprague-Dawley rats

	Chemistry	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)
PBS	—	52	110	3.7
ISIS 588563	5-10-5 MOE	175	291	2.9
ISIS 599024	3-10-4 MOE	139	173	1.4
ISIS 599093	5-7-5 MOE	116	238	2.6
ISIS 599149	4-8-5 MOE	232	190	3.4
ISIS 599155	4-8-5 MOE	108	215	2.5
ISIS 599202	5-8-5 MOE	65	86	3.5
ISIS 599203	5-8-5 MOE	71	97	3.1
ISIS 599208	5-8-5 MOE	257	467	1.9
ISIS 599261	3-10-5 MOE	387	475	1.5
ISIS 599267	3-10-5 MOE	201	337	2.7

Kidney Function

[0499] To evaluate the effect of ISIS oligonucleotides on kidney function, plasma levels of blood urea nitrogen (BUN) and creatinine were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Results are presented in the Table below, expressed in mg/dL. ISIS oligonucleotides that caused changes in the levels of any of the kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 63

Kidney function markers (mg/dL) in Sprague-Dawley rats

	Chemistry	BUN	Creatinine
PBS	—	16	0.3
ISIS 588563	5-10-5 MOE	26	0.4
ISIS 599024	3-10-4 MOE	135	1.2
ISIS 599093	5-7-5 MOE	29	0.4
ISIS 599149	4-8-5 MOE	23	0.4
ISIS 599155	4-8-5 MOE	29	0.4
ISIS 599202	5-8-5 MOE	19	0.4
ISIS 599203	5-8-5 MOE	22	0.4
ISIS 599208	5-8-5 MOE	26	0.3
ISIS 599261	3-10-5 MOE	228	1.6
ISIS 599267	3-10-5 MOE	24	0.4

Weights

[0500] Body weight measurements were taken on day 39. Liver, heart, spleen and kidney weights were measured at the end of the study on day 42, and are presented in the Table below. ISIS oligonucleotides that caused any changes in organ weights outside the expected range for antisense oligonucleotides were excluded from further studies.

TABLE 64

Weights (g)

	Chemistry	Body	Liver	Spleen	Kidney
PBS	—	471	16	1.0	4.1
ISIS 588563	5-10-5 MOE	311	16	3.4	4.1
ISIS 599024	3-10-4 MOE	297	11	1.0	3.5
ISIS 599093	5-7-5 MOE	332	18	4.1	5.0
ISIS 599149	4-8-5 MOE	388	16	2.3	3.7
ISIS 599155	4-8-5 MOE	290	15	2.9	4.5

TABLE 64-continued

Weights (g)

	Chemistry	Body	Liver	Spleen	Kidney
ISIS 599202	5-8-5 MOE	359	13	1.3	3.2
ISIS 599203	5-8-5 MOE	334	14	1.8	3.3
ISIS 599208	5-8-5 MOE	353	29	4.7	4.6
ISIS 599261	3-10-5 MOE	277	10	0.9	3.2
ISIS 599267	3-10-5 MOE	344	21	3.9	4.7

Study 4 (with MOE Gapmers)

[0501] Male Sprague-Dawley rats, nine- to ten-week old, were maintained on a 12-hour light/dark cycle and fed ad libitum with Purina normal rat chow, diet 5001. Groups of 4 Sprague-Dawley rats each were injected subcutaneously once a week for 6 weeks with 100 mg/kg of MOE gapmers. One control group of 6 rats was injected subcutaneously once a week for 6 weeks with PBS. Forty eight hours after the last dose, rats were euthanized and organs and plasma were harvested for further analysis.

Liver Function

[0502] To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma levels of transaminases were measured on day 42 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Plasma levels of ALT (alanine transaminase) and AST (aspartate transaminase) were measured and the results are presented in the Table below expressed in IU/L. ISIS oligonucleotides that caused changes in the levels of any markers of liver function outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 65

Liver function markers in Sprague-Dawley rats

	Chemistry	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)
PBS	—	48	77	3.9
ISIS 532800	5-10-5 MOE	72	111	3.4
ISIS 532809	5-10-5 MOE	59	89	3.8
ISIS 588540	5-10-5 MOE	146	259	3.8
ISIS 599268	3-10-5 MOE	175	206	2.7
ISIS 599322	6-7-6 MOE	523	567	3.3
ISIS 599374	5-9-5 MOE	114	176	3.0
ISIS 599378	5-9-5 MOE	124	116	3.2
ISIS 599380	5-9-5 MOE	148	210	3.4
ISIS 599441	6-8-6 MOE	51	91	2.6

Kidney Function

[0503] To evaluate the effect of ISIS oligonucleotides on kidney function, plasma levels of blood urea nitrogen (BUN) and creatinine were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Results are presented in the Table below, expressed in mg/dL. ISIS oligonucleotides that caused changes in the levels of any of the kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 66

Kidney function markers (mg/dL) in Sprague-Dawley rats

	Chemistry	BUN	Creatinine
PBS	—	15	0.4
ISIS 532800	5-10-5 MOE	26	0.5
ISIS 532809	5-10-5 MOE	18	0.5
ISIS 588540	5-10-5 MOE	22	0.5
ISIS 599268	3-10-5 MOE	28	0.5
ISIS 599322	6-7-6 MOE	24	0.5
ISIS 599374	5-9-5 MOE	29	0.5
ISIS 599378	5-9-5 MOE	22	0.4
ISIS 599380	5-9-5 MOE	26	0.5
ISIS 599441	6-8-6 MOE	24	0.4

Weights

[0504] Body weight measurements were taken on day 39. Liver, heart, spleen and kidney weights were measured at the end of the study on day 42, and are presented in the Table below. ISIS oligonucleotides that caused any changes in organ weights outside the expected range for antisense oligonucleotides were excluded from further studies.

TABLE 67

Weights (g)

	Chemistry	Body	Liver	Spleen	Kidney
PBS	—	502	16	0.9	3.7
ISIS 532800	5-10-5 MOE	376	16	2.0	3.4
ISIS 532809	5-10-5 MOE	430	16	1.4	3.4
ISIS 588540	5-10-5 MOE	391	16	1.8	3.5
ISIS 599268	3-10-5 MOE	332	16	3.6	3.6
ISIS 599322	6-7-6 MOE	348	13	2.1	3.4
ISIS 599374	5-9-5 MOE	302	12	2.0	3.3
ISIS 599378	5-9-5 MOE	332	11	1.1	2.8
ISIS 599380	5-9-5 MOE	350	11	1.5	3.3
ISIS 599441	6-8-6 MOE	368	16	2.5	3.3

Study 5 (with MOE Gapmers and Deoxy, MOE and cEt Oligonucleotides)

[0505] Male Sprague-Dawley rats, nine- to ten-week old, were maintained on a 12-hour light/dark cycle and fed ad libitum with Purina normal rat chow, diet 5001. Groups of 4 Sprague-Dawley rats each were injected subcutaneously once a week for 6 weeks with 100 mg/kg of MOE gapmer or with 50 mg/kg of deoxy, MOE and cEt oligonucleotides. One control group of 4 rats was injected subcutaneously once a week for 6 weeks with PBS. Forty eight hours after the last dose, rats were euthanized and organs and plasma were harvested for further analysis.

Liver Function

[0506] To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma levels of transaminases were measured on day 42 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Plasma levels of ALT (alanine transaminase) and AST (aspartate transaminase) were measured and the results are presented in the Table below expressed in IU/L. ISIS oligonucleotides that caused changes in the levels of any markers of liver function outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 68

Liver function markers in Sprague-Dawley rats

	Chemistry	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)
PBS	—	49	74	3.3
ISIS 532770	5-10-5 MOE	95	132	3.3
ISIS 588851	Deoxy, MOE, and cEt	47	72	3.1
ISIS 588856	Deoxy, MOE, and cEt	56	75	3.0
ISIS 588865	Deoxy, MOE, and cEt	62	84	2.9
ISIS 588867	Deoxy, MOE, and cEt	73	214	2.9
ISIS 588868	Deoxy, MOE, and cEt	59	83	3.1
ISIS 588870	Deoxy, MOE, and cEt	144	144	3.4

Kidney Function

[0507] To evaluate the effect of ISIS oligonucleotides on kidney function, plasma and urine levels of blood urea nitrogen (BUN) and creatinine were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Results are presented in the Tables below, expressed in mg/dL. ISIS oligonucleotides that caused changes in the levels of any of the kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 69

Kidney function markers (mg/dL) in the plasma of Sprague-Dawley rats

	Chemistry	BUN	Creatinine
PBS	—	18	0.3
ISIS 532770	5-10-5 MOE	20	0.4
ISIS 588851	Deoxy, MOE, and cEt	20	0.4
ISIS 588856	Deoxy, MOE, and cEt	22	0.4
ISIS 588865	Deoxy, MOE, and cEt	24	0.5
ISIS 588867	Deoxy, MOE, and cEt	22	0.4
ISIS 588868	Deoxy, MOE, and cEt	19	0.4
ISIS 588870	Deoxy, MOE, and cEt	20	0.5

TABLE 70

Kidney function markers (mg/dL) in the urine of Sprague-Dawley rats

	Chemistry	Total protein	Creatinine
PBS	—	80	92
ISIS 532770	5-10-5 MOE	466	69
ISIS 588851	Deoxy, MOE, and cEt	273	64
ISIS 588856	Deoxy, MOE, and cEt	259	68
ISIS 588865	Deoxy, MOE, and cEt	277	67
ISIS 588867	Deoxy, MOE, and cEt	337	68
ISIS 588868	Deoxy, MOE, and cEt	326	75
ISIS 588870	Deoxy, MOE, and cEt	388	82

Weights

[0508] Body weight measurements were taken on day 39. Liver, heart, spleen and kidney weights were measured at the end of the study on day 42, and are presented in the Table below. ISIS oligonucleotides that caused any changes in organ weights outside the expected range for antisense oligonucleotides were excluded from further studies.

TABLE 71

Weights (g)

	Chemistry	Body	Liver	Spleen	Kidney
PBS	—	489	16	0.9	3.5
ISIS 532770	5-10-5 MOE	372	15	1.7	3.1
ISIS 588851	Deoxy, MOE, and cEt	285	14	1.4	3.2
ISIS 588856	Deoxy, MOE, and cEt	415	15	1.1	3.3
ISIS 588865	Deoxy, MOE, and cEt	362	14	2.0	3.3
ISIS 588867	Deoxy, MOE, and cEt	406	15	2.4	3.4
ISIS 588868	Deoxy, MOE, and cEt	399	15	1.5	3.4
ISIS 588870	Deoxy, MOE, and cEt	446	14	1.4	3.3

Study 6 (with MOE Gapmers, Deoxy, MOE and cEt Oligonucleotides, and cEt Gapmers)

[0509] Male rats were maintained on a 12-hour light/dark cycle and fed ad libitum with Purina normal rat chow, diet 5001. Groups of 4 rats each were injected subcutaneously once a week for 6 weeks with 100 mg/kg of MOE gapmers or with 50 mg/kg of deoxy, MOE and cEt oligonucleotide or cEt gapmer. One control group of 4 rats was injected subcutaneously once a week for 6 weeks with PBS. Forty eight hours after the last dose, rats were euthanized and organs and plasma were harvested for further analysis.

Liver Function

[0510] To evaluate the effect of ISIS oligonucleotides on hepatic function, plasma levels of transaminases were measured on day 42 using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Plasma levels of ALT (alanine transaminase) and AST (aspartate transaminase) were measured and the results are presented in the Table below expressed in IU/L.

TABLE 72

Liver function markers

	Chemistry	Dose (mg/kg/wk)	ALT (IU/L)	AST (IU/L)	Albumin (g/dL)
PBS	—	—	54	73	4.3
ISIS 532770	5-10-5 MOE	100	57	114	4.4
ISIS 532800	5-10-5 MOE	100	176	180	4.3
ISIS 532809	5-10-5 MOE	100	71	132	4.1
ISIS 588540	5-10-5 MOE	100	89	202	4.4
ISIS 588544	5-10-5 MOE	100	75	152	3.9
ISIS 588548	5-10-5 MOE	100	50	71	4.1
ISIS 588550	5-10-5 MOE	100	80	133	3.6
ISIS 588553	5-10-5 MOE	100	59	112	3.9
ISIS 588555	5-10-5 MOE	100	97	142	3.8
ISIS 588848	Deoxy, MOE and cEt	50	53	82	3.9
ISIS 594430	3-10-3 cEt	50	198	172	4.4

Kidney Function

[0511] To evaluate the effect of ISIS oligonucleotides on kidney function, urine levels of total protein and creatinine were measured using an automated clinical chemistry analyzer (Hitachi Olympus AU400e, Melville, N.Y.). Results are presented in the Table below. ISIS oligonucleotides that caused changes in the levels of any of the kidney function markers outside the expected range for antisense oligonucleotides were excluded in further studies.

TABLE 73

Total protein/creatinine ratio in the urine of rats

	Chemistry	Dose (mg/kg/wk)	P/C ratio
PBS	—	—	1.1
ISIS 532770	5-10-5 MOE	100	8.3
ISIS 532800	5-10-5 MOE	100	6.5
ISIS 532809	5-10-5 MOE	100	6.1
ISIS 588540	5-10-5 MOE	100	10.1
ISIS 588544	5-10-5 MOE	100	7.9
ISIS 588548	5-10-5 MOE	100	6.6
ISIS 588550	5-10-5 MOE	100	7.6
ISIS 588553	5-10-5 MOE	100	7.0
ISIS 588555	5-10-5 MOE	100	6.2
ISIS 588848	Deoxy, MOE and cEt	50	5.2
ISIS 594430	3-10-3 cEt	50	5.3

Weights

[0512] Body weight measurements were taken on day 39. Liver, heart, spleen and kidney weights were measured at the end of the study on day 42, and are presented in the Table below. The results for the organ weights were expressed as a ratio to the body weights and normalized to the PBS control ratio.

TABLE 74

Organ weights/Body weight (BW) ratios

	Chemistry	Dose (mg/kg/wk)	Spleen/ BW	Liver/ BW	Kidney/ BW
PBS	—	—	1.0	1.0	1.0
ISIS 532770	5-10-5 MOE	100	2.0	1.2	1.0
ISIS 532800	5-10-5 MOE	100	2.8	1.3	1.0
ISIS 532809	5-10-5 MOE	100	2.2	1.1	1.0
ISIS 588540	5-10-5 MOE	100	2.2	1.4	1.0
ISIS 588544	5-10-5 MOE	100	2.5	1.3	1.1
ISIS 588548	5-10-5 MOE	100	2.1	1.3	1.1
ISIS 588550	5-10-5 MOE	100	3.9	1.4	1.1
ISIS 588553	5-10-5 MOE	100	4.1	1.4	1.4
ISIS 588555	5-10-5 MOE	100	1.8	1.3	1.0
ISIS 588848	Deoxy, MOE and cEt	50	3.1	1.3	1.1
ISIS 594430	3-10-3 cEt	50	1.7	1.0	1.1

Example 14

Efficacy of Antisense Oligonucleotides Against CFB mRNA in hCFB Transgenic Mice

[0513] Selected compounds were tested for efficacy in human CFB transgenic mice, founder line #6. The human CFB gene is located on chromosome 6: position 31913721-31919861. A Fosmid (ABC14-50933200C23) containing the CFB sequence was selected to make transgenic mice expressing the human CFB gene. Cla I (31926612) and Age I (31926815) restriction enzymes were used to generate a 22,127 bp fragment containing the CFB gene for pronuclear injection. DNA was confirmed by restriction enzyme analysis using Pvu I. The 22,127 bp DNA fragment was injected into C57BL/6NTac embryos. 6 positive founders were bred. Founder #6 expressed the liver human CFB mRNA and was crossbreed to the 3^{rd} generation. Progeny from 3^{rd} generation mice were used to evaluate human CFB ASOs for human CFB mRNA reduction.

Treatment

[0514] Groups of 3 mice each were injected subcutaneously twice a week for the first week with 50 mg/kg of ISIS oligonucleotides, followed by once a week dosing with 50 mg/kg of ISIS oligonucleotides for an additional three weeks. One control group of 4 mice was injected subcutaneously twice a week for 2 weeks for the first week with PBS for the first week for an additional three weeks. Forty eight hours after the last dose, mice were euthanized and organs and plasma were harvested for further analysis.

RNA Analysis

[0515] At the end of the dosing period, RNA was extracted from the liver and kidney for real-time PCR analysis of CFB mRNA levels. Human CFB mRNA levels were measured using the human primer probe set RTS3459. CFB mRNA levels were normalized to RIBOGREEN®, and also to the housekeeping gene, Cyclophilin. Results were calculated as percent inhibition of CFB mRNA expression compared to the control. All the antisense oligonucleotides effected inhibition of human CFB mRNA levels in the liver.

TABLE 75

Percent reduction of CFB mRNA levels in hCFB mice

ISIS No	Normalized to RIBOGREEN	Normalized s to Cyclophilin
532770	86	87
532800	88	87
532809	69	69
588540	95	94
588544	91	91
588548	78	77
588550	89	88
588553	94	94
588555	94	94
588848	83	82
594430	78	76

Example 15

In Vivo Antisense Inhibition of Murine CFB

[0516] Several antisense oligonucleotides were designed that were targeted to murine CFB mRNA (GENBANK Accession No. NM_008198.2, incorporated herein as SEQ ID NO: 5). The target start sites and sequences of each oligonucleotide are described in the table below. The chimeric antisense oligonucleotides in the table below were designed as 5-10-5 MOE gapmers. The gapmers are 20 nucleosides in length, wherein the central gap segment is comprised of 10 2'-deoxynucleosides and is flanked on both sides (in the 5' and 3' directions) by wings comprising 5 nucleosides each. Each nucleoside in the 5' wing segment and each nucleoside in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine residues throughout each gapmer are 5-methylcytosines.

TABLE 76

Gapmers targeting murine CFB

ISIS No	Sequence	Target Start Site on SEQ ID NO: 5	SEQ ID NO
516269	GCATAAGAGGGTACCAGCTG	2593	804
516272	GTCCTTTAGCCAGGGCAGCA	2642	805
516323	TCCACCCATGTTGTGCAAGC	1568	806
516330	CCACACCATGCCACAGAGAC	1826	807
516341	TTCCGAGTCAGGCTCTTCCC	2308	808

Treatment

[0517] Groups of four C57BL/6 mice each were injected with 50 mg/kg of ISIS 516269, ISIS 516272, ISIS 516323, ISIS 516330, or ISIS 516341 administered weekly for 3 weeks. A control group of mice was injected with phosphate buffered saline (PBS) administered weekly for 3 weeks.

CFB RNA Analysis

[0518] At the end of the study, RNA was extracted from liver tissue for real-time PCR analysis of CFB, using primer probe set RTS3430 (forward sequence GGGCAAACAGCAATTTGTGA, designated herein as SEQ ID NO: 816; reverse sequence TGGCTACCCACCTTCCTTGT, designated herein as SEQ ID NO: 817; probe sequence CTGGATACTGTCCCAATCCCGGTATTCCX, designated herein as SEQ ID NO: 818). The mRNA levels were normalized using RIBOGREEN®. As shown in the Table below, some of the antisense oligonucleotides achieved reduction of murine CFB over the PBS control. Results are presented as percent inhibition of CFB, relative to control.

TABLE 77

Percent inhibition of murine CFB mRNA in C57BL/6 mice

ISIS No	%
516269	29
516272	72
516323	77
516330	62
516341	72

Protein Analysis

[0519] CFB protein levels were measured in the kidney, liver, plasma, and in the eye by western Blot using goat anti-CFB antibody (Sigma Aldrich). Results are presented as percent inhibition of CFB, relative to PBS control. 'n/a' indicates that measurements were not taken for that sample. As shown in the Table below, antisense inhibition of CFB by ISIS oligonucleotides resulted in a reduction of CFB protein in various tissues. As shown in the Table below, systemic administration of ISIS oligonucleotides was effective in reducing CFB levels in the eye.

TABLE 78

Percent inhibition of murine CFB protein in C57BL/6 mice

ISIS No	Kidney	Liver	Plasma	Eye
516269	20	58	n/a	70
516272	48	74	n/a	99
516323	73	85	90	93
516330	77	80	n/a	n/a
516341	80	88	68	n/a

Example 16

Dose-Dependent Antisense Inhibition of Murine CFB

[0520] Groups of four C57BL/6 mice each were injected with 25 mg/kg, 50 mg/kg, or 100 mg/kg of ISIS 516272, and ISIS 516323 administered weekly for 6 weeks. Another two groups of mice were injected with 100 mg/kg of ISIS 516330 or ISIS 516341 administered weekly for 6 weeks. Two control groups of mice were injected with phosphate buffered saline (PBS) administered weekly for 6 weeks.

CFB RNA Analysis

[0521] RNA was extracted from liver and kidney tissues for real-time PCR analysis of CFB, using primer probe set RTS3430. The mRNA levels were normalized using RIBOGREEN®. As shown in the Table below, the antisense oligonucleotides achieved dose-dependent reduction of murine CFB over the PBS control. Results are presented as percent inhibition of CFB, relative to control.

TABLE 79

Percent inhibition of murine CFB mRNA in C57BL/6 mice

ISIS No	Dose (mg/kg/wk)	Liver	Kidney
516272	25	39	32
	50	73	36
	100	87	42
516323	25	36	41
	50	65	47
	100	79	71
516330	100	85	45
516341	200	89	65

Protein Analysis

[0522] CFB protein levels were measured in the plasma by western Blot using goat anti-CFB antibody (Sigma Aldrich). As shown in the table below, antisense inhibition of CFB by the ISIS oligonucleotides resulted in a reduction of CFB protein. Results are presented as percent inhibition of CFB, relative to PBS control. 'n/a' indicates that measurements were not taken for that sample.

[0523] CFB protein levels were also measured in the eye by Western Blot. All treatment groups demonstrated an inhibition of CFB by 95%, with some sample measurements being below detection levels of the assay.

TABLE 80

Percent inhibition of murine CFB protein in C57BL/6 mice

ISIS No	Dose (mg/kg/wk)	Liver
516272	25	32
	50	70
	100	83
516323	25	43
	50	80
	100	90
516330	100	n/a
516341	200	n/a

Example 17

Effect of Antisense Inhibition of CFB in the NZB/W F1 Mouse Model

[0524] The NZB/W F1 is the oldest classical model of lupus, where the mice develop severe lupus-like phenotypes comparable to that of lupus patients (Theofilopoulos, A. N. and Dixon, F. J. Advances in Immunology, vol. 37, pp. 269-390, 1985). These lupus-like phenotypes include lymphadenopathy, splenomegaly, elevated serum antinuclear autoantibodies (ANA) including anti-dsDNA IgG, a majority of which are IgG2a and IgG3, and immune complex-mediated glomerulonephritis (GN) that becomes apparent at 5-6 months of age, leading to kidney failure and death at 10-12 months of age.

Study 1

[0525] A study was conducted to demonstrate that treatment with antisense oligonucleotides targeting CFB would improve renal pathology in the mouse model. Female NZB/W F1 mice, 17 weeks old, were purchased from Jackson Laboratories. Groups of 16 mice each received doses of 100 μg/kg/week of ISIS 516272 or ISIS 516323 for 20 weeks. Another group of 16 mice received doses of 100 μg/kg/week of control oligonucleotide ISIS 141923 for 20 weeks. Another group of 10 mice received doses of PBS for 20 weeks and served as the control group to which all the other groups were compared. Terminal endpoints were collected 48 hours after the last dose was injected.

CFB RNA Analysis

[0526] RNA was extracted from liver and kidney tissue for real-time PCR analysis of CFB, using primer probe set RTS3430. The mRNA levels were normalized using RIBOGREEN®. As shown in the Table below, some of the antisense oligonucleotides achieved reduction of murine CFB over the PBS control. Results are presented as percent inhibition of CFB, relative to control.

TABLE 81

Percent inhibition of murine CFB mRNA in NZB/W F1 mice

ISIS No	Liver	Kidney
516272	55	25
516323	63	43
141923	0	0

Proteinuria

[0527] Proteinuria is expected in 60% of animals in this mouse model. The cumulative incidence of severe proteinuria was measured by calculating the total protein to creatinine ratio using a clinical analyzer. The results are presented in the table below and demonstrate that treatment with antisense oligonucleotides targeting CFB achieved reduction of proteinuria in the mice compared to the PBS control and the control oligonucleotide treated mice.

TABLE 82

Percent cumulative incidence of severe proteinuria in NZB/W F1 mice

	%
PBS	40
ISIS 516272	6
ISIS 516323	0
ISIS 141923	25

Survival

[0528] Survival of the mice was monitored by keeping count of the mice at the start of treatment and then again at week 20. The results are presented in the table below and demonstrate that treatment with antisense oligonucleotides targeting CFB increased survival in the mice compared to the PBS control and the control oligonucleotide treated mice.

TABLE 83

Number of surviving mice and % survival

	Week 1	Week 20	% survival at week 20
PBS	10	6	60
ISIS 516272	16	15	94
ISIS 516323	16	16	100
ISIS 141923	16	12	75

Glomerular Deposition

[0529] The amount of C3 deposition, as well as IgG deposition, in the glomeruli of the kidneys was measured by immunohistochemistry with an anti-C3 antibody. The results are presented in the table below and demonstrate that treatment with antisense oligonucleotides targeting CFB achieved reduction of both C3 and IgG depositions in the kidney glomeruli compared to the PBS control and the control oligonucleotide treated mice.

TABLE 84

Percent inhibition of *glomerula* deposition in NZB/W F1 mice

ISIS No	C3	IgG
516272	45	20
516323	48	2
141923	0	0

Study 2

[0530] Female NZB/W F1 mice, 16 weeks old, were purchased from Jackson Laboratories. A group of 10 mice received doses of 100 μg/kg/week of ISIS 516323 for 12 weeks. Another group of 10 mice received doses of 100 μg/kg/week of control oligonucleotide ISIS 141923 for 12 weeks. Another group of 10 mice received doses of PBS for 12 weeks and served as the control group to which all the other groups were compared. Terminal endpoints were collected 48 hours after the last dose was injected.

CFB RNA Analysis

[0531] RNA was extracted from liver and kidney tissue for real-time PCR analysis of CFB, using primer probe set RTS3430. As shown in the table below, treatment with ISIS 516323 achieved reduction of murine CFB over the PBS control. Results are presented as percent inhibition of CFB, relative to control.

TABLE 85

Percent inhibition of murine CFB mRNA in NZB/W F1 mice

ISIS No	Liver	Kidney
516323	75	46
141923	0	6

Proteinuria

[0532] The cumulative incidence of severe proteinuria was assessed by measuring urine total protein to creatinine ratio, as well as by measuring total microalbumin levels. The results are presented in the tables below and demonstrate that treatment with antisense oligonucleotides targeting CFB reduced proteinuria in the mice compared to the PBS control and the control oligonucleotide treated mice.

TABLE 86

Proteinuria in NZB/W F1 mice measured as urine microalbumin levels (mg/dl)

ISIS No	Week 0	Week 6	Week 8	Week 10
516323	0	0	5.4	0.4
141923	0	8.28	8.6	5.6

TABLE 87

Proteinuria in NZB/W F1 mice measured as total protein to creatinine ratio

ISIS No	Week 0	Week 6	Week 8	Week 10
516323	5.5	7.8	8.6	7.2
141923	6.9	10.0	13.5	7.2

Survival

[0533] Survival of the mice was monitored by keeping count of the mice at the start of treatment and then again at week 12. The results are presented in the table below and demonstrate that treatment with antisense oligonucleotides targeting CFB increased survival in the mice compared to the PBS control and the control oligonucleotide treated mice.

TABLE 88

Number of surviving mice		
	Week 1	Week 12
PBS	10	9
ISIS 516323	10	10
ISIS 141923	10	9

Example 18

Effect of Antisense Inhibition of CFB in the MRL Mouse Model

[0534] The MRL/lpr lupus nephritis mouse model develops an SLE-like phenotype characterized by lymphadenopathy due to an accumulation of double negative ($CD4^-$ $CD8^-$) and $B220^+$ T-cells. These mice display an accelerated mortality rate. In addition, the mice have high concentrations of circulating immunoglobulins, which included elevated levels of autoantibodies such as ANA, anti-ssDNA, anti-dsDNA, anti-Sm, and rheumatoid factors, resulting in large amounts of immune complexes (Andrews, B. et al., J. Exp. Med. 148: 1198-1215, 1978).

Treatment

[0535] A study was conducted to investigate whether treatment with antisense oligonucleotides targeting CFB would reverse renal pathology in the mouse model. Female MRL/lpr mice, 14 weeks old, were purchased from Jackson Laboratories. A group of 10 mice received doses of 50 μg/kg/week of ISIS 516323 for 7 weeks. Another group of 10 mice received doses of 50 μg/kg/week of control oligonucleotide ISIS 141923 for 7 weeks. Another group of 10 mice received doses of PBS for 7 weeks and served as the control group to which all the other groups were compared. Terminal endpoints were collected 48 hours after the last dose was injected.

CFB RNA Analysis

[0536] RNA was extracted from liver tissue for real-time PCR analysis of CFB, using primer probe set RTS3430. As shown in the Table below, ISIS 516323 reduced CFB over the PBS control. Results are presented as percent inhibition of CFB, relative to control.

TABLE 89

Percent inhibition of murine CFB mRNA in MRL/lpr mice	
ISIS No	%
516323	68
141923	4

Renal Pathology

[0537] Renal pathology was evaluated by two methods. Histological sections of the kidney were stained with Haematoxylin & Eosin. The PBS control demonstrated presence of multiglomerular crescents tubular casts, which is a symptom of glomerulosclerosis. In contrast, the sections from mice treated with ISIS 516323 showed absent crescents tubular casts with minimal bowman capsule fibrotic changes, moderate to severe segmental mesangial cell expansion and glomerular basement membrane thickening.

[0538] Accumulation of C3 in the kidney was also assessed by immunohistochemistry with anti-C3 antibodies. The whole kidney C3 immunohistochemistry intensity score was calculated by intensity scoring system, which was computed by capturing 10 glomeruli per kidney and calculation the intensity of positive C3 staining. The results are presented in the table below and demonstrate that treatment with ISIS 516323 reduced renal C3 accumulation compared to the control groups.

TABLE 90

Renal C3 accumulation in MRL/lpr mice		
	Whole kidney C3 intensity score	C3 quantification (area/total area) % of average PBS
PBS	2.5	100
ISIS 516323	1.6	68
ISIS 141923	2.2	99

Plasma C3 Levels

[0539] Reduction of CFB inhibits activation of the alternative complement pathway, preventing C3 consumption and leading to an apparent elevation of plasma C3 levels. Plasma C3 levels from terminal bleed were measured by clinical analyzer. The results are presented in the table below and demonstrate that treatment with ISIS 516323 increased C3 levels ($p<0.001$) in the plasma compared to the control groups.

TABLE 91

Plasma C3 levels (mg/dL) in MRL/lpr mice	
ISIS No	C3
516323	28
141923	16

The results indicate that treatment with antisense oligonucleotides targeting CFB reverses renal pathology in the lupus mouse model.

Example 19

Effect of Antisense Inhibition of CFB in the CFH Het Mouse Model

[0540] CFH heterozygous (CFH Het, $CFH^{+/-}$) mouse model expresses a mutant Factor H protein in combination with the full-length mouse protein (Pickering, M. C. et al., J. Exp. Med. 2007. 204: 1249-56). Renal histology remains normal in these mice up to six months old.

Study 1

[0541] Groups of 8 $CFH^{+/-}$ mice, 6 weeks old, each received doses of 75 mg/kg/week of ISIS 516323 or ISIS 516341 for 6 weeks. Another group of 8 mice received doses of 75 mg/kg/week of control oligonucleotide ISIS 141923 for 6 weeks. Another group of 8 mice received doses of PBS for 6 weeks and served as the control group to which all the other

groups were compared. Terminal endpoints were collected 48 hours after the last dose was injected.

CFB RNA Analysis

[0542] RNA was extracted from liver and kidney tissue for real-time PCR analysis of CFB, using primer probe set RTS3430. As shown in the Table below, the antisense oligonucleotides reduced CFB over the PBS control. Results are presented as percent inhibition of CFB, relative to control.

TABLE 92

Percent inhibition of murine CFB mRNA in $CFH^{+/-}$ mice

ISIS No	Liver	Kidney
516323	80	38
516341	90	44
141923	0	17

Plasma C3 Levels

[0543] Reduction of CFB inhibits activation of the alternative complement pathway, preventing C3 consumption and leading to an apparent elevation of plasma C3 levels. Plasma C3 levels from terminal plasma collection were measured by clinical analyzer. The results are presented in the table below and demonstrate that treatment with ISIS 516323 increased C3 to normal levels in the plasma.

TABLE 93

Plasma C3 levels (mg/dL) in $CFH^{+/-}$ mice

ISIS No	C3
516323	15
516341	17
141923	8

Study 2

[0544] Groups of 5 $CFH^{+/-}$ mice each received doses of 12.5 mg/kg/week, 25 mg/kg/week, 50 mg/kg/week, 75 mg/kg/week, or 100 mg/kg/week of ISIS 516323 or ISIS 516341 for 6 weeks. Another group of 5 mice received doses of 75 μg/kg/week of control oligonucleotide ISIS 141923 for 6 weeks. Another group of 5 mice received doses of PBS for 6 weeks and served as the control group to which all the other groups were compared. Terminal endpoints were collected 48 hours after the last dose was injected.

CFB RNA Analysis

[0545] RNA was extracted from liver and kidney tissue for real-time PCR analysis of CFB, using primer probe set RTS3430. As shown in the Table below, the antisense oligonucleotides reduced CFB over the PBS control in a dose dependent manner. Results are presented as percent inhibition of CFB, relative to control.

TABLE 94

Percent inhibition of murine CFB mRNA in the liver of $CFH^{+/-}$ mice

ISIS No	Dose (mg/kg/week)	%
516323	12.5	34
	25	51
	50	72
	75	79
	100	92
516341	12.5	38
	25	57
	50	89
	75	92
	100	90
141923	75	13

Plasma C3 Levels

[0546] Reduction of CFB inhibits activation of the alternative complement pathway, preventing C3 consumption and leading to an apparent elevation of plasma C3 levels. Plasma C3 levels from terminal plasma collection were measured by clinical analyzer. The results are presented in the table below and demonstrate that treatment with ISIS oligonucleotides targeting CFB increased C3 levels in the plasma.

TABLE 95

Plasma C3 levels (mg/dL) in $CFH^{+/-}$ mice

	Dose (mg/kg/week)	C3
PBS	—	10.1
516323	12.5	11.4
	25	15.5
	50	17.0
	75	18.3
	100	18.8
516341	12.5	12.1
	25	16.3
	50	18.6
	75	22.1
	100	19.1
141923	75	8.9

Example 20

Effect of ISIS Antisense Oligonucleotides Targeting Human CFB in Cynomolgus Monkeys

[0547] Cynomolgus monkeys were treated with ISIS antisense oligonucleotides selected from studies described in the Examples above. Antisense oligonucleotide efficacy and tolerability, as well as their pharmacokinetic profile in the liver and kidney, were evaluated.

[0548] At the time this study was undertaken, the cynomolgus monkey genomic sequence was not available in the National Center for Biotechnology Information (NCBI) database; therefore cross-reactivity with the cynomolgus monkey gene sequence could not be confirmed. Instead, the sequences of the ISIS antisense oligonucleotides used in the cynomolgus monkeys was compared to a rhesus monkey sequence for homology. The human antisense oligonucleotides tested below are cross-reactive (with 0 or 1 mismatches) with the rhesus genomic sequence (GENBANK Accession No.

NW_001116486.1 truncated from nucleotides 536000 to 545000, designated herein as SEQ ID NO: 3). The start and stop sites of each oligonucleotide targeted to SEQ ID NO: 3 is presented in the Table below. "Start site" indicates the 5'-most nucleotide to which the gapmer is targeted in the rhesus monkey gene sequence. 'Mismatches' indicates the number of nucleobases in the human oligonucleotide that are mismatched with the rhesus genomic sequence.

TABLE 96

Antisense oligonucleotides complementary to the rhesus CFB genomic sequence (SEQ ID NO: 3)

ISIS No	Target Start Site	Mismatches	Chemistry	SEQ ID NO
532770	6788	0	5-10-5 MOE	198
532800	7500	0	5-10-5 MOE	228
532809	7614	0	5-10-5 MOE	237
588540	7627	1	5-10-5 MOE	440
588544	7631	1	5-10-5 MOE	444
588548	7635	1	5-10-5 MOE	448
588550	7637	1	5-10-5 MOE	450
588553	7640	1	5-10-5 MOE	453
588555	7643	0	5-10-5 MOE	455
588848	7639	1	Deoxy, MOE and cEt	598
594430	6790	0	3-10-3 cEt	549

Treatment

[0549] Prior to the study, the monkeys were kept in quarantine for at least a 30 day period, during which the animals were observed daily for general health. The monkeys were 2-4 years old and weighed between 2 and 4 kg. Eleven groups of 4-6 randomly assigned male cynomolgus monkeys each were injected subcutaneously with ISIS oligonucleotide or PBS at four sites on the back in a clockwise rotation (i.e. left, top, right, and bottom), one site per dose. The monkeys were given four loading doses of PBS or 40 mg/kg of ISIS 532800, ISIS 532809, ISIS 588540, ISIS 588544, ISIS 588548, ISIS 588550, ISIS 588553, ISIS 588555, ISIS 588848, or ISIS 594430 for the first week (days 1, 3, 5, and 7), and were subsequently dosed once a week for 12 weeks (days 14, 21, 28, 35, 42, 49, 56, 63, 70, 77, and 84) with PBS or 40 mg/kg of ISIS oligonucleotide. ISIS 532770 was tested in a separate study with similar conditions with two male and two female cynomolgus monkeys in the group.

Hepatic Target Reduction

RNA Analysis

[0550] On day 86, liver and kidney samples were collected in duplicate (approximately 250 mg each) for CFB mRNA analysis. The samples were flash frozen in liquid nitrogen at necropsy within approximately 10 minutes of sacrifice.

[0551] RNA was extracted from liver and kidney for real-time PCR analysis of measurement of mRNA expression of CFB. Results are presented as percent change of mRNA, relative to PBS control, normalized with RIBOGREEN®. RNA levels were also normalized with the house-keeping gene, Cyclophilin A. RNA levels were measured with the primer probe sets RTS3459, described above, or RTS4445_MGB (forward sequence CGAAGAAGCTCAGTGAAATCAA, designated herein as SEQ ID NO: 819; reverse sequence TGCCTGGAGGGCCCTCTT, designated herein as SEQ ID NO: 820; probe sequence AGACCACAAGTTGAAGTC, designated herein as SEQ ID NO: 815).

[0552] As shown in the Tables below, treatment with ISIS antisense oligonucleotides resulted in reduction of CFB mRNA in comparison to the PBS control. Analysis of CFB mRNA levels revealed that several of the ISIS oligonucleotides reduced CFB levels in liver and/or kidney. Here '0' indicates that the expression levels were not inhibited. '*' indicates that the oligonucleotide was tested in a separate study with similar conditions.

TABLE 97

Percent inhibition of CFB mRNA in the cynomolgus monkey liver relative to the PBS control

ISIS No	RTS3459/ Cyclophilin A	RTS3459/ RIBOGREEN	RTS445_MGB/Cyclophilin A	RTS445_MGB/ RIBOGREEN
532770*	12	37	24	45
532800	54	45	56	46
588540	31	27	28	24
588548	68	67	68	67
588550	53	39	51	37
588553	74	59	74	59
588555	73	71	71	69
588848	9	0	6	0
594430	24	26	23	25

TABLE 98

Percent inhibition of CFB mRNA in the cynomolgus monkey kidney relative to the PBS control

ISIS No	RTS3459/ Cyclophilin A	RTS3459/ RIBOGREEN	RTS445_MGB/Cyclophilin A	RTS445_MGB/ RIBOGREEN
532770*	34	56	2	31
532800	36	30	43	37
588540	70	71	67	69
588548	83	84	82	83
588550	81	77	78	74
588553	86	84	86	85
588555	32	34	48	50
588848	89	91	87	90
594430	33	37	19	23

Protein Analysis

[0553] Approximately 1 mL of blood was collected from all available animals at day 85 and placed in tubes containing the potassium salt of EDTA. The blood samples were placed in wet-ice or Kryorack immediately, and centrifuged (3000 rpm for 10 min at 4° C.) to obtain plasma (approximately 0.4 mL) within 60 minutes of collection. Plasma levels of CFB were measured in the plasma by radial immunodiffusion (RID), using a polyclonal anti-Factor B antibody. The results are presented in the Table below. ISIS 532770 was tested in a separate study and plasma protein levels were measured on day 91 or 92 in that group.

[0554] Analysis of plasma CFB revealed that several ISIS oligonucleotides reduced protein levels in a sustained manner. ISIS 532770, which was tested in a separate study, reduced CFB protein levels on day 91/92 by 50% compared to baseline values. The reduction in plasma CFB protein levels correlates well with liver CFB mRNA level reduction in the corresponding groups of animals.

TABLE 99

Plasma protein levels (% baseline values) in the cynomolgus monkey

	Day 1	Day 30	Day 58	Day 72	Day 86
PBS	113	115	95	83	86
ISIS 532800	117	68	52	39	34
ISIS 532809	104	121	100	80	71
ISIS 588540	108	72	61	40	38
ISIS 588544	118	74	53	33	29
ISIS 588548	110	41	28	20	16
ISIS 588550	104	64	54	38	37
ISIS 588553	97	42	35	18	16
ISIS 588555	107	35	37	18	18
ISIS 588848	116	95	92	69	71
ISIS 594430	104	64	59	45	46

Tolerability Studies

Body Weight Measurements

[0555] To evaluate the effect of ISIS oligonucleotides on the overall health of the animals, body and organ weights were measured and are presented in the Table below. '*' indicates that the oligonucleotide was tested in a separate study with similar conditions and is the average of the measurements from male and female monkeys. The results indicate that effect of treatment with antisense oligonucleotides on body and organ weights was within the expected range for antisense oligonucleotides.

TABLE 100

Final body weights (g) in cynomolgus monkey

	Day 1	Day 14	Day 28	Day 42	Day 56	Day 70	Day 84
PBS	2887	2953	3028	3094	3125	3143	3193
ISIS 532770*	2963	2947	2966	3050	3097	3138	3160
ISIS 532800	2886	2976	3072	3149	3220	3269	3265
ISIS 532809	2755	2836	2927	2983	3019	3071	3098
ISIS 588540	2779	2834	2907	2934	2981	3034	3057
ISIS 588544	2837	2896	3009	3064	3132	3163	3199
ISIS 588548	2694	2816	2882	2990	3073	3149	3161
ISIS 588550	2855	2988	3062	3188	3219	3282	3323
ISIS 588553	3033	3156	3256	3335	3379	3372	3442
ISIS 588555	2757	2863	2965	3022	3075	3088	3158
ISIS 588848	2850	3018	3032	3187	3230	3212	3291
ISIS 594430	2884	2963	2953	3149	3187	3204	3256

TABLE 101

Final organ weights (g) in cynomolgus monkey

	Spleen	Heart	Kidney	Liver
PBS	2.8	11.6	11.9	55.8
ISIS 532770*	5.0	11.3	20.6	77.9
ISIS 532800	6.2	11.9	18.6	94.4
ISIS 588540	4.0	11.4	13.5	67.1
ISIS 588548	4.1	11.7	17.3	72.0
ISIS 588550	5.8	10.9	18.5	81.8
ISIS 588553	5.0	12.7	17.2	85.9
ISIS 588555	4.7	11.8	15.9	88.3
ISIS 588848	5.0	12.7	14.4	75.7
ISIS 594430	3.9	11.9	14.8	69.9

Liver Function

[0556] To evaluate the effect of ISIS oligonucleotides on hepatic function, blood samples were collected from all the study groups. The blood samples were collected from the cephalic, saphenous, or femoral veins, 48 hours post-dosing. The monkeys were fasted overnight prior to blood collection. Blood (1.5 mL) was collected in tubes without anticoagulant for serum separation. The tubes were kept at room temperature for a minimum of 90 minutes and then centrifuged (approximately 3,000 rpm for 10 min) to obtain serum. Levels of various liver function markers were measured using a Toshiba 200FR NEO chemistry analyzer (Toshiba Co., Japan).

[0557] Plasma levels of ALT and AST were measured and the results are presented in the Table below, expressed in IU/L. Bilirubin, a liver function marker, was similarly measured and is presented in the Table below expressed in mg/dL. '*' indicates that the oligonucleotide was tested in a separate study with similar conditions and is the average of the measurements from male and female monkeys. The results indicate that most of the antisense oligonucleotides had no effect on liver function outside the expected range for antisense oligonucleotides.

TABLE 102

Liver chemistry marker levels in cynomolgus monkey plasma on day 86

	ALT (IU/L)	AST (IU/L)	Bilirubin (mg/dL)
PBS	71	57	0.3
ISIS 532770*	59	58	0.1
ISIS 532800	65	86	0.1
ISIS 532809	35	58	0.1
ISIS 588540	70	88	0.2
ISIS 588544	55	97	0.2
ISIS 588548	61	85	0.2
ISIS 588550	94	84	0.2
ISIS 588553	44	65	0.2
ISIS 588555	63	84	0.2
ISIS 588848	69	65	0.2
ISIS 594430	86	53	0.2

Kidney Function

[0558] To evaluate the effect of ISIS oligonucleotides on kidney function, blood samples were collected from all the study groups. The blood samples were collected from the cephalic, saphenous, or femoral veins, 48 hours post-dosing. The monkeys were fasted overnight prior to blood collection. Blood was collected in tubes without anticoagulant for serum separation. The tubes were kept at room temperature for a minimum of 90 minutes and then centrifuged (approximately 3,000 rpm for 10 min) to obtain serum. Levels of BUN and creatinine were measured using a Toshiba 200FR NEO chemistry analyzer (Toshiba Co., Japan). Results are presented in the Table below, expressed in mg/dL. '*' indicates that the oligonucleotide was tested in a separate study with similar conditions and is the average of the measurements from male and female monkeys.

[0559] For urinalysis, fresh urine from all the animals was collected in the morning using a clean cage pan on wet ice. Food was removed overnight the day before urine collection but water was supplied. Urine samples (approximately 1 mL) were analyzed for protein to creatinine (P/C) ratio using a Toshiba 200FR NEO automated chemistry analyzer (Toshiba

Co., Japan). 'n.d.' indicates that the urine protein level was under the detection limit of the analyzer.

[0560] The plasma and urine chemistry data indicate that most of the ISIS oligonucleotides did not have any effect on the kidney function outside the expected range for antisense oligonucleotides.

TABLE 103

Renal chemistry marker levels (mg/dL) in cynomolgus monkey plasma on day 86

	BUN	Creatinine	Total protein
PBS	28	0.9	8.0
ISIS 532770*	20	0.9	6.9
ISIS 532800	25	0.9	7.5
ISIS 532809	23	0.8	7.4
ISIS 588540	30	0.8	7.5
ISIS 588544	26	0.9	7.4
ISIS 588548	25	0.9	7.6
ISIS 588550	24	0.9	7.2
ISIS 588553	25	0.8	7.2
ISIS 588555	25	0.8	7.6
ISIS 588848	24	0.9	7.5
ISIS 594430	25	0.8	7.2

TABLE 104-continued

Total Protein/Creatinine ratio in cynomolgus monkey urine

	Day 44	Day 86
ISIS 588848	0.09	n.d.
ISIS 594430	0.03	n.d.

Hematology

[0561] To evaluate any effect of ISIS oligonucleotides in cynomolgus monkeys on hematologic parameters, blood samples of approximately 0.5 mL of blood was collected from each of the available study animals in tubes containing K_2-EDTA. Samples were analyzed for red blood cell (RBC) count, white blood cells (WBC) count, individual white blood cell counts, such as that of monocytes, neutrophils, lymphocytes, as well as for platelet count, hemoglobin content and hematocrit, using an ADVIA120 hematology analyzer (Bayer, USA). The data is presented in the Tables below. '*' indicates that the oligonucleotide was tested in a separate study with similar conditions and is the average of the measurements from male and female monkeys.

[0562] The data indicate the oligonucleotides did not cause any changes in hematologic parameters outside the expected range for antisense oligonucleotides at this dose.

TABLE 105

Blood cell counts in cynomolgus monkeys

	RBC ($\times 10^6$/μL)	Platelets ($\times 10^3$/μL)	WBC ($\times 10^3$/μL)	Neutrophils (% WBC)	Lymphocytes (% total)	Monocytes (% total)
PBS	5.8	347	9.4	42.7	53.1	3.0
ISIS 532770*	5.4	386	10.8	22.3	71.7	3.3
ISIS 532800	5.6	360	13.1	29.5	61.1	6.5
ISIS 532809	5.2	400	11.5	56.6	38.2	2.5
ISIS 588540	5.5	367	11.7	50.9	42.7	2.1
ISIS 588544	5.2	373	14.3	56.6	37.6	4.3
ISIS 588548	5.1	373	9.7	40.4	54.3	3.9
ISIS 588550	6.1	343	9.9	32.1	61.7	4.6
ISIS 588553	5.2	424	9.3	41.7	53.2	3.6
ISIS 588555	5.1	411	9.6	45.1	49.7	3.5
ISIS 588848	5.7	370	10.0	39.8	55.8	3.1
ISIS 594430	5.7	477	10.6	47.3	47.8	3.6

TABLE 104

Total Protein/Creatinine ratio in cynomolgus monkey urine

	Day 44	Day 86
PBS	0.03	n.d.
ISIS 532800	0.01	n.d.
ISIS 532809	0.01	n.d.
ISIS 588540	0.03	n.d.
ISIS 588544	0.01	0.09
ISIS 588548	0.01	0.01
ISIS 588550	0.04	0.01
ISIS 588553	0.05	n.d.
ISIS 588555	0.03	0.03

TABLE 106

Hematologic parameters in cynomolgus monkeys

	Hemoglobin (g/dL)	HCT (%)
PBS	14.1	46.6
ISIS 532770*	12.4	40.9
ISIS 532800	12.3	40.5
ISIS 532809	12.2	40.4
ISIS 588540	12.5	41.5
ISIS 588544	11.9	38.1
ISIS 588548	12.3	39.6
ISIS 588550	13.4	45.0

TABLE 106-continued

Hematologic parameters in cynomolgus monkeys

	Hemoglobin (g/dL)	HCT (%)
ISIS 588553	12.6	39.8
ISIS 588555	11.6	38.1
ISIS 588848	13.2	42.7
ISIS 594430	13.4	43.1

Measurement of Oligonucleotide Concentration

[0563] The concentration of the full-length oligonucleotide was measured in the kidney and liver tissues. The method used is a modification of previously published methods (Leeds et al., 1996; Geary et al., 1999) which consist of a phenol-chloroform (liquid-liquid) extraction followed by a solid phase extraction. Tissue sample concentrations were calculated using calibration curves, with a lower limit of quantitation (LLOQ) of approximately 1.14 μg/g. The results are presented in the Table below, expressed as μg/g liver or kidney tissue.

TABLE 107

Antisense oligonucleotide distribution

	Kidney (μg/g)	Liver (μg/g)	Kidney/Liver ratio
ISIS 532800	3881	1633	2.4
ISIS 588540	3074	1410	2.2
ISIS 588548	3703	1233	3.0
ISIS 588550	4242	860	4.9
ISIS 588553	3096	736	4.2
ISIS 588555	4147	1860	2.2
ISIS 588848	2235	738	3.0
ISIS 594430	1548	752	2.1

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 820

<210> SEQ ID NO 1
<211> LENGTH: 2646
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 1

gacttctgca gtttctgttt ccttgactgg cagctcagcg gggccctccc gcttggatgt 60

tccgggaaag tgatgtgggt aggacaggcg gggcgagccg caggtgccag aacacagatt 120

gtataaaagg ctgggggctg gtggggagca ggggaaggga atgtgaccag gtctaggtct 180

ggagtttcag cttggacact gagccaagca gacaagcaaa gcaagccagg acacaccatc 240

ctgccccagg cccagcttct ctcctgcctt ccaacgccat ggggagcaat ctcagccccc 300

aactctgcct gatgcccttt atcttgggcc tcttgtctgg aggtgtgacc accactccat 360

ggtctttggc ccggccccag ggatcctgct ctctggaggg ggtagagatc aaaggcggct 420

ccttccgact tctccaagag ggccaggcac tggagtacgt gtgtccttct ggcttctacc 480

cgtaccctgt gcagacacgt acctgcagat ctacggggtc ctggagcacc ctgaagactc 540

aagaccaaaa gactgtcagg aaggcagagt gcagagcaat ccactgtcca agaccacacg 600

acttcgagaa cggggaatac tggccccggt ctccctacta caatgtgagt gatgagatct 660

ctttccactg ctatgacggt tacactctcc ggggctctgc caatcgcacc tgccaagtga 720

atggccgatg gagtgggcag acagcgatct gtgacaacgg agcggggtac tgctccaacc 780

cgggcatccc cattggcaca aggaaggtgg gcagccagta ccgccttgaa gacagcgtca 840

cctaccactg cagccggggg cttaccctgc gtggctccca gcggcgaacg tgtcaggaag 900

gtggctcttg gagcgggacg gagccttcct gccaagactc cttcatgtac gacacccctc 960

aagaggtggc cgaagctttc ctgtcttccc tgacagagac catagaagga gtcgatgctg 1020

aggatgggca cggcccaggg gaacaacaga agcggaagat cgtcctggac ccttcaggct 1080

ccatgaacat ctacctggtg ctagatggat cagacagcat tggggccagc aacttcacag 1140

gagccaaaaa gtgtctagtc aacttaattg agaaggtggc aagttatggt gtgaagccaa 1200

gatatggtct agtgacatat gccacatacc ccaaaatttg ggtcaaagtg tctgaagcag 1260

-continued

acagcagtaa tgcagactgg gtcacgaagc agctcaatga aatcaattat gaagaccaca 1320

agttgaagtc agggactaac accaagaagg ccctccaggc agtgtacagc atgatgagct 1380

ggccagatga cgtccctcct gaaggctgga accgcacccg ccatgtcatc atcctcatga 1440

ctgatggatt gcacaacatg ggcggggacc caattactgt cattgatgag atccgggact 1500

tgctatacat tggcaaggat cgcaaaaacc caagggagga ttatctggat gtctatgtgt 1560

ttggggtcgg gcctttggtg aaccaagtga acatcaatgc tttggcttcc aagaaagaca 1620

atgagcaaca tgtgttcaaa gtcaaggata tggaaaacct ggaagatgtt ttctaccaaa 1680

tgatcgatga aagccagtct ctgagtctct gtggcatggt ttgggaacac aggaagggta 1740

ccgattacca caagcaacca tggcaggcca agatctcagt cattcgccct tcaaagggac 1800

acgagagctg tatgggggct gtggtgtctg agtactttgt gctgacagca gcacattgtt 1860

tcactgtgga tgacaaggaa cactcaatca aggtcagcgt aggaggggag aagcgggacc 1920

tggagataga agtagtccta tttcacccca actacaacat taatgggaaa aaagaagcag 1980

gaattcctga attttatgac tatgacgttg ccctgatcaa gctcaagaat aagctgaaat 2040

atggccagac tatcaggccc atttgtctcc cctgcaccga gggaacaact cgagctttga 2100

ggcttcctcc aactaccact tgccagcaac aaaaggaaga gctgctccct gcacaggata 2160

tcaaagctct gtttgtgtct gaggaggaga aaaagctgac tcggaaggag gtctacatca 2220

agaatgggga taagaaaggc agctgtgaga gagatgctca atatgcccca ggctatgaca 2280

aagtcaagga catctcagag gtggtcaccc ctcggttcct ttgtactgga ggagtgagtc 2340

cctatgctga ccccaatact tgcagaggtg attctggcgg ccccttgata gttcacaaga 2400

gaagtcgttt cattcaagtt ggtgtaatca gctggggagt agtggatgtc tgcaaaaacc 2460

agaagcggca aaagcaggta cctgctcacg cccgagactt tcacatcaac ctctttcaag 2520

tgctgccctg gctgaaggag aaactccaag atgaggattt gggttttcta taaggggttt 2580

cctgctggac aggggcgtgg gattgaatta aaacagctgc gacaacaaaa aaaaaaaaaa 2640

aaaaaa 2646

<210> SEQ ID NO 2
<211> LENGTH: 9001
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 2

ggaggtgagg gtctcaggtt ggggatgctg ggatcccccc gtgacagctc ccagaatgtc 60

tctcttcctt ctccaggtct ggctgctttc tctctctgac gcgggtcacc cctcctccca 120

agcctcacaa acctgctagg tgtccctggg tctgcttatt ctttttttgt tgttattgag 180

atggagtctt gctctgtctc ccaggctgga gtgcagtggc acgacctcag ctcactgcaa 240

cttctgcctc ctgggttcaa gcgattctcc tacttcagcc tcccgagtag ctgagattac 300

aggtgcccac caccacacca gctaattttt gtatttttag tagagacggg atttcgccat 360

gttggccagg atggtcttga actcctgacc tcaagtgatc tgcctgcctc aacctcccaa 420

agtgctgaga ttacaggcgt gagccactgc acccacccgg gtctgcttat tctacccttc 480

tctctggttc caccctgct gcagtggaca agctgtgccg aggttgtctc ccaagaaaaa 540

accatgttcc ccaacttgac agatgtcagg gaggtggtga cagaccagtt cctatgcagt 600

-continued

gggacccagg aggatgagag tccctgcaag ggtgagtccc tcaccatgcc tggattccca 660

aggggaaggc cacctgtgtc tctgtggcca gcatgcatgc cagaacacca gtccactgcc 720

ctagatgaca ctgtctcctg tcacccttg ctggcaggag aatctggggg agcagttttc 780

cttgagcgga gattcaggtt ttttcaggtg agaaggtaga agcttgcagg acccaggggt 840

tacaggatct cagccttgtt gggggggatga gggaggcctt tgagggatct agggaggttg 900

gggcttacag ttggggctgt ggcagcctcc cagccagttc tctccttttc tccaggtggg 960

tctggtgagc tggggtcttt acaacccctg ccttggctct gctgacaaaa actcccgcaa 1020

aagggcccct cgtagcaagg tcccgccgcc acgagacttt cacatcaatc tcttccgcat 1080

gcagccctgg ctgaggcagc acctgggggga tgtcctgaat tttttacccc tctagccatg 1140

gccactgagc cctctgctgc cctgccagaa tctgccgccc ctccatcttc tacctctgaa 1200

tggccaccct tagaccctgt gatccatcct ctctcctagc tgagtaaatc cgggtctcta 1260

ggatgccaga ggcagcgcac acaagctggg aaatcctcag ggctcctacc agcaggactg 1320

cctcgctgcc ccacctcccg ctccttggcc tgtccccaga ttccttccct ggttgacttg 1380

actcatgctt gtttcacttt cacatggaat ttcccagtta tgaaattaat aaaaatcaat 1440

ggtttccaca tctctcagtg cctctatctg gaggccaggt agggctggcc ttgggggagg 1500

gggaggccag aatgactcca agagctacag gaaggcaggt cagagacccc actggacaaa 1560

cagtggctgg actctgcacc ataacacaca atcaacaggg gagtgagctg gatccttatt 1620

tctggtccct aagtgggtgg tttgggctta ctggggagga gctaaggccg gagaggaggt 1680

actgaagggg agagtcctgg acctttggca gcaaagggtg ggacttctgc agtttctgtt 1740

tccttgactg gcagctcagc ggggccctcc cgcttggatg ttccgggaaa gtgatgtggg 1800

taggacaggc ggggcgagcc gcaggtgcca gaacacagat tgtataaaag gctgggggct 1860

ggtggggagc aggggaaggg aatgtgacca ggtctaggtc tggagtttca gcttggacac 1920

tgagccaagc agacaagcaa agcaagccag gacacaccat cctgccccag gcccagcttc 1980

tctcctgcct tccaacgcca tggggagcaa tctcagcccc caactctgcc tgatgccctt 2040

tatcttgggc ctcttgtctg gaggtaagcg agggtaacct tcccttcctg ctgtctccag 2100

catccctcct tggccttttg gggccaggct tcatcagcct ttctcttcag gtgtgaccac 2160

cactccatgg tctttggccc ggccccaggg atcctgctct ctggaggggg tagagatcaa 2220

aggcggctcc ttccgacttc tccaagaggg ccaggcactg gagtacgtgt gtccttctgg 2280

cttctacccg taccctgtgc agacacgtac ctgcagatct acggggtcct ggagcaccct 2340

gaagactcaa gaccaaaaga ctgtcaggaa ggcagagtgc agaggtttga gggcaatgag 2400

tgtgggcagt ggcctaaggc agaaacaggg caggcggcag caaggtcagg actaggatga 2460

gactaggcag ggtgacaagg tgggctgacc gggagtagga gcagttttag ggtggcaggc 2520

ggaaaggggg caagaaaaag cggagttaac ccttactaag catttaccct gggcttccag 2580

gcagccctgg aagtcaagag aacactcaga aatggggagg gagaagcagt ggaaatccat 2640

atgggttgag gagtaggtaa gatgctgctt ctgcgggact gggaatgcgc tgtttctcag 2700

tgacatggtc tccgagacca ggagggatac acctaaggca gcctttccct cttgatgact 2760

tctacttgtc ccccttctc aaagcaatcc actgtccaag accacacgac ttcgagaacg 2820

gggaatactg gccccggtct ccctactaca atgtgagtga tgagatctct ttccactgct 2880

-continued

atgacggtta cactctccgg ggctctgcca atcgcacctg ccaagtgaat ggccgatgga 2940

gtgggcagac agcgatctgt gacaacggag gtgagaagca tcccctcccc ctacattgct 3000

gtctccctga cggcgcccag cccgaggagt gggcactcgg ctccggacac tgtaactctt 3060

gctctctacc ttgctcacgg ggcctcaggc ttcagtgctt acctcgatgt ctcatacctc 3120

tgcagcgggg tactgctcca acccgggcat ccccattggc acaaggaagg tgggcagcca 3180

gtaccgcctt gaagacagcg tcacctacca ctgcagccgg gggcttaccc tgcgtggctc 3240

ccagcggcga acgtgtcagg aaggtggctc ttggagcggg acggagcctt cctgccaagg 3300

tgacctttga cctgtacccc caggtcagat cctggtcttc catcctactg tcttctctcc 3360

ccacctcaac cctgctcttt cctcactttg tttaaacctc cctgtacaac tatctcactt 3420

ctgagccttt tataccctgg aaacccatga tcccccgtct ctttggtcac tgtatccctg 3480

acactcccag acatttgacc tcatttctga ctctcccaga ctccttcatg tacgacaccc 3540

ctcaagaggt ggccgaagct ttcctgtctt ccctgacaga gaccatagaa ggagtcgatg 3600

ctgaggatgg gcacggccca ggtttgaaga cagagaaggg aggcagggca gggaactggg 3660

ggaaaatgga gaagggacag aactgttaat gctggagcct gagccactct cctggcaccc 3720

aggggaacaa cagaagcgga agatcgtcct ggacccttca ggctccatga acatctacct 3780

ggtgctagat ggatcagaca gcattggggc cagcaacttc acaggagcca aaaagtgtct 3840

agtcaactta attgagaagg tggaatcctc ctatccctga actcgggggа atggaatctc 3900

gctgatcttc caggactagc tccctgatca ttccagcccc tctgaacaac agggccccag 3960

gaaaatctcc aggtcctatt ctgtcctcct tccctttтac ttgaagcagt ttcttgactg 4020

gtaattcctc catgaacctc agcccttgag cctcttactg agagcctccc tgtcccagca 4080

aagtcgctga aatctcccaa tcacagtatt ctattttcaa tgccatggcg ccttgttctc 4140

ctcacccaca ggtggcaagt tatggtgtga agccaagata tggtctagtg acatatgcca 4200

catacccсaa aatttgggtc aaagtgtctg aagcagacag cagtaatgca gactgggtca 4260

cgaagcagct caatgaaatc aattatgaag gtcagaggtt agggaatggt gggaggttca 4320

ctttggggtc aggaggttca gggtggaggg ggtcatgaga ctaccttgag ggcgacaggg 4380

aggaccactt tgtagtcaaa agttgaacag caggatcgtt gggcaatgga ggttagtggg 4440

aacctgttgg gggctggaag ggccactttg tggtcaaagg gaagtccgtg taatgatgat 4500

taacttaaaa agttgaaaga tgtgggattt cagttgcaga ttggtctctg gggttaaaag 4560

atggcttgga agaccaggtg aggtgatggt ctcttccctc tccacagacc acaagttgaa 4620

gtcagggact aacaccaaga aggccctcca ggcagtgtac agcatgatga gctggccaga 4680

tgacgtccct cctgaaggct ggaaccgcac ccgccatgtc atcatcctca tgactgatgg 4740

tcagaaggga cctctctcct gtcccagcct ccccaccttc tcagaccagc atgtggccct 4800

taagtccact tgtaacacta tacccatggt tggggccctg aatgtgactc atagctggct 4860

gttcatctct cctgtgaccc ttcataagga attcttccta agccctgtga tcaactatct 4920

ctaacccttc ctcaacttgc tcaccctgcc atgtgtatcc ctgcctttag ccagtttatc 4980

ttccttatct cctaccctca tggtcctgtc tcttctgcag gattgcacaa catgggcggg 5040

gacccaatta ctgtcattga tgagatccgg gacttgctat acattggcaa ggatcgcaaa 5100

aacccaaggg aggattatct gggtgagtaa cctgcctagg acccagcacc ccacttcctc 5160

-continued

agggcttgga ccctcatcct tccttttttat ccctcagatg tctatgtgtt tggggtcggg 5220

cctttggtga accaagtgaa catcaatgct ttggcttcca agaaagacaa tgagcaacat 5280

gtgttcaaag tcaaggatat ggaaaacctg gaagatgttt tctaccaaat gatcggtagg 5340

gagatacaag ggaataaaga acacaactct cctcaggttc ccctgaagta attcattctt 5400

cctctacacc tgaagctcta gttgcctgga aagccttctt cattcctcct tctctacctc 5460

agtgtcacta ttcttgtttc ctggcactgt tcacttaacc ttagaatcac agagctctga 5520

gcacttcaga gatctttcta tagtcctaca tttgacacgt ggaaacagaa gccaaaggag 5580

gtcaagggac agcaagttag caacaagggt gggcttgaaa acagccaggc ctctgacagc 5640

ttgatcccaa gttctttccc ttttcagtcc accatagcag ttttctccta acacgaggaa 5700

acaaataccc gtggtctttc cctttctcct tttgggcctt tgctccccat agactcctac 5760

ccaaaaggct gctgccattt gggaatgaag tgttccgagt tttcagcaca ttctccttct 5820

ctgccagatg aaagccagtc tctgagtctc tgtggcatgg tttgggaaca caggaagggt 5880

accgattacc acaagcaacc atggcaggcc aagatctcag tcattgtaag cacagaatcc 5940

cagtagtggg gacttggggg aggtgaggtc aaggtgaaat gggagtaggg gaaggaaaaa 6000

atggccataa gagatggtgg tttgtgaaag ttgagctttc cctctctact gttgtgtccc 6060

cagcgccctt caaagggaca cgagagctgt atgggggctg tggtgtctga gtactttgtg 6120

ctgacagcag cacattgttt cactgtggat gacaaggaac actcaatcaa ggtcagcgta 6180

ggtaaggatg caactgaagg tcctgggctg cacctatgct ctccaggcaa cacctcccac 6240

tttctacaga tcctacactc cacccatcct caatgcagcc ccattccttg caccccagac 6300

cagtcaggga tgggggaaga cgtgaagtta ggaatgacac ggggccagag gcaggaagct 6360

gcccacaaag aggtggtacc tactctccta cttcaggagg ggagaagcgg gacctggaga 6420

tagaagtagt cctatttcac cccaactaca acattaatgg gaaaaaagaa gcaggaattc 6480

ctgaatttta tgactatgac gttgccctga tcaagctcaa gaataagctg aaatatggcc 6540

agactatcag gtgagagcgt ccagatccct gaggaaaggc tgggaaaggc tggaggactg 6600

gggtgaggag caggcctggt ttgctgttct ccttgtcctt tataggccca tttgtctccc 6660

ctgcaccgag ggaacaactc gagctttgag gcttcctcca actaccactt gccagcaaca 6720

aagtaagaca tacttggcaa gaggataagg atgagatccc aagagacaag tggggcatga 6780

gagggaggtg caataggaag agatgatgcc tggcccagaa cctagctcta gaagggctta 6840

ggggacatct actgagtgac aaaggcaatg gggagatgac agtggtggga gcagctgaag 6900

tgacgcagtc tattcgtcca gaggaagagc tgctccctgc acaggatatc aaagctctgt 6960

ttgtgtctga ggaggagaaa aagctgactc ggaaggaggt ctacatcaag aatggggata 7020

aggtgagaaa cgggcatcct aaggaggcac tctaggcccc aatccttcct aagccacttc 7080

tgttcattac ttctccatgc ttcccacctc ccctacagaa aggcagctgt gagagagatg 7140

ctcaatatgc cccaggctat gacaaagtca aggacatctc agaggtggtc acccctcggt 7200

tcctttgtac tggaggagtg agtccctatg ctgaccccaa tacttgcaga ggtgagagaa 7260

tgctctttgg ttgtgctaca agtgcccaag gcccaacagt ccttttctct acagcttctc 7320

ctctccttgc aggtgattct ggcggcccct tgatagttca caagagaagt cgtttcattc 7380

aagtgagtcc tccctttcct atctggggag atgccaagtg gtcagcatgg gccccaaagc 7440

-continued

aggaaagctc aatgcatgtg gctagtaatt cgaggtaggc agagcctgcc tcaccttagg 7500

accgcatgtc ttgcctgcgt gtgtcaagaa cgaggctgag ctgggtccct agtctgattc 7560

ctttaggtca gctaagacac aagcaggaac agccatgctt ccaggattag gaattctact 7620

gaatgatcca tggcacccca ctgcctctgc aggttggtgt aatcagctgg ggagtagtgg 7680

atgtctgcaa aaaccagaag cggcaaaagc aggtacctgc tcacgcccga gactttcaca 7740

tcaacctctt tcaagtgctg ccctggctga aggagaaact ccaagatgag gatttgggtt 7800

ttctataagg ggtttcctgc tggacagggg cgtgggattg aattaaaaca gctgcgacaa 7860

cacctgtgtt ccagatcctt ttggggcaag ggagtgggga acaggcactg gccatgttgt 7920

tacactgaga tcaaacctga cagccgtttt taaaggttta accccaatcc caagtgctga 7980

aaaaccagag gctgagggag atgtgtaagc ttccacctca gtgttttact gagaccagca 8040

ttggggcata tgaggcacaa ggaatccagc tctgttccct agaagccatc cacaaggttt 8100

tccttgtaga cgtcatcact gtagacaatc tgggtcctct tgtcccggtg gcaaccctta 8160

gggctgttct ggacagctag ggagggagga gaggaacagt taaggtctaa aggagatcat 8220

agaacagacc ctgaggctga ctcctgacca cctcactcct ggccactggc ccctggaagc 8280

ccagtttcca cgctgccctc tggtggccag gatggcctgt cttccttagc tcctttgtgc 8340

caacccatgg ccaagaaaag tataagtgga cattttgatg aatgttttgt tcttagaaaa 8400

atcccaaatg tcattgttga gacacgtgaa tgatattaac ccactactta cagtcagtat 8460

gtcagaagct aaaaactaga aaacctctgt agccctttt tgacatgctg gtcaattcta 8520

gttccttct tttgcctgaa gggccactgt agctgagccc ttctttctgc tcactccttt 8580

cccaggaaaa tctactttca gggaaaatgg attattcaca ctaagaaatg ctactagctc 8640

caccagaact cattcagggt gtagctttgg ccctcaccat tctctctcaa gcctctagct 8700

gtttcttccc cttcctcttt cctccctcca ccagacatgt tactctcttc accccatcca 8760

atggttccat ccccaccacc cttgagctac agagaatctc tctcacccac tcccatcctg 8820

tgatctctgt gcctcaacac tgctggctac tccctctttc tcaaagtgtg tgtccttttg 8880

cttcagtggc ccaggcccct gcggtgctgc tcccagccct ccgacccctc ctcctgtctc 8940

ctttgctaac gttaggctca acgttagcct aacatgtcag gacagctggg gacatgtggg 9000

g 9001

<210> SEQ ID NO 3
<211> LENGTH: 9001
<212> TYPE: DNA
<213> ORGANISM: Macaca mulatta

<400> SEQUENCE: 3

gatggaatct tgctctgtct cccacactgg agtgcagtgg cacgatcttg gctcactgcg 60

acttctgcct cccagattta agtgattctc ctacctcggc ctcccaagta gctgggatta 120

taggtgcttg ccaccacatg cagctaattt ttgtatttttt agtagagaca ggattccgcc 180

atgttggcca ggatggtctt gaactcctga cctcaagtga ttcgcccacc tcagcctccc 240

aaactgctgg gattacaggc gtgagccatt gcacccagtc aggtctgctt attcttccct 300

tctctctggt tccaccccta cggcagtgga caagctgtgc cgaggtcgtc tcccaagaaa 360

aaaccatgtt ccccaacttg acagatgtca gggaggtggt gacagaccag tttctatgca 420

-continued

gtgggaccca ggaggatgag agtccctgca agggtgagtc cctcaccatg cctggattcc 480

caaaggggaa ggccacctgt gtctctgtgg ccagggtgca tgccagaaca ccagtccact 540

gccctgtatg acgctgtctc ctgtcaccct ttgctggcag gagaatctgg gggagcagtt 600

ttccttgagc ggagattcag gttttttcag gtgagaaggt ggaagcttgc aggacccagg 660

ggttacagga tgtcagcctt gttgggggga tgagggaggc ctttgaggga tctagggagg 720

ttggggctta cagctggagc tgtggcagcc tcccagccag ttctctcctt ttctccaggt 780

gggtctggtg agctggggtc tttacaaccc ctgccttggc tctgctgaca aaaactcccg 840

caaaagggcc cctcgtagca aggtcccgcc gccacgagac tttcacatca atctcttccg 900

catgcagccc tggctgaggc agcacctggg ggatgtcctg aatttttttac ccctttagtc 960

atggccactg agccctctgc tgtcctgtta gaatccgccc cccctccatc ttctacctct 1020

gaatgcccac ccttagactc tgtgacccat gctgtctcct agttgagtaa atctgggtct 1080

ctaggatgcc aggggcagcg cacacaagct gggaaatcct cagggctcct accagcggga 1140

ctgcctcgct gccccacctc ccgctccttg gcctgtcccc aaattcctcc cctggttgac 1200

ttgactcatg ctcatttcac tttcatatgg aatttcccag ttatgaaatt aataaaaatc 1260

agtggtttcc acatctgtct gtgactctat ctggaggcca ggtagggctg gcctgggggg 1320

aaggggaggc cagaatgact ccaagagcca caggaaggca ggtcagagac cccactggac 1380

aaacagtggc tggactctgt accataacac acaagcaaca ggggagtgag ctggatcctt 1440

atttctggtc cctaagtggg tggtctgggc ttgctgggga ggagctgagg ccagaaggag 1500

gtactgaagg ggagagtcct ggaccttggg cagcaaaggg tgggacttct gcagtttctg 1560

cttccttgac tggcagctca gcggggccct cccgcttgga tgttccggga aagtgatgag 1620

ggtaggacag gcggggcaag ctgcaggtgc cagaacacag attgcataaa aggccgggag 1680

ctggtggggg gcaggggaag ggaatgtgac caggtctagg tctggagttt cagcttggac 1740

actgagctaa gtagacaagc aaaacaagcc aggacacgcc atcctgcccc aggcccagct 1800

tctctcctgc cttctaacgc catggggagc agtctcagcc cccagctcta cctgatgccc 1860

ttcatcttgg gcctcttatc tggaggtaag tgagggtaac cttcccttcc tgctgtcccc 1920

agcatccctc cttggccttt tggggccagg cttcatcagc ctttctcttc aggtgtgacc 1980

accactccat tgtcttcggc ccagcctcaa ggatcctgct ctctggaggg ggtagagatc 2040

aaaggtggct ccttccgact tctccaagag ggccaggcac tggaatacgt gtgtccttct 2100

ggcttctacc cgtaccctgt gcagacacgt acctgcagat ccacggggtc ctggagcacc 2160

ctgcagactc aagatcgaaa aactgtcaag aaggcagagt gcagaggttt gagggcaatg 2220

agtgtgggca gtggcctaag ggagaaacag ggcagatggc agcaaggtca ggactaggat 2280

gagactaggc agggtgacaa ggtgggctga ccaggagtag gagcagtttt agggttgtag 2340

agggaaagga agggaaaaaa aaaggggagt taacctttag taagcattta ccctgggctt 2400

ccacgcagcc ctggaagtca agagaacact cagcaatggg gagggaggag cagcggaaac 2460

ccctatgggt tgaagggtag gtaagatgca gcttctgcag gactgggaat gctctgtttc 2520

tcagtgacct ggtctctgag accaggaggg aaacacctaa ggcagccttt ccctcttaat 2580

gacttctact tctcccctct tctcaaagca atccgctgtc cacgaccaca ggacttcgag 2640

aacggggaat accggccccg gtctccctac tacaatgtga gtgatgagat ctctttccac 2700

-continued

tgctatgacg gttacactct ccggggctct gccaatcgca cctgccaagt gaatggccgg 2760

tggagtgggc agacagcgat ctgtgacaac ggaggtgaga agcatcctct ccccccacat 2820

tgctgtctcc ctgacagcgc ctagcctgag gagtgggcat ttgcccccgg acactgtaac 2880

tcttgctctc taccttgccc tcggggcctc aggcttcagc gcttacctcc atgtctcatg 2940

cctctgcagc ggggtactgc tccaacccag gcatccccat tggcacaagg aaggtgggca 3000

gccggtaccg ccttgaagac agcgtcacct accactgcag ccgggggctt accctgcgtg 3060

gctcccagcg gcgaacatgt caggaaggtg gctcttggag cgggacggag ccttcctgcc 3120

aaggtgaccc ttgacctgta cccccaggtc agatcctgat cttgcatcct actgtcttct 3180

ctccccacct caaccctgct ctttcctcac ttcttttaaa ccttcctcta gaactgtctc 3240

acttctgagc cttttctacc ctggaaaccc acaatcccct gtctctttgg tcactgtgtc 3300

cctgacactc ccagacattt gacctcattt ctgactctcc cagactcctt catgtacgac 3360

acccctcaag aggtggccga agctttcctg tcttccctga cggagaccat agaaggagtc 3420

gatgccgagg atgggcacag cccaggtttg aaggcagaga ggggaggcaa ggcagggaac 3480

tgggggaaaa tggagaaggg acaagataat cgttcatgct ggagcctgag tcactctcct 3540

ggcacccagg ggaacaacag aagcggagga tcatcctaga cccttcaggc tccatgaaca 3600

tctacctggt gctagatgga tcagacagca ttggggccgg caacttcaca ggagccaaaa 3660

agtgtctagt caacttaatt gagaaggtgg agtcctccta tccctgaact tgggggaatg 3720

gaatcttgct gatcttccag gactagctcc ctgatcattc cagcccctct gaaccgcagg 3780

gccccaggaa agtctccagg tcctattctg tcctccttcc cttgtacttg attcctccat 3840

gaacctgtgc ttgagcctct tcctaagagc ctccctgtcc cagcaacgtt gctgaagtct 3900

cccaatcaca gtattctact ttcaatgcca tggcgccttg ttctcctcac ccacaggtgg 3960

caagttatgg tgtgaagcca agatatgctc tagtgacata tgccacatac cccagaattt 4020

gggtcaaagt gtctgaccaa gagagcagca atgcagactg ggtcacgaag aagctcagtg 4080

aaatcaatta tgaaggtcag aggttaggga atggtgggag gttcactttg gggtcaggag 4140

gttcaggagt gttgtgtgga gggggtcatg agactacctt gagggcaaca gggggaccac 4200

tttgtagtca aaggttgaac agcaggatca ttgggcaatg gaggttagtg ggaacctgct 4260

gagggctgga agggccactt tgtggtcaaa gggaagtcca tatgatgatt aacttaaaaa 4320

gttgaagatg tgagatttca gttgcagatt ggtctctggg gttaaaagat ggcttggaag 4380

accaggtgag gcgatgctct cttccctccc cacagaccac aagttgaagt cagggactaa 4440

caccaagagg gccctccagg cagtgtacag catgatgagt tggccagagg acatccctcc 4500

tgaaggctgg aaccgcaccc gccatgtcat catcctcatg accgatggtc agaagggacc 4560

tctctcctgt cccagcctcc ccaccttctc agaccagcat gtggccctta agtccacttg 4620

taacactata cccatggttg gggccctgaa tgtgactcgt aactggctgt tcatctctcc 4680

tgtgaccctt cataaagaat tattcctaaa gccctgtgat caactacctc taacccttcc 4740

tcaacttact caccctgcca cgtgtatcac tgcctctagc caatttatct tatctcctac 4800

cctcatggtc ccgtctcttc tgcaggattg cacaacatgg gcggggaccc aattactgtc 4860

attgatgaga tccgggactt gttatacatc ggcaaggatc gtaaaaaccc gagggaggat 4920

tatctgggtg agtaacctgc ctaggaccca gcaccctact tcctcagggc ttggaccgtc 4980

-continued

atccttcctt tttctccctc agatgtctat gtgtttgggg ttggaccttt ggtggaccaa 5040

gtgaacatca atgctttggc ttccaagaaa gacaatgagc aacatgtgtt caaagtcaag 5100

gatatggaaa acctggaaga cgttttcttc caaatgattg gtaggcagac acaagggaat 5160

caagaacgca actctcctca gcttcccctg aaataattca ttcttcctct acccctgaag 5220

ctctagttgc ctggaaagcc ttcttcattc ctccttctct acctcagtat cactattctt 5280

gtttcctggc actgtttgct tcttaacctt agaatcacag agctctaggc acttcagaga 5340

tctttctatt gtcctacatt tgacacatgt ggaaacaaag gccaaaggag gtcaaggggc 5400

agcaagctag caacagggct gggcttgaaa acagccaggc ctctgatagc ttgatcccaa 5460

gttctttccc ttttcactcc accacagcag ttttctccta acacgaggaa acaaatacct 5520

gtggcctttc cctttctcct tttgggcctc tgccccccac agacttctac ccaaaggctg 5580

ctgccgtttg ggaatgaagt gttccaagtt ttcagcacat tctccttctc tgccagatga 5640

aagccagtct ctgagtctct gtggcatggt ttgggaacac agcaagggta ccgattacca 5700

caagcaacca tggcaggcca agatctcagt cactgtaagc acagaatccc agtagtgagg 5760

acttgggggа ggtgaggtca aggtgaaatg ggagtagggg aagggcaaaa tggccgtaag 5820

agatggtggt ttgtgaaagt tgagttttcc ctttctactg ttctgttccc agcgcccttc 5880

gaagggacat gagagctgta tgggggctgt ggtgtctgag tactttgtgc tgacagcagc 5940

acattgtttt actgtggacg acaaggaaca ctcaatcaag gtcagcgtgg gtaaggatgc 6000

aactgaaggt cccgggctgc acctacgccc tccaggcaac acctcccact ttctacagat 6060

cccacactcc actcatctgc aatgcagccc catcccttgc accccagacc agtcagggat 6120

ggggaagact tgaagttagg aatgacatgg ggccagaggc aagaagctgc ccacaaagag 6180

gtggtaccta ttctcctact tcaagggaag aagcgggacc tggagataga aaaagtccta 6240

tttcaccccg actacaacat tagcgagaaa aaagaagcag gaattcctga attttatgac 6300

tatgacgttg ccctgatcaa gctcaagaat aagttgaatt atgacccgac tatcaggtga 6360

gagcatccag atccctgagg aaaggctggg aaaggctgga ggactggggt gaggagcagg 6420

cctagtttgc tgttctttct ccatccttta taggcccatt tgtctcccct gcaccgaggg 6480

aacaactcga gctttgaggc ttcctccaac taccacttgc cagcaacaga gtaagacata 6540

ctaggggggа ggataaggat gagatcccga gacaagtgag gcatgagagg gagatgcaat 6600

aggaagagac gatgcctggc ccagaaccta gcactaggaa gggcttaggg gacatctgct 6660

gagtgacaaa gtcaataggg agatgacagt ggtgggagca gctgaagtga tgcagtctat 6720

ttgtccagag gaagagctgc tccctgcaca ggatatcaaa gctctgtttg tgtctgagga 6780

ggagaagaag ctgactcgga aggaggtcta catcaagaat ggggataagg tgagaaatgg 6840

gcatcctaag gaggcactct aggccctaat ccttcctaag ccacctctgt tcattacctt 6900

tctccatgct tcccacctcc cctacagaaa ggcagctgtg agagagatgc tcaatatgcc 6960

ccaggctatg acaaagtcaa ggacatctcg gaggtggtca cccctcggtt cctttgtact 7020

ggaggagtga gtccctatgc tgaccccaat acttgcagag gtgagagaac gctctctggt 7080

tgtgctccaa gtgcccgagg gccaagagtc cttttcccta cagcttctcc tctccttgca 7140

ggtgattctg gcggcccctt gatagttcac aagagaagtc gtttcattca agtgagtcct 7200

ccctttccta tctggggaga tgccaagtgg tcagcatggg ccccaaagca ggaaagcaca 7260

-continued

atgcatgtgg ctagtaattc gaggtgggca gagcctgcct cactttagga ctgcatgtct 7320

ggcctgtgtg tgtcaagaat gaggctgagc tgggtcccta gcctgattcc tttaggtcag 7380

ctaagacaca atcaggaaca gtcatgcttc caggattagg aattctatga atgatccatg 7440

gcaccccact gcctctgcag gttggtgtca tcagctgggg agtagtggat gtctgcaaaa 7500

accagaagcg gcaaaagcag gtacctgctc acgcccgaga ctttcacgtc aacctcttcc 7560

aagtgctgcc ctggctgaag gagaaactcc aagatgagga tttgggtttt ctctaagggg 7620

tttcctgctg gacaggggcg cgggattgaa ttaaaacagc tgcgacaaca cttgtgttcc 7680

agatcctttt ggggcaaggg agtggggaac gggcactggc catgttgtta cactgagatc 7740

aaacctgaca cccatttta aaggcttaac cccaatccca agtgctgaaa aaccagaggc 7800

tgagggagat atgtaagctt ccacctcagt gttttactga gaccagcatt ggggcatttg 7860

aggcacaagg aatccagctc tgttccctag aagccatcca caaggttttc cttgtagacg 7920

tcatcactgt agacaatctg ggtcctcttg tcccggtggc aacccttagg gctgttctgg 7980

acagctaggg agggaggaga ggaacagtta aggtctaaag gagatcatag atcagaccct 8040

gaggctgact cctgaccacc tcagtcctgg ctgctggccc ctggaaaccc agtttccacg 8100

ctgccctctg gtggccagga tggcctgtct tccttagctc ctttgtgcca acccatggcc 8160

aaggagagtg taagtggaca ttttgatgaa tgttttgttc ttagaaaaat cccaaatgtc 8220

attgttgaga tatatgaatg atattaaccc actacttata gtcagtatgt cagaagctaa 8280

aaactagaaa acctctgtag ccctttattg acatgctggt caactctagt tcctttcttt 8340

tgcctgaaag gccactgttg ctctgagtcc ttctttctgc tcactccttt cccaggaaaa 8400

tctactttca ggtaaatggg ttactcatac taaggaatgc tactagctcc accagaactc 8460

atccagcatg tagctttggc cctcaccatt ctctctcaag cctctagctg tttcttcccc 8520

ttcctctttt cctccctcca ccagacatgt tactctcttc accccatcca aagattccat 8580

ccccaccacc cttgacctag agagaatctc tcccacccac ttctcatcct gtgatctctg 8640

taccttgaca ctgctggcta ctcccctctt ctcaaagcat gtgtcctttc gcttcagtgg 8700

cccaggcccc tctggtgctg ctcccagccc tctgacccct cctcctgtct cctttgctaa 8760

cgttaggctc aacgttagcc taacgtgtca ggagagctgg agacacgtgg ggcgtaaggt 8820

ggacagtcct gtttcctaac atagtccctg agtattcctc aagtctagtc ctgggtcgtt 8880

ttttttctcc gaaatcagtc tccctcatga tcggggagcc accctgtgat gcagatgact 8940

taatctatgt tttcattcct tacctcacac ctgagttcca gacccctaat ttcaaatact 9000

t 9001

<210> SEQ ID NO 4
<211> LENGTH: 4086
<212> TYPE: DNA
<213> ORGANISM: Macaca mulatta

<400> SEQUENCE: 4

atagatatat tagcatcagg gagacagggc aaaggttcca cccttcagct cagtccccag 60

tccctgctta ttatttccct aacagaagac catccccctt gccactccct gggttttctt 120

ctctggcagc aatgaagcag ctgctgagcc agctctggtt ttcgggaagt cagatgacct 180

tttccctccc gcggctctct gcctctcgct gtccctaggg aggacaccat ggacccactg 240

-continued

atggttcttt tttgcctgct gttcctgtac ccaggtccgg cagactcggc tacctcctgc 300

cctcagaacg tgaatatctc tggtggcacc ttcaccctca gccatggctg ggcccctggg 360

agccttctca tctactcctg tccccagggc ctgtacccat ccccagcgtc acggctgtgc 420

aagagcagcg gacagtggca gaccccaaga gccacccggt ctctgactaa ggcggtctgc 480

aaacctggcc actgccccaa ccccggcatt tcgctgggcg cggtgcggac aggctcccgc 540

tttggtcatg gggacaaggt ccgctatcgc tgctcctcga atcttgtgct cacggggtct 600

gcggagcggg agtgccaggg caacggggtc tggagtggaa cggagcccat ctgccgccag 660

ccctactctt atgacttccc tgaggacgtg gcccctgccc tgggcacctc cttctcccac 720

atgcttgggg ccaccaatcc cacccagagg acaaaggatc atgaaaatgg aactgggact 780

aacacctatg cagccctaaa cagtgtctat ctcatgatga acaatcaaat gcaactcctt 840

ggcatgaaaa cgatggcctg gcaggaaatc cgacatgcca tcatccttct gacagatgga 900

aagtccaata tgggtggctc tcccaaaaca gctgttgacc aaatcagaga gatcttgaat 960

atcaaccaga agaggaatga ctatctggac atctatgcca tcggggtggg caagctggat 1020

gtggactgga gagaactgaa tgagctgggg tccaagaagg atggcgagag gcatgccttc 1080

attctgcagg acacaaaggc tctgcaccag gtctttgaac atatgctgga tgtctccaag 1140

ctcacagaca ccatctgcgg ggtggggaac atgtcagcaa acgcctctga ccaagagagg 1200

acaccctggc atgtcactat taagcccaag agccaagaga cctgccgggg agccctcatc 1260

tccgaccaat gggtcctgac agcggctcac tgcttccgcg atggcaacga ccactcccta 1320

tggagggtca atgtgggaga ccccaaatcc cagtggggca aagaattcct tattgagaag 1380

gcagtgattt ccccaggatt tgatgtcttt gccaaaaaga accagggaat cctggagttc 1440

tatggtgatg acatcgccct gctgaagctg gcccagaaag taaagatgtc cacccatgcc 1500

aggcccatct gccttccctg caccatggag gccaatctgg ctctgcggag acctcaaggc 1560

agcacctgta gggaccatga gaatgaactg ctgaacaaac agagtgttcc tgctcatttt 1620

gtcgccttga atgggagcaa actgaacatt aaccttaaga tgggagtgga gtggacaagc 1680

tgtgccgagg tcgtctccca agaaaaaacc atgttcccca acttgacaga tgtcagggag 1740

gtggtgacag accagtttct atgcagtggg acccaggagg atgagagtcc ctgcaagggt 1800

gtgaccacca ctccattgtc ttcggcccag cctcaaggat cctgctctct ggaggggtga 1860

gagatcaaag gtggctcctt ccgacttctc caagagggcc aggcactgga atacgtgtgt 1920

ccttctggct tctacccgta ccctgtgcag acacgtacct gcagatccac ggggtcctgg 1980

agcaccctgc agactcaaga tcgaaaaact gtcaagaagg cagagtgcag agcaatccgc 2040

tgtccacgac cacaggactt cgagaacggg gaataccggc cccggtctcc ctactacaat 2100

gtgagtgatg agatctcttt ccactgctat gacggttaca ctctccgggg ctctgccaat 2160

cgcacctgcc aagtgaatgg ccggtggagt gggcagacag cgatctgtga caacggagcg 2220

gggtactgct ccaacccagg catccccatt ggcacaagga aggtgggcag ccggtaccgc 2280

cttgaagaca gcgtcaccta ccactgcagc cgggggcttа ccctgcgtgg ctcccagcgg 2340

cgaacatgtc aggaaggtgg ctcttggagc gggacggagc cttcctgcca agactccttc 2400

atgtacgaca cccctcaaga ggtggccgaa gctttcctgt cttccctgac ggagaccata 2460

gaaggagtcg atgccgagga tgggcacagc ccaggggaac aacagaagcg gaggatcatc 2520

-continued

ctagaccctt caggctccat gaacatctac ctggtgctag atggatcaga cagcattggg 2580

gccggcaact tcacaggagc caaaaagtgt ctagtcaact taattgagaa ggtggcaagt 2640

tatggtgtga agccaagata tgctctagtg acatatgcca catccccag aatttgggtc 2700

aaagtgtctg accaagagag cagcaatgca gactgggtca cgaagaagct cagtgaaatc 2760

aattatgaag accacaagtt gaagtcaggg actaacacca agagggccct ccaggcagtg 2820

tacagcatga tgagttggcc agaggacatc cctcctgaag gctggaaccg cacccgccat 2880

gtcatcatcc tcatgaccga tggattgcac aacatgggcg gggacccaat tactgtcatt 2940

gatgagatcc gggacttgtt atacatcggc aaggatcgta aaaacccgag ggaggattat 3000

ctggatgtct atgtgtttgg ggttggacct ttggtggacc aagtgaacat caatgctttg 3060

gcttccaaga aagacaatga gcaacatgtg ttcaaagtca aggatatgga aaacctggaa 3120

gacgttttct tccaaatgat tgatgaaagc cagtctctga gtctctgtgg catggtttgg 3180

gaacacagca agggtaccga ttaccacaag caaccatggc aggccaagat ctcagtcact 3240

cgcccttcga agggacatga gagctgtatg ggggctgtgg tgtctgagta ctttgtgctg 3300

acagcagcac attgttttac tgtggacgac aaggaacact caatcaaggt cagcgtggga 3360

gggaagaagc gggacctgga gatagaaaaa gtcctatttc accccgacta caacattagc 3420

gagaaaaaag aagcaggaat tcctgaattt tatgactatg acgttgccct gatcaagctc 3480

aagaataagt tgaattatga cccgactatc aggcccattt gtctcccctg caccgaggga 3540

acaactcgag ctttgaggct tcctccaact accacttgcc agcaacagaa ggaagagctg 3600

ctccctgcac aggatatcaa agctctgttt gtgtctgagg aggagaagaa gctgactcgg 3660

aaggaggtct acatcaagaa tggggataag aaaggcagct gtgagagaga tgctcaatat 3720

gccccaggct atgacaaagt caaggacatc tcggaggtgg tcacccctcg gttccctttgt 3780

actggaggag tgagtcccta tgctgacccc aatacttgca gaggtgattc tggcggcccc 3840

ttgatagttc acaagagaag tcgtttcatt caagttggtg tcatcagctg gggagtagtg 3900

gatgtctgca aaaaccagaa gcggcaaaag caggtacctg ctcacgcccg agactttcac 3960

gtcaacctct tccaagtgct gccctggctg aaggagaaac tccaagatga ggatttgggt 4020

tttctctaag gggtttcctg ctggacaggg gcgcgggatt gaattaaaac agctgcgaca 4080

acactt 4086

<210> SEQ ID NO 5
<211> LENGTH: 2767
<212> TYPE: DNA
<213> ORGANISM: Mus musculus

<400> SEQUENCE: 5

gctccatcac acagtccatg gaaagactga tcttttaaat tgggggtagt ggaggtggtg 60

gtctgtgctt gttaggaggg gtctgggggc taagagggag ctttgaaagg gaagttctgg 120

cccttggtca gtcaagggtg gggctcacat agtttctgtt tcctcagttg gcagttcagc 180

tggggccctc cttcatgaat gttccgggaa gcagtggctg cgtgcgcagg gtaggctggc 240

caggctgcag atgccagagc agattgcata aaaggttagg ggacagtggg aaaggggtgt 300

agccagatcc agcatttggg tttcagtttg gacaggaggt caaataggca cccagagtga 360

cctggagagg gctttgggcc actggactct ctggtgcttt ccatgacaat ggagagcccc 420

-continued

cagctctgcc tcgtcctctt ggtcttaggc ttctcctctg gaggtgtgag cgcaactcca 480

gtgcttgagg cccggcccca agtctcctgc tctctggagg gagtagagat caaaggcggc 540

tcctttcaac ttctccaagg cggtcaggcc ctggagtacc tatgtccctc tggcttctac 600

ccataccccg tgcagactcg aacctgcaga tccacaggct cctggagcga cctgcagacc 660

cgagaccaaa agattgtcca gaaggcggaa tgcagagcaa tacgctgccc acgaccgcag 720

gactttgaaa atggggaatt ctggccccgg tcccccttct acaacctgag tgaccagatt 780

tcttttcaat gctatgatgg ttacgttctc cggggctctg ctaatcgcac ctgccaagag 840

aatggccggt gggatgggca aacagcaatt tgtgatgatg gagctggata ctgtcccaat 900

cccggtattc ctattgggac aaggaaggtg ggtagccaat accgccttga agacattgtt 960

acttaccact gcagccgggg acttgtcctg cgtggctccc agaagcgaaa gtgtcaagaa 1020

ggtggctcat ggagtgggac agagccttcc tgccaagatt ccttcatgta tgacagccct 1080

caagaagtgg ccgaagcatt cctatcctcc ctgacagaga ccatcgaagg agccgatgct 1140

gaggatgggc acagcccagg agaacagcag aagaggaaga ttgtcctaga cccctcgggc 1200

tccatgaata tctacctggt gctagatgga tcagacagca tcggaagcag caacttcaca 1260

ggggctaagc ggtgcctcac caacttgatt gagaaggtgg cgagttacgg ggtgaggcca 1320

cgatatggtc tcctgacata tgctacagtc cccaaagtgt tggtcagagt gtctgatgag 1380

aggagtagcg atgccgactg ggtcacagag aagctcaacc aaatcagtta tgaagaccac 1440

aagctgaagt cagggaccaa caccaagagg gctctccagg ctgtgtatag catgatgagc 1500

tgggcagggg atgccccgcc tgaaggctgg aatagaaccc gccatgtcat catcattatg 1560

actgatggct tgcacaacat gggtggaaac cctgtcactg tcattcagga catccgagcc 1620

ttgctggaca tcggcaggga tcccaaaaat cccagggagg attacctgga tgtgtatgtg 1680

tttggggtcg ggcctctggt ggactccgtg aacatcaatg ccttagcttc caaaaaggac 1740

aatgagcatc atgtgtttaa agtcaaggat atggaagacc tggagaatgt tttctaccaa 1800

atgattgatg aaaccaaatc tctgagtctc tgtggcatgg tgtgggagca taaaaaaggc 1860

aacgattatc ataagcaacc atggcaagcc aagatctcag tcactcgccc tctgaaagga 1920

catgagacct gtatgggggc cgtggtgtct gagtacttcg tgctgacagc agcgcactgc 1980

ttcatggtgg atgatcagaa acattccatc aaggtcagcg tgggggggtca gaggcgggac 2040

ctggagattg aagaggtcct gttccacccc aaatacaata ttaatgggaa aaaggcagaa 2100

gggatccctg agttctatga ttatgatgtg gccctagtca agctcaagaa caagctcaag 2160

tatggccaga ctctcaggcc catctgtctc ccctgcacgg agggaaccac acgagccttg 2220

aggcttcctc agacagccac ctgcaagcag cacaaggaac agttgctccc tgtgaaggat 2280

gtcaaagctc tgtttgtatc tgagcaaggg aagagcctga ctcggaagga ggtgtacatc 2340

aagaatgggg acaagaaagc cagttgtgag agagatgcta caaaggccca aggctatgag 2400

aaggtcaaag atgcctctga ggtggtcact ccacggttcc tctgcacagg aggggtggat 2460

ccctatgctg accccaacac atgcaaagga gattccgggg gccctctcat tgttcacaag 2520

agaagccgct tcattcaagt tggtgtgatt agctggggag tagtagatgt ctgcagagac 2580

cagaggcggc aacagctggt accctcttat gcccgggact tccacatcaa cctcttccag 2640

gtgctgccct ggctaaagga caagctcaaa gatgaggatt tgggttttct ataaagagct 2700

-continued

tcctgcaggg agagtgtgag gacagattaa agcagttaca ataacaaaaa aaaaaaaaaa 2760

aaaaaaa 2767

<210> SEQ ID NO 6
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 6

gctgagctgc cagtcaagga 20

<210> SEQ ID NO 7
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 7

ggccccgctg agctgccagt 20

<210> SEQ ID NO 8
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 8

cggaacatcc aagcgggagg 20

<210> SEQ ID NO 9
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 9

ctttcccgga acatccaagc 20

<210> SEQ ID NO 10
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 10

atctgtgttc tggcacctgc 20

<210> SEQ ID NO 11
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 11

gtcacattcc cttcccctgc 20

-continued

<210> SEQ ID NO 12
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 12

gacctggtca cattcccttc 20

<210> SEQ ID NO 13
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 13

gacctagacc tggtcacatt 20

<210> SEQ ID NO 14
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 14

actccagacc tagacctggt 20

<210> SEQ ID NO 15
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 15

gctgaaactc cagacctaga 20

<210> SEQ ID NO 16
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 16

gtccaagctg aaactccaga 20

<210> SEQ ID NO 17
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 17

ctcagtgtcc aagctgaaac 20

<210> SEQ ID NO 18
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 18

aggagagaag ctgggcctgg 20

<210> SEQ ID NO 19
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 19

gaaggcagga gagaagctgg 20

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

<400> SEQUENCE: 20

gtggtggtca cacctccaga 20

<210> SEQ ID NO 21
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 21

ccctccagag agcaggatcc 20

<210> SEQ ID NO 22
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 22

tctacccccct ccagagagca 20

<210> SEQ ID NO 23
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 23

ttgatctcta ccccctccag 20

<210> SEQ ID NO 24
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 24

tggagaagtc ggaaggagcc 20

<210> SEQ ID NO 25
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 25

ccctcttgga gaagtcggaa 20

<210> SEQ ID NO 26
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 26

gcctggccct cttggagaag 20

<210> SEQ ID NO 27
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 27

tccagtgcct ggccctcttg 20

<210> SEQ ID NO 28
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 28

agaagccaga aggacacacg 20

<210> SEQ ID NO 29
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 29

acgggtagaa gccagaagga 20

<210> SEQ ID NO 30
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 30

cgtgtctgca cagggtacgg 20

-continued

<210> SEQ ID NO 31
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 31

agggtgctcc aggaccccgt 20

<210> SEQ ID NO 32
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 32

ttgctctgca ctctgccttc 20

<210> SEQ ID NO 33
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 33

tattccccgt tctcgaagtc 20

<210> SEQ ID NO 34
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 34

cattgtagta gggagaccgg 20

<210> SEQ ID NO 35
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 35

cactcacatt gtagtaggga 20

<210> SEQ ID NO 36
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 36

tctcatcact cacattgtag 20

<210> SEQ ID NO 37
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 37

aagagatctc atcactcaca 20

<210> SEQ ID NO 38
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 38

agtggaaaga gatctcatca 20

<210> SEQ ID NO 39
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 39

catagcagtg gaaagagatc 20

<210> SEQ ID NO 40
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 40

aaccgtcata gcagtggaaa 20

<210> SEQ ID NO 41
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 41

gagtgtaacc gtcatagcag 20

<210> SEQ ID NO 42
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 42

cccggagagt gtaaccgtca 20

<210> SEQ ID NO 43
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 43

cagagccccg gagagtgtaa 20

<210> SEQ ID NO 44
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 44

gattggcaga gccccggaga 20

<210> SEQ ID NO 45
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 45

aggtgcgatt ggcagagccc 20

<210> SEQ ID NO 46
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 46

cttggcaggt gcgattggca 20

<210> SEQ ID NO 47
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 47

cattcacttg gcaggtgcga 20

<210> SEQ ID NO 48
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 48

atcgctgtct gcccactcca 20

<210> SEQ ID NO 49
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 49

tcacagatcg ctgtctgccc 20

-continued

<210> SEQ ID NO 50
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 50

ccgttgtcac agatcgctgt 20

<210> SEQ ID NO 51
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 51

cccgctccgt tgtcacagat 20

<210> SEQ ID NO 52
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 52

cagtaccccg ctccgttgtc 20

<210> SEQ ID NO 53
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 53

ttggagcagt accccgctcc 20

<210> SEQ ID NO 54
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 54

accttccttg tgccaatggg 20

<210> SEQ ID NO 55
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 55

ctgcccacct tccttgtgcc 20

<210> SEQ ID NO 56
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 56

cgctgtcttc aaggcggtac 20

<210> SEQ ID NO 57
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 57

gctgcagtgg taggtgacgc 20

<210> SEQ ID NO 58
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 58

cccccggctg cagtggtagg 20

<210> SEQ ID NO 59
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 59

ggtaagcccc cggctgcagt 20

<210> SEQ ID NO 60
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 60

acgcagggta agcccccggc 20

<210> SEQ ID NO 61
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 61

ggagccacgc agggtaagcc 20

<210> SEQ ID NO 62
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 62

gccgctggga gccacgcagg 20

<210> SEQ ID NO 63
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 63

caagagccac cttcctgaca 20

<210> SEQ ID NO 64
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 64

ccgctccaag agccaccttc 20

<210> SEQ ID NO 65
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 65

tccgtcccgc tccaagagcc 20

<210> SEQ ID NO 66
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 66

gaaggctccg tcccgctcca 20

<210> SEQ ID NO 67
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 67

tggcaggaag gctccgtccc 20

<210> SEQ ID NO 68
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 68

gagtcttggc aggaaggctc 20

-continued

<210> SEQ ID NO 69
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 69

atgaaggagt cttggcagga 20

<210> SEQ ID NO 70
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 70

cttcggccac ctcttgaggg 20

<210> SEQ ID NO 71
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 71

ggaaagcttc ggccacctct 20

<210> SEQ ID NO 72
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 72

aagacaggaa agcttcggcc 20

<210> SEQ ID NO 73
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 73

tcagggaaga caggaaagct 20

<210> SEQ ID NO 74
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 74

tcgactcctt ctatggtctc 20

<210> SEQ ID NO 75
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 75

cttctgttgt tcccctgggc 20

<210> SEQ ID NO 76
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 76

ttcatggagc ctgaagggtc 20

<210> SEQ ID NO 77
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 77

tagatgttca tggagcctga 20

<210> SEQ ID NO 78
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 78

accaggtaga tgttcatgga 20

<210> SEQ ID NO 79
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 79

tctagcacca ggtagatgtt 20

<210> SEQ ID NO 80
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 80

gatccatcta gcaccaggta 20

<210> SEQ ID NO 81
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 81

ctgtctgatc catctagcac 20

<210> SEQ ID NO 82
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 82

ccaatgctgt ctgatccatc 20

<210> SEQ ID NO 83
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 83

tttggctcct gtgaagttgc 20

<210> SEQ ID NO 84
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 84

acacttttg gctcctgtga 20

<210> SEQ ID NO 85
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 85

gactagacac tttttggctc 20

<210> SEQ ID NO 86
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 86

taagttgact agacactttt 20

<210> SEQ ID NO 87
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 87

ctcaattaag ttgactagac 20

-continued

<210> SEQ ID NO 88
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 88

caccttctca attaagttga 20

<210> SEQ ID NO 89
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 89

acttgccacc ttctcaatta 20

<210> SEQ ID NO 90
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 90

accataactt gccaccttct 20

<210> SEQ ID NO 91
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 91

cttcacacca taacttgcca 20

<210> SEQ ID NO 92
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 92

tcttggcttc acaccataac 20

<210> SEQ ID NO 93
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 93

atgtggcata tgtcactaga 20

<210> SEQ ID NO 94
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 94

cagacacttt gacccaaatt 20

<210> SEQ ID NO 95
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 95

ggtcttcata attgatttca 20

<210> SEQ ID NO 96
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 96

acttgtggtc ttcataattg 20

<210> SEQ ID NO 97
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 97

acttcaactt gtggtcttca 20

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

<400> SEQUENCE: 98

tccctgactt caacttgtgg 20

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

<400> SEQUENCE: 99

tgttagtccc tgacttcaac 20

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

-continued

<400> SEQUENCE: 100

tcttggtgtt agtccctgac 20

<210> SEQ ID NO 101
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 101

tgtacactgc ctggagggcc 20

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

<400> SEQUENCE: 102

tcatgctgta cactgcctgg 20

<210> SEQ ID NO 103
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 103

gttccagcct tcaggaggga 20

<210> SEQ ID NO 104
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 104

ggtgcggttc agccttcag 20

<210> SEQ ID NO 105
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 105

atggcgggtg cggttccagc 20

<210> SEQ ID NO 106
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 106

gatgacatgg cgggtgcggt 20

-continued

<210> SEQ ID NO 107
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 107

gaggatgatg acatggcggg 20

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

<400> SEQUENCE: 108

cccatgttgt gcaatccatc 20

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

<400> SEQUENCE: 109

tccccgccca tgttgtgcaa 20

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

<400> SEQUENCE: 110

attgggtccc cgcccatgtt 20

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

<400> SEQUENCE: 111

acagtaattg ggtccccgcc 20

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

<400> SEQUENCE: 112

tcaatgacag taattgggtc 20

<210> SEQ ID NO 113
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 113

atctcatcaa tgacagtaat 20

<210> SEQ ID NO 114
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 114

tcccggatct catcaatgac 20

<210> SEQ ID NO 115
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 115

acatccagat aatcctccct 20

<210> SEQ ID NO 116
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 116

acatagacat ccagataatc 20

<210> SEQ ID NO 117
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 117

ccaaacacat agacatccag 20

<210> SEQ ID NO 118
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 118

agcattgatg ttcacttggt 20

<210> SEQ ID NO 119
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 119

agccaaagca ttgatgttca 20

<210> SEQ ID NO 120
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 120

cttggaagcc aaagcattga 20

<210> SEQ ID NO 121
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 121

gtctttcttg gaagccaaag 20

<210> SEQ ID NO 122
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 122

ctcattgtct ttcttggaag 20

<210> SEQ ID NO 123
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 123

atgttgctca ttgtctttct 20

<210> SEQ ID NO 124
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 124

gaacacatgt tgctcattgt 20

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

<400> SEQUENCE: 125

gactttgaac acatgttgct 20

-continued

<210> SEQ ID NO 126
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 126

atccttgact ttgaacacat 20

<210> SEQ ID NO 127
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 127

ttccatatcc ttgactttga 20

<210> SEQ ID NO 128
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 128

caggttttcc atatccttga 20

<210> SEQ ID NO 129
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 129

ctcagagact ggctttcatc 20

<210> SEQ ID NO 130
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 130

cagagactca gagactggct 20

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

<400> SEQUENCE: 131

atgccacaga gactcagaga 20

<210> SEQ ID NO 132
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 132

caaaccatgc cacagagact 20

<210> SEQ ID NO 133
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 133

tgttcccaaa ccatgccaca 20

<210> SEQ ID NO 134
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 134

ttgtggtaat cggtaccctt 20

<210> SEQ ID NO 135
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 135

ggttgcttgt ggtaatcggt 20

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

<400> SEQUENCE: 136

tgccatggtt gcttgtggta 20

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

<400> SEQUENCE: 137

ttggcctgcc atggttgctt 20

<210> SEQ ID NO 138
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 138

gagatcttgg cctgccatgg 20

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

<400> SEQUENCE: 139

acagccccca tacagctctc 20

<210> SEQ ID NO 140
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 140

gacaccacag cccccataca 20

<210> SEQ ID NO 141
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 141

tactcagaca ccacagcccc 20

<210> SEQ ID NO 142
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 142

acaaagtact cagacaccac 20

<210> SEQ ID NO 143
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 143

gtcagcacaa agtactcaga 20

<210> SEQ ID NO 144
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 144

ttgattgagt gttccttgtc 20

-continued

<210> SEQ ID NO 145
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 145

ctgaccttga ttgagtgttc 20

<210> SEQ ID NO 146
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 146

tatctccagg tcccgcttct 20

<210> SEQ ID NO 147
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 147

gaattcctgc ttctttttc 20

<210> SEQ ID NO 148
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 148

attcaggaat tcctgcttct 20

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

<400> SEQUENCE: 149

cataaaattc aggaattcct 20

<210> SEQ ID NO 150
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 150

catagtcata aaattcagga 20

<210> SEQ ID NO 151
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 151

tgagcttgat cagggcaacg 20

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

<400> SEQUENCE: 152

tattcttgag cttgatcagg 20

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

<400> SEQUENCE: 153

gacaaatggg cctgatagtc 20

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

<400> SEQUENCE: 154

gttgttccct cggtgcaggg 20

<210> SEQ ID NO 155
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 155

gctcgagttg ttccctcggt 20

<210> SEQ ID NO 156
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 156

ctcaaagctc gagttgttcc 20

<210> SEQ ID NO 157
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 157

ggaagcctca aagctcgagt 20

<210> SEQ ID NO 158
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 158

gttggaggaa gcctcaaagc 20

<210> SEQ ID NO 159
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 159

gtggtagttg gaggaagcct 20

<210> SEQ ID NO 160
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 160

tggcaagtgg tagttggagg 20

<210> SEQ ID NO 161
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 161

tgttgctggc aagtggtagt 20

<210> SEQ ID NO 162
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 162

tccagctcac tcccctgttg 20

<210> SEQ ID NO 163
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 163

taaggatcca gctcactccc 20

-continued

<210> SEQ ID NO 164
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 164

cagaaataag gatccagctc 20

<210> SEQ ID NO 165
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 165

agggaccaga aataaggatc 20

<210> SEQ ID NO 166
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 166

ccacttaggg accagaaata 20

<210> SEQ ID NO 167
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 167

tccaggactc tccccttcag 20

<210> SEQ ID NO 168
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 168

aagtcccacc ctttgctgcc 20

<210> SEQ ID NO 169
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 169

ctgcagaagt cccacccttt 20

<210> SEQ ID NO 170
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 170

cagaaactgc agaagtccca 20

<210> SEQ ID NO 171
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 171

aacctctgca ctctgccttc 20

<210> SEQ ID NO 172
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 172

ccctcaaacc tctgcactct 20

<210> SEQ ID NO 173
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 173

tcattgccct caaacctctg 20

<210> SEQ ID NO 174
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 174

ccacactcat tgccctcaaa 20

<210> SEQ ID NO 175
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 175

cactgcccac actcattgcc 20

<210> SEQ ID NO 176
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 176

ttaggccact gcccacactc 20

<210> SEQ ID NO 177
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 177

ctagtcctga ccttgctgcc 20

<210> SEQ ID NO 178
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 178

ctcatcctag tcctgacctt 20

<210> SEQ ID NO 179
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 179

cctagtctca tcctagtcct 20

<210> SEQ ID NO 180
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 180

accctgccta gtctcatcct 20

<210> SEQ ID NO 181
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 181

cttgtcaccc tgcctagtct 20

<210> SEQ ID NO 182
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 182

gcccaccttg tcaccctgcc 20

-continued

<210> SEQ ID NO 183
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 183

cctaaaactg ctcctactcc 20

<210> SEQ ID NO 184
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 184

gagtcagaaa tgaggtcaaa 20

<210> SEQ ID NO 185
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 185

ccctactccc atttcacctt 20

<210> SEQ ID NO 186
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 186

tgttgtgcaa tcctgcagaa 20

<210> SEQ ID NO 187
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 187

aaaggctgat gaagcctggc 20

<210> SEQ ID NO 188
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 188

cctttgacca caaagtggcc 20

<210> SEQ ID NO 189
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 189

aggtaccacc tctttgtggg 20

<210> SEQ ID NO 190
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 190

tggtggtcac acctgaagag 20

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

<400> SEQUENCE: 191

gcagggagca gctcttcctt 20

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

<400> SEQUENCE: 192

tcctgtgcag ggagcagctc 20

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

<400> SEQUENCE: 193

ttgatatcct gtgcagggag 20

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

<400> SEQUENCE: 194

agagctttga tatcctgtgc 20

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

-continued

<400> SEQUENCE: 195

acaaacagag ctttgatatc 20

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

<400> SEQUENCE: 196

tcagacacaa acagagcttt 20

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

<400> SEQUENCE: 197

tcctcctcag acacaaacag 20

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

<400> SEQUENCE: 198

acctccttcc gagtcagctt 20

<210> SEQ ID NO 199
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 199

atgtagacct ccttccgagt 20

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

<400> SEQUENCE: 200

ttcttgatgt agacctcctt 20

<210> SEQ ID NO 201
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 201

tccccattct tgatgtagac 20

-continued

<210> SEQ ID NO 202
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 202

ttcttatccc cattcttgat 20

<210> SEQ ID NO 203
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 203

ctgcctttct tatccccatt 20

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

<400> SEQUENCE: 204

tcacagctgc ctttcttatc 20

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

<400> SEQUENCE: 205

tctctctcac agctgccttt 20

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

<400> SEQUENCE: 206

tgagcatctc tctcacagct 20

<210> SEQ ID NO 207
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 207

gcatattgag catctctctc 20

<210> SEQ ID NO 208
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 208

tgactttgtc atagcctggg 20

<210> SEQ ID NO 209
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 209

tgtccttgac tttgtcatag 20

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

<400> SEQUENCE: 210

cagtacaaag gaaccgaggg 20

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

<400> SEQUENCE: 211

ctcctccagt acaaaggaac 20

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

<400> SEQUENCE: 212

gactcactcc tccagtacaa 20

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

<400> SEQUENCE: 213

catagggact cactcctcca 20

<210> SEQ ID NO 214
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 214

ggtcagcata gggactcact 20

<210> SEQ ID NO 215
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 215

tcacctctgc aagtattggg 20

<210> SEQ ID NO 216
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 216

ccagaatcac ctctgcaagt 20

<210> SEQ ID NO 217
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 217

gggccgccag aatcacctct 20

<210> SEQ ID NO 218
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 218

ctcttgtgaa ctatcaaggg 20

<210> SEQ ID NO 219
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 219

cgacttctct tgtgaactat 20

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

<400> SEQUENCE: 220

atgaaacgac ttctcttgtg 20

-continued

<210> SEQ ID NO 221
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 221

acttgaatga aacgacttct 20

<210> SEQ ID NO 222
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 222

acaccaactt gaatgaaacg 20

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

<400> SEQUENCE: 223

tccactactc cccagctgat 20

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

<400> SEQUENCE: 224

cagacatcca ctactcccca 20

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

<400> SEQUENCE: 225

tttttgcaga catccactac 20

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

<400> SEQUENCE: 226

ttctggtttt tgcagacatc 20

<210> SEQ ID NO 227
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 227

tgccgcttct ggtttttgca 20

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

<400> SEQUENCE: 228

tgcttttgcc gcttctggtt 20

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

<400> SEQUENCE: 229

ggtacctgct tttgccgctt 20

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

<400> SEQUENCE: 230

tgagcaggta cctgcttttg 20

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

<400> SEQUENCE: 231

ttcagccagg gcagcacttg 20

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

<400> SEQUENCE: 232

ttctccttca gccagggcag 20

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

-continued

<400> SEQUENCE: 233

tggagtttct ccttcagcca 20

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

<400> SEQUENCE: 234

tcatcttgga gtttctcctt 20

<210> SEQ ID NO 235
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 235

aaatcctcat cttggagttt 20

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

<400> SEQUENCE: 236

aaacccaaat cctcatcttg 20

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

<400> SEQUENCE: 237

gtccagcagg aaacccctta 20

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

<400> SEQUENCE: 238

gcccctgtcc agcaggaaac 20

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

<400> SEQUENCE: 239

agctgtttta attcaatccc 20

-continued

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

<400> SEQUENCE: 240

aacttgccac ctgtgggtga 20

<210> SEQ ID NO 241
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 241

tcaccttatc cccattcttg 20

<210> SEQ ID NO 242
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 242

tcaactttca caaaccacca 20

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

<400> SEQUENCE: 243

ccgccagaat cacctgcaag 20

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

<400> SEQUENCE: 244

aggaggaatg aagaaggctt 20

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

<400> SEQUENCE: 245

gcctttcctc agggatctgg 20

<210> SEQ ID NO 246
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 246

aaatgtctgg gagtgtcagg 20

<210> SEQ ID NO 247
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 247

gcctagagtg cctccttagg 20

<210> SEQ ID NO 248
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 248

ggcatctccc cagataggaa 20

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

<400> SEQUENCE: 249

agggagctag tcctggaaga 20

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

<400> SEQUENCE: 250

acacctgaag agaaaggctg 20

<210> SEQ ID NO 251
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 251

ccctttgacc acaaagtggc 20

<210> SEQ ID NO 252
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 252

gccctcaagg tagtctcatg 20

<210> SEQ ID NO 253
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 253

aagggaagga ggacagaata 20

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

<400> SEQUENCE: 254

aaaggccaag gagggatgct 20

<210> SEQ ID NO 255
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 255

agaggtccct tctgaccatc 20

<210> SEQ ID NO 256
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 256

gctgggacag gagagaggtc 20

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

<400> SEQUENCE: 257

tcaaatgtct gggagtgtca 20

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

<400> SEQUENCE: 258

agaaggagaa tgtgctgaaa 20

-continued

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

<400> SEQUENCE: 259

tgctgaccac ttggcatctc 20

<210> SEQ ID NO 260
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 260

caactttcac aaaccaccat 20

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

<400> SEQUENCE: 261

agctctgtga ttctaaggtt 20

<210> SEQ ID NO 262
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 262

ccacctgtgg gtgaggagaa 20

<210> SEQ ID NO 263
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 263

gaggactcac ttgaatgaaa 20

<210> SEQ ID NO 264
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 264

tggaatgatc agggagctag 20

<210> SEQ ID NO 265
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 265

gtcccttctc cattttcccc 20

<210> SEQ ID NO 266
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 266

tcaacttttt aagttaatca 20

<210> SEQ ID NO 267
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 267

gggtgaggag aacaaggcgc 20

<210> SEQ ID NO 268
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 268

cttccaagcc atcttttaac 20

<210> SEQ ID NO 269
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 269

aggactcact tgaatgaaac 20

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

<400> SEQUENCE: 270

ttccaggcaa ctagagcttc 20

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

-continued

<400> SEQUENCE: 271

cagagtccag ccactgtttg 20

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

<400> SEQUENCE: 272

ccaacctgca gaggcagtgg 20

<210> SEQ ID NO 273
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 273

tgcaaggaga ggagaagctg 20

<210> SEQ ID NO 274
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 274

ctaggcaggt tactcaccca 20

<210> SEQ ID NO 275
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 275

caccataact tgccacctgt 20

<210> SEQ ID NO 276
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 276

taggtaccac ctctttgtgg 20

<210> SEQ ID NO 277
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 277

cttgacctca cctcccccaa 20

-continued

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

<400> SEQUENCE: 278

ccacctcttt gtgggcagct 20

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

<400> SEQUENCE: 279

ttcacaaacc accatctctt 20

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

<400> SEQUENCE: 280

ttctcacctc cgttgtcaca 20

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

<400> SEQUENCE: 281

gaaagtggga ggtgttgcct 20

<210> SEQ ID NO 282
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 282

acagcaggaa gggaaggtta 20

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

<400> SEQUENCE: 283

catgctgacc acttggcatc 20

<210> SEQ ID NO 284
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 284

ggtcaccttg gcaggaaggc 20

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

<400> SEQUENCE: 285

gtatagtgtt acaagtggac 20

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

<400> SEQUENCE: 286

ggacttccct ttgaccacaa 20

<210> SEQ ID NO 287
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 287

tcaccttgac ctcacctccc 20

<210> SEQ ID NO 288
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 288

tagagtgcct ccttaggatg 20

<210> SEQ ID NO 289
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 289

tgacttcaac ttgtggtctg 20

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

-continued

<400> SEQUENCE: 290

cagagaagga gaatgtgctg 20

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

<400> SEQUENCE: 291

agggagcagc tcttcctctg 20

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

<400> SEQUENCE: 292

tgttcccctg ggtgccagga 20

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

<400> SEQUENCE: 293

ggcctggctg ttttcaagcc 20

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

<400> SEQUENCE: 294

gactggcttt catctggcag 20

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

<400> SEQUENCE: 295

gaaggctttc caggcaacta 20

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

<400> SEQUENCE: 296

tcacttgaat gaaacgactt 20

-continued

<210> SEQ ID NO 297
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 297

ggccccaaaa ggccaaggag 20

<210> SEQ ID NO 298
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 298

aatcacctgc aaggagagga 20

<210> SEQ ID NO 299
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 299

gaccttcagt tgcatcctta 20

<210> SEQ ID NO 300
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 300

tgatgaagcc tggccccaaa 20

<210> SEQ ID NO 301
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 301

tagaaagtgg gaggtgttgc 20

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

<400> SEQUENCE: 302

cccatccctg actggtctgg 20

<210> SEQ ID NO 303
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 303

ccatgggtat agtgttacaa 20

<210> SEQ ID NO 304
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 304

gtgttctctt gacttccagg 20

<210> SEQ ID NO 305
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 305

ggcctgctcc tcaccccagt 20

<210> SEQ ID NO 306
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 306

gaggcctggc tgttttcaag 20

<210> SEQ ID NO 307
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 307

gactctcccc ttcagtacct 20

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

<400> SEQUENCE: 308

catgggtata gtgttacaag 20

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

-continued

<400> SEQUENCE: 309

gaaggagaat gtgctgaaaa 20

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

<400> SEQUENCE: 310

tcacctggtc ttccaagcca 20

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

<400> SEQUENCE: 311

ctccccagat aggaaaggga 20

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

<400> SEQUENCE: 312

ggactcactt gaatgaaacg 20

<210> SEQ ID NO 313
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 313

ggccgccaga atcacctgca 20

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

<400> SEQUENCE: 314

ctcacttgaa tgaaacgact 20

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

<400> SEQUENCE: 315

ctttcccagc ctttcctcag 20

-continued

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

<400> SEQUENCE: 316

agaaagtggg aggtgttgcc 20

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

<400> SEQUENCE: 317

gtcgcagctg ttttaattca 20

<210> SEQ ID NO 318
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 318

ccaggactct ccccttcagt 20

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

<400> SEQUENCE: 319

agggaaggag gacagaatag 20

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

<400> SEQUENCE: 320

gaaatgaggt caaatgtctg 20

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

<400> SEQUENCE: 321

ggagagtcag aaatgaggtc 20

<210> SEQ ID NO 322
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 322

gtagaaagtg ggaggtgttg 20

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

<400> SEQUENCE: 323

tagaaagatc tctgaagtgc 20

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

<400> SEQUENCE: 324

ctgctcctca ccccagtcct 20

<210> SEQ ID NO 325
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 325

ctactgggat tctgtgctta 20

<210> SEQ ID NO 326
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 326

cccaaaaggc caaggaggga 20

<210> SEQ ID NO 327
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 327

tgaccacttg gcatctcccc 20

<210> SEQ ID NO 328
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 328

cctgcaagga gaggagaagc 20

<210> SEQ ID NO 329
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 329

ctctcacctc tgcaagtatt 20

<210> SEQ ID NO 330
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 330

ccccaaaagg ccaaggaggg 20

<210> SEQ ID NO 331
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 331

gtcttccaag ccatctttta 20

<210> SEQ ID NO 332
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 332

gttacaagtg gacttaaggg 20

<210> SEQ ID NO 333
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 333

cccatgttgt gcaatcctgc 20

<210> SEQ ID NO 334
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 334

gaggtgggaa gcatggagaa 20

-continued

<210> SEQ ID NO 335
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 335

tgctcccacc actgtcatct 20

<210> SEQ ID NO 336
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 336

aggcaggtta ctcacccaga 20

<210> SEQ ID NO 337
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 337

tactgggatt ctgtgcttac 20

<210> SEQ ID NO 338
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 338

gcctttccca gcctttcctc 20

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

<400> SEQUENCE: 339

gtgcaatcct gcagaagaga 20

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

<400> SEQUENCE: 340

acaggagaga ggtcccttct 20

<210> SEQ ID NO 341
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 341

cccaaaagga gaaagggaaa 20

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

<400> SEQUENCE: 342

aagcccaggg taaatgctta 20

<210> SEQ ID NO 343
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 343

gatgaagcct ggccccaaaa 20

<210> SEQ ID NO 344
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 344

tggcagagaa ggagaatgtg 20

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

<400> SEQUENCE: 345

ttcccagcct ttcctcaggg 20

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

<400> SEQUENCE: 346

ggcagagaag gagaatgtgc 20

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

-continued

<400> SEQUENCE: 347

acagtgccag gaaacaagaa 20

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

<400> SEQUENCE: 348

taggcaggtt actcacccag 20

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

<400> SEQUENCE: 349

ttctcttgac ttccagggct 20

<210> SEQ ID NO 350
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 350

cctgctcctc accccagtcc 20

<210> SEQ ID NO 351
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 351

tcccactaac ctccattgcc 20

<210> SEQ ID NO 352
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 352

ttccctttga ccacaaagtg 20

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

<400> SEQUENCE: 353

ctgggtccta ggcaggttac 20

-continued

<210> SEQ ID NO 354
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 354

tccaggcaac tagagcttca 20

<210> SEQ ID NO 355
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 355

gcccatgttg tgcaatcctg 20

<210> SEQ ID NO 356
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 356

ggttcccact aacctccatt 20

<210> SEQ ID NO 357
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 357

aggtagagag caagagttac 20

<210> SEQ ID NO 358
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 358

ccactaacct ccattgccca 20

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

<400> SEQUENCE: 359

tcacaaacca ccatctctta 20

<210> SEQ ID NO 360
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 360

tactcaccca gataatcctc 20

<210> SEQ ID NO 361
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 361

tgctcctcac cccagtcctc 20

<210> SEQ ID NO 362
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 362

tctcacagct gcctttctgt 20

<210> SEQ ID NO 363
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 363

gaaagggagg actcacttga 20

<210> SEQ ID NO 364
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 364

ccatctttta accccagaga 20

<210> SEQ ID NO 365
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 365

tcctcacccc agtcctccag 20

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

-continued

<400> SEQUENCE: 366

ctggcagaga aggagaatgt 20

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

<400> SEQUENCE: 367

tctccccaga taggaaaggg 20

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

<400> SEQUENCE: 368

acttcagctg ctcccaccac 20

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

<400> SEQUENCE: 369

gacagcagga agggaaggtt 20

<210> SEQ ID NO 370
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 370

ggagacaaat gggcctataa 20

<210> SEQ ID NO 371
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 371

ctgctcccac cactgtcatc 20

<210> SEQ ID NO 372
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 372

aggaatgaag aaggctttcc 20

-continued

<210> SEQ ID NO 373
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 373

gggatctcat ccttatcctc 20

<210> SEQ ID NO 374
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 374

gtgctgggtc ctaggcaggt 20

<210> SEQ ID NO 375
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 375

caaaaggcca aggagggatg 20

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

<400> SEQUENCE: 376

ccatgctgac cacttggcat 20

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

<400> SEQUENCE: 377

ggaggctggg acaggagaga 20

<210> SEQ ID NO 378
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 378

ggagcagctc ttcctctgga 20

<210> SEQ ID NO 379
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 379

tctcacctcc gttgtcacag 20

<210> SEQ ID NO 380
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 380

cagtcctcca gcctttccca 20

<210> SEQ ID NO 381
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 381

agtcctccag cctttcccag 20

<210> SEQ ID NO 382
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 382

tgaaggagtc tgggagagtc 20

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

<400> SEQUENCE: 383

cagaatcacc tgcaaggaga 20

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

<400> SEQUENCE: 384

taggaaaggg aggactcact 20

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

-continued

<400> SEQUENCE: 385

accttggcag gaaggctccg 20

<210> SEQ ID NO 386
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 386

gagacaaatg ggcctataaa 20

<210> SEQ ID NO 387
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 387

ctgaagagaa aggctgatga 20

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

<400> SEQUENCE: 388

aatgatcagg gagctagtcc 20

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

<400> SEQUENCE: 389

cttagctgac ctaaaggaat 20

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

<400> SEQUENCE: 390

tgggtatagt gttacaagtg 20

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

<400> SEQUENCE: 391

tgaagagaaa ggctgatgaa 20

-continued

<210> SEQ ID NO 392
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 392

gtgttacaag tggacttaag 20

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

<400> SEQUENCE: 393

acctgtgggt gaggagaaca 20

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

<400> SEQUENCE: 394

tcacccagat aatcctccct 20

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

<400> SEQUENCE: 395

tgttgtcgca gctgttttaa 20

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

<400> SEQUENCE: 396

tggtcacatt cccttcccct 20

<210> SEQ ID NO 397
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 397

cctggtcaca ttcccttccc 20

<210> SEQ ID NO 398
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 398

tagacctggt cacattccct 20

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

<400> SEQUENCE: 399

cctagacctg gtcacattcc 20

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

<400> SEQUENCE: 400

ccttccgagt cagctttttc 20

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

<400> SEQUENCE: 401

ctccttccga gtcagctttt 20

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

<400> SEQUENCE: 402

agacctcctt ccgagtcagc 20

<210> SEQ ID NO 403
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 403

gtagacctcc ttccgagtca 20

<210> SEQ ID NO 404
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 404

tttgccgctt ctggtttttg 20

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

<400> SEQUENCE: 405

cttttgccgc ttctggtttt 20

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

<400> SEQUENCE: 406

cctgcttttg ccgcttctgg 20

<210> SEQ ID NO 407
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 407

tacctgcttt tgccgcttct 20

<210> SEQ ID NO 408
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 408

agaaaaccca aatcctcatc 20

<210> SEQ ID NO 409
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 409

tagaaaaccc aaatcctcat 20

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

<400> SEQUENCE: 410

atagaaaacc caaatcctca 20

-continued

<210> SEQ ID NO 411
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 411

tatagaaaac ccaaatcctc 20

<210> SEQ ID NO 412
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 412

ttatagaaaa cccaaatcct 20

<210> SEQ ID NO 413
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 413

cttatagaaa acccaaatcc 20

<210> SEQ ID NO 414
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 414

ccttatagaa aacccaaatc 20

<210> SEQ ID NO 415
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 415

cccttataga aaacccaaat 20

<210> SEQ ID NO 416
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 416

ccccttatag aaaacccaaa 20

<210> SEQ ID NO 417
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 417

acccctttata gaaaacccaa 20

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

<400> SEQUENCE: 418

aacccctttat agaaaaccca 20

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

<400> SEQUENCE: 419

aaacccctta tagaaaaccc 20

<210> SEQ ID NO 420
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 420

gaaacccctt atagaaaacc 20

<210> SEQ ID NO 421
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 421

ggaaacccct tatagaaaac 20

<210> SEQ ID NO 422
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 422

aggaaacccc ttatagaaaa 20

<210> SEQ ID NO 423
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 423

caggaaaccc cttatagaaa 20

<210> SEQ ID NO 424
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 424

gcaggaaacc ccttatagaa 20

<210> SEQ ID NO 425
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 425

agcaggaaac cccttataga 20

<210> SEQ ID NO 426
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 426

cagcaggaaa ccccttatag 20

<210> SEQ ID NO 427
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 427

ccagcaggaa acccccttata 20

<210> SEQ ID NO 428
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 428

tccagcagga aacccccttat 20

<210> SEQ ID NO 429
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 429

tgtccagcag gaaacccctt 20

-continued

<210> SEQ ID NO 430
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 430

ctgtccagca ggaaacccct 20

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

<400> SEQUENCE: 431

cctgtccagc aggaaacccc 20

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

<400> SEQUENCE: 432

ccctgtccag caggaaaccc 20

<210> SEQ ID NO 433
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 433

cccctgtcca gcaggaaacc 20

<210> SEQ ID NO 434
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 434

cgcccctgtc cagcaggaaa 20

<210> SEQ ID NO 435
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 435

acgcccctgt ccagcaggaa 20

<210> SEQ ID NO 436
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 436

cacgcccctg tccagcagga 20

<210> SEQ ID NO 437
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 437

ccacgcccct gtccagcagg 20

<210> SEQ ID NO 438
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 438

cccacgcccc tgtccagcag 20

<210> SEQ ID NO 439
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 439

tcccacgccc ctgtccagca 20

<210> SEQ ID NO 440
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 440

atcccacgcc cctgtccagc 20

<210> SEQ ID NO 441
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 441

aatcccacgc ccctgtccag 20

<210> SEQ ID NO 442
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 442

caatcccacg cccctgtcca 20

<210> SEQ ID NO 443
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 443

tcaatcccac gcccctgtcc 20

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

<400> SEQUENCE: 444

ttcaatccca cgcccctgtc 20

<210> SEQ ID NO 445
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 445

attcaatccc acgcccctgt 20

<210> SEQ ID NO 446
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 446

aattcaatcc cacgcccctg 20

<210> SEQ ID NO 447
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 447

taattcaatc ccacgcccct 20

<210> SEQ ID NO 448
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 448

ttaattcaat cccacgcccc 20

-continued

<210> SEQ ID NO 449
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 449

tttaattcaa tcccacgccc 20

<210> SEQ ID NO 450
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 450

ttttaattca atcccacgcc 20

<210> SEQ ID NO 451
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 451

gttttaattc aatcccacgc 20

<210> SEQ ID NO 452
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 452

tgttttaatt caatcccacg 20

<210> SEQ ID NO 453
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 453

ctgttttaat tcaatcccac 20

<210> SEQ ID NO 454
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 454

gctgttttaa ttcaatccca 20

<210> SEQ ID NO 455
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 455

cagctgtttt aattcaatcc 20

<210> SEQ ID NO 456
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 456

gcagctgttt taattcaatc 20

<210> SEQ ID NO 457
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 457

cgcagctgtt ttaattcaat 20

<210> SEQ ID NO 458
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 458

tcgcagctgt tttaattcaa 20

<210> SEQ ID NO 459
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 459

tgtcgcagct gttttaattc 20

<210> SEQ ID NO 460
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 460

ttgtcgcagc tgttttaatt 20

<210> SEQ ID NO 461
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 461

gttgtcgcag ctgttttaat 20

<210> SEQ ID NO 462
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 462

ttgttgtcgc agctgtttta 20

<210> SEQ ID NO 463
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 463

tttgttgtcg cagctgtttt 20

<210> SEQ ID NO 464
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 464

ttttgttgtc gcagctgttt 20

<210> SEQ ID NO 465
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 465

tttttgttgt cgcagctgtt 20

<210> SEQ ID NO 466
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 466

ggatccagct cactcccctg 20

<210> SEQ ID NO 467
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 467

aaataaggat ccagctcact 20

-continued

<210> SEQ ID NO 468
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 468

gaccagaaat aaggatccag 20

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

<400> SEQUENCE: 469

cttagggacc agaaataagg 20

<210> SEQ ID NO 470
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 470

cacccactta gggaccagaa 20

<210> SEQ ID NO 471
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 471

accacccact tagggaccag 20

<210> SEQ ID NO 472
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 472

aggtccagga ctctcccctt 20

<210> SEQ ID NO 473
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 473

aaggtccagg actctcccct 20

<210> SEQ ID NO 474
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 474

aaactgcaga agtcccaccc 20

<210> SEQ ID NO 475
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 475

ggagggcccc gctgagctgc 20

<210> SEQ ID NO 476
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 476

tcccggaaca tccaagcggg 20

<210> SEQ ID NO 477
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 477

catcactttc ccggaacatc 20

<210> SEQ ID NO 478
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 478

ctggtcacat tcccttcccc 20

<210> SEQ ID NO 479
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 479

ctagacctgg tcacattccc 20

<210> SEQ ID NO 480
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 480

ggagtggtgg tcacacctcc 20

<210> SEQ ID NO 481
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 481

acccccctcca gagagcagga 20

<210> SEQ ID NO 482
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 482

atctctaccc cctccagaga 20

<210> SEQ ID NO 483
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 483

ggtacgggta gaagccagaa 20

<210> SEQ ID NO 484
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 484

ggagagtgta accgtcatag 20

<210> SEQ ID NO 485
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 485

tgcgattggc agagccccgg 20

<210> SEQ ID NO 486
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 486

ggcaggtgcg attggcagag 20

-continued

<210> SEQ ID NO 487
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 487

ggccattcac ttggcaggtg 20

<210> SEQ ID NO 488
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 488

ttgtcacaga tcgctgtctg 20

<210> SEQ ID NO 489
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 489

aaggagtctt ggcaggaagg 20

<210> SEQ ID NO 490
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 490

gtacatgaag gagtcttggc 20

<210> SEQ ID NO 491
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 491

aagcttcggc cacctcttga 20

<210> SEQ ID NO 492
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 492

ccatctagca ccaggtagat 20

<210> SEQ ID NO 493
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 493

ggccccaatg ctgtctgatc 20

<210> SEQ ID NO 494
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 494

aattaagttg actagacact 20

<210> SEQ ID NO 495
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 495

tgccaccttc tcaattaagt 20

<210> SEQ ID NO 496
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 496

taacttgcca ccttctcaat 20

<210> SEQ ID NO 497
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 497

cataacttgc caccttctca 20

<210> SEQ ID NO 498
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 498

acaccataac ttgccacctt 20

<210> SEQ ID NO 499
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 499

tcacaccata acttgccacc 20

<210> SEQ ID NO 500
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 500

tagtccctga cttcaacttg 20

<210> SEQ ID NO 501
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 501

tggtgttagt ccctgacttc 20

<210> SEQ ID NO 502
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 502

gcggttccag ccttcaggag 20

<210> SEQ ID NO 503
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 503

tcatgaggat gatgacatgg 20

<210> SEQ ID NO 504
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 504

ccgcccatgt tgtgcaatcc 20

<210> SEQ ID NO 505
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 505

gtaattgggt ccccgcccat 20

-continued

<210> SEQ ID NO 506
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 506

aagtcccgga tctcatcaat 20

<210> SEQ ID NO 507
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 507

aacacataga catccagata 20

<210> SEQ ID NO 508
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 508

caaagcattg atgttcactt 20

<210> SEQ ID NO 509
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 509

tttgaacaca tgttgctcat 20

<210> SEQ ID NO 510
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 510

cttccaggtt ttccatatcc 20

<210> SEQ ID NO 511
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 511

tcttccaggt tttccatatc 20

<210> SEQ ID NO 512
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 512

agactcagag actggctttc 20

<210> SEQ ID NO 513
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 513

gcctgccatg gttgcttgtg 20

<210> SEQ ID NO 514
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 514

tgactgagat cttggcctgc 20

<210> SEQ ID NO 515
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 515

ttctatctcc aggtcccgct 20

<210> SEQ ID NO 516
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 516

agtcataaaa ttcaggaatt 20

<210> SEQ ID NO 517
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 517

cgagttgttc cctcggtgca 20

<210> SEQ ID NO 518
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 518

agcctcaaag ctcgagttgt 20

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

<400> SEQUENCE: 519

ggaggaagcc tcaaagctcg 20

<210> SEQ ID NO 520
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 520

gtagttggag gaagcctcaa 20

<210> SEQ ID NO 521
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 521

caagtggtag ttggaggaag 20

<210> SEQ ID NO 522
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 522

tcctcagaca caaacagagc 20

<210> SEQ ID NO 523
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 523

ttctcctcct cagacacaaa 20

<210> SEQ ID NO 524
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 524

tagacctcct tccgagtcag 20

-continued

<210> SEQ ID NO 525
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 525

ttgatgtaga cctccttccg 20

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

<400> SEQUENCE: 526

ctttcttatc cccattcttg 20

<210> SEQ ID NO 527
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 527

gcctttctta tccccattct 20

<210> SEQ ID NO 528
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 528

agctgccttt cttatcccca 20

<210> SEQ ID NO 529
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 529

cagctgcctt tcttatcccc 20

<210> SEQ ID NO 530
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 530

acagctgcct ttcttatccc 20

<210> SEQ ID NO 531
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 531

gcatctctct cacagctgcc 20

<210> SEQ ID NO 532
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 532

agatgtcctt gactttgtca 20

<210> SEQ ID NO 533
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 533

cagcataggg actcactcct 20

<210> SEQ ID NO 534
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 534

ccgccagaat cacctctgca 20

<210> SEQ ID NO 535
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 535

tgaatgaaac gacttctctt 20

<210> SEQ ID NO 536
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 536

acatccacta ctccccagct 20

<210> SEQ ID NO 537
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 537

cgcttctggt ttttgcagac 20

<210> SEQ ID NO 538
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 538

ttttgccgct tctggttttt 20

<210> SEQ ID NO 539
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 539

gcaggtacct gcttttgccg 20

<210> SEQ ID NO 540
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 540

tcttggagtt tctccttcag 20

<210> SEQ ID NO 541
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 541

ggaacatcca agcggg 16

<210> SEQ ID NO 542
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 542

tggtcacatt cccttc 16

<210> SEQ ID NO 543
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 543

cctggtcaca ttccct 16

-continued

<210> SEQ ID NO 544
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 544

gacctggtca cattcc 16

<210> SEQ ID NO 545
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 545

taacttgcca ccttct 16

<210> SEQ ID NO 546
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 546

cataacttgc cacctt 16

<210> SEQ ID NO 547
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 547

accataactt gccacc 16

<210> SEQ ID NO 548
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 548

ccttccgagt cagctt 16

<210> SEQ ID NO 549
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 549

ctccttccga gtcagc 16

<210> SEQ ID NO 550
<211> LENGTH: 16

-continued

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

<400> SEQUENCE: 550

acctccttcc gagtca 16

<210> SEQ ID NO 551
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 551

ctttcttatc cccatt 16

<210> SEQ ID NO 552
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 552

gcctttctta tcccca 16

<210> SEQ ID NO 553
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 553

ctgcctttct tatccc 16

<210> SEQ ID NO 554
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 554

tttgccgctt ctggtt 16

<210> SEQ ID NO 555
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 555

cttttgccgc ttctgg 16

<210> SEQ ID NO 556
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 556

tgcttttgcc gcttct 16

<210> SEQ ID NO 557
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 557

aaacccaaat cctcat 16

<210> SEQ ID NO 558
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 558

gaaaacccaa atcctc 16

<210> SEQ ID NO 559
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 559

tagaaaaccc aaatcc 16

<210> SEQ ID NO 560
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 560

atagaaaacc caaatc 16

<210> SEQ ID NO 561
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 561

cttatagaaa acccaa 16

<210> SEQ ID NO 562
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 562

ccttatagaa aaccca 16

-continued

<210> SEQ ID NO 563
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 563

ccctttataga aaaccc 16

<210> SEQ ID NO 564
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 564

ccccttatag aaaacc 16

<210> SEQ ID NO 565
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 565

acccctttata gaaaac 16

<210> SEQ ID NO 566
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 566

aacccctttat agaaaa 16

<210> SEQ ID NO 567
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 567

aaacccctta tagaaa 16

<210> SEQ ID NO 568
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 568

gaaacccctt atagaa 16

<210> SEQ ID NO 569
<211> LENGTH: 16

-continued

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

<400> SEQUENCE: 569

ggaaacccct tataga 16

<210> SEQ ID NO 570
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 570

aggaaacccc ttatag 16

<210> SEQ ID NO 571
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 571

caggaaaccc cttata 16

<210> SEQ ID NO 572
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 572

gcaggaaacc ccttat 16

<210> SEQ ID NO 573
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 573

agcaggaaac ccctta 16

<210> SEQ ID NO 574
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 574

cagcaggaaa cccctt 16

<210> SEQ ID NO 575
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 575

ccagcaggaa acccct 16

<210> SEQ ID NO 576
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 576

tccagcagga aacccc 16

<210> SEQ ID NO 577
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 577

gtccagcagg aaaccc 16

<210> SEQ ID NO 578
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 578

tgtccagcag gaaacc 16

<210> SEQ ID NO 579
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 579

ctgtccagca ggaaac 16

<210> SEQ ID NO 580
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 580

cctgtccagc aggaaa 16

<210> SEQ ID NO 581
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 581

ccctgtccag caggaa 16

-continued

<210> SEQ ID NO 582
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 582

cccctgtcca gcagga 16

<210> SEQ ID NO 583
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 583

gcccctgtcc agcagg 16

<210> SEQ ID NO 584
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 584

cgcccctgtc cagcag 16

<210> SEQ ID NO 585
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 585

acgcccctgt ccagca 16

<210> SEQ ID NO 586
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 586

cacgcccctg tccagc 16

<210> SEQ ID NO 587
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 587

ccacgcccct gtccag 16

<210> SEQ ID NO 588
<211> LENGTH: 16

-continued

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

<400> SEQUENCE: 588

cccacgcccc tgtcca 16

<210> SEQ ID NO 589
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 589

tcccacgccc ctgtcc 16

<210> SEQ ID NO 590
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 590

atcccacgcc cctgtc 16

<210> SEQ ID NO 591
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 591

aatcccacgc ccctgt 16

<210> SEQ ID NO 592
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 592

caatcccacg cccctg 16

<210> SEQ ID NO 593
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 593

tcaatcccac gcccct 16

<210> SEQ ID NO 594
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 594

ttcaatccca cgcccc 16

<210> SEQ ID NO 595
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 595

attcaatccc acgccc 16

<210> SEQ ID NO 596
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 596

aattcaatcc cacgcc 16

<210> SEQ ID NO 597
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 597

taattcaatc ccacgc 16

<210> SEQ ID NO 598
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 598

ttaattcaat cccacg 16

<210> SEQ ID NO 599
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 599

tttaattcaa tcccac 16

<210> SEQ ID NO 600
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 600

ttttaattca atccca 16

-continued

<210> SEQ ID NO 601
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 601

gttttaattc aatccc 16

<210> SEQ ID NO 602
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 602

tgttttaatt caatcc 16

<210> SEQ ID NO 603
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 603

ctgttttaat tcaatc 16

<210> SEQ ID NO 604
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 604

gctgttttaa ttcaat 16

<210> SEQ ID NO 605
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 605

agctgtttta attcaa 16

<210> SEQ ID NO 606
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 606

cagctgtttt aattca 16

<210> SEQ ID NO 607
<211> LENGTH: 16

-continued

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

<400> SEQUENCE: 607

gcagctgttt taattc 16

<210> SEQ ID NO 608
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 608

cgcagctgtt ttaatt 16

<210> SEQ ID NO 609
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 609

tcgcagctgt tttaat 16

<210> SEQ ID NO 610
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 610

gtcgcagctg ttttaa 16

<210> SEQ ID NO 611
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 611

tgtcgcagct gtttta 16

<210> SEQ ID NO 612
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 612

ttgtcgcagc tgtttt 16

<210> SEQ ID NO 613
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 613

gttgtcgcag ctgttt 16

<210> SEQ ID NO 614
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 614

tgttgtcgca gctgtt 16

<210> SEQ ID NO 615
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 615

ttgttgtcgc agctgt 16

<210> SEQ ID NO 616
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 616

tttgttgtcg cagctg 16

<210> SEQ ID NO 617
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 617

ttttgttgtc gcagct 16

<210> SEQ ID NO 618
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 618

tttttgttgt cgcagc 16

<210> SEQ ID NO 619
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 619

gaaaacccaa atcctca 17

-continued

<210> SEQ ID NO 620
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 620

agaaaaccca aatcctc 17

<210> SEQ ID NO 621
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 621

tagaaaaccc aaatcct 17

<210> SEQ ID NO 622
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 622

atagaaaacc caaatcc 17

<210> SEQ ID NO 623
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 623

ttatagaaaa cccaaat 17

<210> SEQ ID NO 624
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 624

cttatagaaa acccaaa 17

<210> SEQ ID NO 625
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 625

ccttatagaa aacccaa 17

<210> SEQ ID NO 626
<211> LENGTH: 17

-continued

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

<400> SEQUENCE: 626

cccttataga aaaccca 17

<210> SEQ ID NO 627
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 627

ccccttatag aaaaccc 17

<210> SEQ ID NO 628
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 628

accccttata gaaaacc 17

<210> SEQ ID NO 629
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 629

aaccccttat agaaaac 17

<210> SEQ ID NO 630
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 630

aaaccccttа tagaaaa 17

<210> SEQ ID NO 631
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 631

gaaaccccтt atagaaa 17

<210> SEQ ID NO 632
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 632

ggaaacccct tatagaa 17

<210> SEQ ID NO 633
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 633

aggaaacccc ttataga 17

<210> SEQ ID NO 634
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 634

caggaaaccc cttatag 17

<210> SEQ ID NO 635
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 635

gcaggaaacc ccttata 17

<210> SEQ ID NO 636
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 636

agcaggaaac cccttat 17

<210> SEQ ID NO 637
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 637

cagcaggaaa ccccttа 17

<210> SEQ ID NO 638
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 638

ccagcaggaa acccctt 17

-continued

<210> SEQ ID NO 639
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 639

tccagcagga aacccct 17

<210> SEQ ID NO 640
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 640

gtccagcagg aaacccc 17

<210> SEQ ID NO 641
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 641

tgtccagcag gaaaccc 17

<210> SEQ ID NO 642
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 642

ctgtccagca ggaaacc 17

<210> SEQ ID NO 643
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 643

cctgtccagc aggaaac 17

<210> SEQ ID NO 644
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 644

ccctgtccag caggaaa 17

<210> SEQ ID NO 645
<211> LENGTH: 17

-continued

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

<400> SEQUENCE: 645

gcccctgtcc agcagga 17

<210> SEQ ID NO 646
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 646

cgcccctgtc cagcagg 17

<210> SEQ ID NO 647
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 647

acgcccctgt ccagcag 17

<210> SEQ ID NO 648
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 648

cacgcccctg tccagca 17

<210> SEQ ID NO 649
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 649

ccacgcccct gtccagc 17

<210> SEQ ID NO 650
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 650

cccacgcccc tgtccag 17

<210> SEQ ID NO 651
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 651

tcccacgccc ctgtcca 17

<210> SEQ ID NO 652
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 652

atcccacgcc cctgtcc 17

<210> SEQ ID NO 653
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 653

aatcccacgc ccctgtc 17

<210> SEQ ID NO 654
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 654

caatcccacg cccctgt 17

<210> SEQ ID NO 655
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 655

tcaatcccac gcccctg 17

<210> SEQ ID NO 656
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 656

ttcaatccca cgccccct 17

<210> SEQ ID NO 657
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 657

attcaatccc acgcccc 17

-continued

<210> SEQ ID NO 658
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 658

aattcaatcc cacgccc 17

<210> SEQ ID NO 659
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 659

taattcaatc ccacgcc 17

<210> SEQ ID NO 660
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 660

ttaattcaat cccacgc 17

<210> SEQ ID NO 661
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 661

tttaattcaa tcccacg 17

<210> SEQ ID NO 662
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 662

ttttaattca atcccac 17

<210> SEQ ID NO 663
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 663

gttttaattc aatccca 17

<210> SEQ ID NO 664
<211> LENGTH: 17

-continued

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

<400> SEQUENCE: 664

tgttttaatt caatccc 17

<210> SEQ ID NO 665
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 665

ctgttttaat tcaatcc 17

<210> SEQ ID NO 666
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 666

gctgttttaa ttcaatc 17

<210> SEQ ID NO 667
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 667

agctgtttta attcaat 17

<210> SEQ ID NO 668
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 668

cagctgtttt aattcaa 17

<210> SEQ ID NO 669
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 669

gcagctgttt taattca 17

<210> SEQ ID NO 670
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 670

cgcagctgtt ttaattc 17

<210> SEQ ID NO 671
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 671

tcgcagctgt tttaatt 17

<210> SEQ ID NO 672
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 672

gtcgcagctg ttttaat 17

<210> SEQ ID NO 673
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 673

tgtcgcagct gttttaa 17

<210> SEQ ID NO 674
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 674

ttgtcgcagc tgtttta 17

<210> SEQ ID NO 675
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 675

gttgtcgcag ctgtttt 17

<210> SEQ ID NO 676
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 676

tgttgtcgca gctgttt 17

-continued

<210> SEQ ID NO 677
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 677

ttgttgtcgc agctgtt 17

<210> SEQ ID NO 678
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 678

tttgttgtcg cagctgt 17

<210> SEQ ID NO 679
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 679

ttttgttgtc gcagctg 17

<210> SEQ ID NO 680
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 680

tttttgttgt cgcagct 17

<210> SEQ ID NO 681
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 681

tagaaaaccc aaatcctca 19

<210> SEQ ID NO 682
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 682

atagaaaacc caaatcctc 19

<210> SEQ ID NO 683
<211> LENGTH: 19

-continued

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

<400> SEQUENCE: 683

tatagaaaac ccaaatcct 19

<210> SEQ ID NO 684
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 684

cttatagaaa acccaaatc 19

<210> SEQ ID NO 685
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 685

ccttatagaa aacccaaat 19

<210> SEQ ID NO 686
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 686

cccttataga aaacccaaa 19

<210> SEQ ID NO 687
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 687

ccccttatag aaaacccaa 19

<210> SEQ ID NO 688
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 688

acccccttata gaaaaccca 19

<210> SEQ ID NO 689
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 689

aacccttat agaaaaccc 19

<210> SEQ ID NO 690
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 690

aaacccctta tagaaaacc 19

<210> SEQ ID NO 691
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 691

gaaacccctt atagaaaac 19

<210> SEQ ID NO 692
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 692

ggaaacccct atagaaaa 19

<210> SEQ ID NO 693
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 693

aggaaacccc ttatagaaa 19

<210> SEQ ID NO 694
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 694

caggaaaccc cttatagaa 19

<210> SEQ ID NO 695
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 695

gcaggaaacc ccttataga 19

-continued

<210> SEQ ID NO 696
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 696

agcaggaaac cccttatag 19

<210> SEQ ID NO 697
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 697

cagcaggaaa ccccttata 19

<210> SEQ ID NO 698
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 698

ccagcaggaa acccccttat 19

<210> SEQ ID NO 699
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 699

tccagcagga aacccctta 19

<210> SEQ ID NO 700
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 700

gtccagcagg aaacccctt 19

<210> SEQ ID NO 701
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 701

tgtccagcag gaaacccct 19

<210> SEQ ID NO 702
<211> LENGTH: 19

-continued

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

<400> SEQUENCE: 702

cctgtccagc aggaaaccc 19

<210> SEQ ID NO 703
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 703

ccctgtccag caggaaacc 19

<210> SEQ ID NO 704
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 704

cccctgtcca gcaggaaac 19

<210> SEQ ID NO 705
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 705

gcccctgtcc agcaggaaa 19

<210> SEQ ID NO 706
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 706

acgcccctgt ccagcagga 19

<210> SEQ ID NO 707
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 707

cacgcccctg tccagcagg 19

<210> SEQ ID NO 708
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 708

ccacgcccct gtccagcag 19

<210> SEQ ID NO 709
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 709

cccacgcccc tgtccagca 19

<210> SEQ ID NO 710
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 710

tcccacgccc ctgtccagc 19

<210> SEQ ID NO 711
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 711

atcccacgcc cctgtccag 19

<210> SEQ ID NO 712
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 712

aatcccacgc ccctgtcca 19

<210> SEQ ID NO 713
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 713

caatcccacg cccctgtcc 19

<210> SEQ ID NO 714
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 714

tcaatcccac gcccctgtc 19

-continued

<210> SEQ ID NO 715
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 715

ttcaatccca cgcccctgt 19

<210> SEQ ID NO 716
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 716

attcaatccc acgcccctg 19

<210> SEQ ID NO 717
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 717

aattcaatcc cacgccccct 19

<210> SEQ ID NO 718
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 718

taattcaatc ccacgcccc 19

<210> SEQ ID NO 719
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 719

ttaattcaat cccacgccc 19

<210> SEQ ID NO 720
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 720

tttaattcaa tcccacgcc 19

<210> SEQ ID NO 721
<211> LENGTH: 19

-continued

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

<400> SEQUENCE: 721

ttttaattca atcccacgc 19

<210> SEQ ID NO 722
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 722

gttttaattc aatcccacg 19

<210> SEQ ID NO 723
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 723

tgttttaatt caatcccac 19

<210> SEQ ID NO 724
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 724

ctgttttaat tcaatccca 19

<210> SEQ ID NO 725
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 725

gctgttttaa ttcaatccc 19

<210> SEQ ID NO 726
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 726

agctgtttta attcaatcc 19

<210> SEQ ID NO 727
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 727

cagctgtttt aattcaatc 19

<210> SEQ ID NO 728
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 728

gcagctgttt taattcaat 19

<210> SEQ ID NO 729
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 729

cgcagctgtt ttaattcaa 19

<210> SEQ ID NO 730
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 730

tcgcagctgt tttaattca 19

<210> SEQ ID NO 731
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 731

gtcgcagctg ttttaattc 19

<210> SEQ ID NO 732
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 732

tgtcgcagct gttttaatt 19

<210> SEQ ID NO 733
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 733

ttgtcgcagc tgttttaat 19

-continued

<210> SEQ ID NO 734
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 734

gttgtcgcag ctgttttaa 19

<210> SEQ ID NO 735
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 735

tgttgtcgca gctgtttta 19

<210> SEQ ID NO 736
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 736

ttgttgtcgc agctgtttt 19

<210> SEQ ID NO 737
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 737

tttgttgtcg cagctgttt 19

<210> SEQ ID NO 738
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 738

ttttgttgtc gcagctgtt 19

<210> SEQ ID NO 739
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 739

tttttgttgt cgcagctgt 19

<210> SEQ ID NO 740
<211> LENGTH: 18

-continued

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

<400> SEQUENCE: 740

ccccttatag aaaaccca 18

<210> SEQ ID NO 741
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 741

accccttata gaaaaccc 18

<210> SEQ ID NO 742
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 742

aaccccttat agaaaacc 18

<210> SEQ ID NO 743
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 743

aaaccccttа tagaaaac 18

<210> SEQ ID NO 744
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 744

gaaaccccttt atagaaaa 18

<210> SEQ ID NO 745
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 745

aggaaacccc ttatagaa 18

<210> SEQ ID NO 746
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 746

caggaaaccc cttataga 18

<210> SEQ ID NO 747
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 747

gcaggaaacc ccttatag 18

<210> SEQ ID NO 748
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 748

agcaggaaac cccttata 18

<210> SEQ ID NO 749
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 749

cagcaggaaa ccccttat 18

<210> SEQ ID NO 750
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 750

ccagcaggaa acccctta 18

<210> SEQ ID NO 751
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 751

tccagcagga aacccctt 18

<210> SEQ ID NO 752
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 752

gtccagcagg aaacccct 18

-continued

<210> SEQ ID NO 753
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 753

tgtccagcag gaaacccc 18

<210> SEQ ID NO 754
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 754

ctgtccagca ggaaaccc 18

<210> SEQ ID NO 755
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 755

cctgtccagc aggaaacc 18

<210> SEQ ID NO 756
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 756

ccctgtccag caggaaac 18

<210> SEQ ID NO 757
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 757

cccctgtcca gcaggaaa 18

<210> SEQ ID NO 758
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 758

cgcccctgtc cagcagga 18

<210> SEQ ID NO 759
<211> LENGTH: 18

-continued

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

<400> SEQUENCE: 759

acgcccctgt ccagcagg 18

<210> SEQ ID NO 760
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 760

cacgcccctg tccagcag 18

<210> SEQ ID NO 761
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 761

ccacgcccct gtccagca 18

<210> SEQ ID NO 762
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 762

cccacgcccc tgtccagc 18

<210> SEQ ID NO 763
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 763

tcccacgccc ctgtccag 18

<210> SEQ ID NO 764
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 764

atcccacgcc cctgtcca 18

<210> SEQ ID NO 765
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 765

aatcccacgc ccctgtcc 18

<210> SEQ ID NO 766
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 766

caatcccacg cccctgtc 18

<210> SEQ ID NO 767
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 767

tcaatcccac gcccctgt 18

<210> SEQ ID NO 768
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 768

ttcaatccca cgcccctg 18

<210> SEQ ID NO 769
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 769

attcaatccc acgccccct 18

<210> SEQ ID NO 770
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 770

aattcaatcc cacgcccc 18

<210> SEQ ID NO 771
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 771

taattcaatc ccacgccc 18

-continued

<210> SEQ ID NO 772
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 772

ttaattcaat cccacgcc 18

<210> SEQ ID NO 773
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 773

tttaattcaa tcccacgc 18

<210> SEQ ID NO 774
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 774

ttttaattca atcccacg 18

<210> SEQ ID NO 775
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 775

gttttaattc aatcccac 18

<210> SEQ ID NO 776
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 776

tgttttaatt caatccca 18

<210> SEQ ID NO 777
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 777

ctgttttaat tcaatccc 18

<210> SEQ ID NO 778
<211> LENGTH: 18

-continued

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

<400> SEQUENCE: 778

gctgttttaa ttcaatcc 18

<210> SEQ ID NO 779
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 779

agctgtttta attcaatc 18

<210> SEQ ID NO 780
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 780

cagctgtttt aattcaat 18

<210> SEQ ID NO 781
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 781

gcagctgttt taattcaa 18

<210> SEQ ID NO 782
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 782

cgcagctgtt ttaattca 18

<210> SEQ ID NO 783
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 783

tcgcagctgt tttaattc 18

<210> SEQ ID NO 784
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 784

gtcgcagctg ttttaatt 18

<210> SEQ ID NO 785
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 785

tagaaaaccc aaatcctc 18

<210> SEQ ID NO 786
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 786

atagaaaacc caaatcct 18

<210> SEQ ID NO 787
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 787

tatagaaaac ccaaatcc 18

<210> SEQ ID NO 788
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 788

ttatagaaaa cccaaatc 18

<210> SEQ ID NO 789
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 789

cttatagaaa acccaaat 18

<210> SEQ ID NO 790
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 790

ccttatagaa aacccaaa 18

-continued

<210> SEQ ID NO 791
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 791

ccctttataga aaacccaa 18

<210> SEQ ID NO 792
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 792

tgtcgcagct gttttaat 18

<210> SEQ ID NO 793
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 793

ttgtcgcagc tgttttaa 18

<210> SEQ ID NO 794
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 794

gttgtcgcag ctgtttta 18

<210> SEQ ID NO 795
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 795

tgttgtcgca gctgtttt 18

<210> SEQ ID NO 796
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 796

ttgttgtcgc agctgttt 18

<210> SEQ ID NO 797
<211> LENGTH: 18

-continued

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

<400> SEQUENCE: 797

tttgttgtcg cagctgtt 18

<210> SEQ ID NO 798
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 798

ttttgttgtc gcagctgt 18

<210> SEQ ID NO 799
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 799

tttttgttgt cgcagctg 18

<210> SEQ ID NO 800
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 800

aaaacccaaa tcctca 16

<210> SEQ ID NO 801
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 801

agaaaaccca aatcct 16

<210> SEQ ID NO 802
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 802

tatagaaaac ccaaat 16

<210> SEQ ID NO 803
<211> LENGTH: 16
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

-continued

<400> SEQUENCE: 803

ttatagaaaa cccaaa 16

<210> SEQ ID NO 804
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 804

gcataagagg gtaccagctg 20

<210> SEQ ID NO 805
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 805

gtcctttagc cagggcagca 20

<210> SEQ ID NO 806
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 806

tccacccatg ttgtgcaagc 20

<210> SEQ ID NO 807
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 807

ccacaccatg ccacagagac 20

<210> SEQ ID NO 808
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 808

ttccgagtca ggctcttccc 20

<210> SEQ ID NO 809
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 809

ccttccctga aggttcctcc 20

-continued

<210> SEQ ID NO 810
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Primer

<400> SEQUENCE: 810

agtctctgtg gcatggtttg g 21

<210> SEQ ID NO 811
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Primer

<400> SEQUENCE: 811

gggcgaatga ctgagatctt g 21

<210> SEQ ID NO 812
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Probe

<400> SEQUENCE: 812

taccgattac cacaagcaac catggca 27

<210> SEQ ID NO 813
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Primer

<400> SEQUENCE: 813

cgaagcagct caatgaaatc aa 22

<210> SEQ ID NO 814
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Primer

<400> SEQUENCE: 814

tgcctggagg gccttctt 18

<210> SEQ ID NO 815
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Probe

<400> SEQUENCE: 815

agaccacaag ttgaagtc 18

<210> SEQ ID NO 816
<211> LENGTH: 20

-continued

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

<400> SEQUENCE: 816

gggcaaacag caatttgtga 20

<210> SEQ ID NO 817
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Primer

<400> SEQUENCE: 817

tggctaccca ccttccttgt 20

<210> SEQ ID NO 818
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Probe

<400> SEQUENCE: 818

ctggatactg tcccaatccc ggtattcc 28

<210> SEQ ID NO 819
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 819

cgaagaagct cagtgaaatc aa 22

<210> SEQ ID NO 820
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic oligonucleotide

<400> SEQUENCE: 820

tgcctggagg gccctctt 18

1.-**94**. (canceled)

95. A compound comprising a modified oligonucleotide consisting of 10 to 30 linked nucleosides having a nucleobase sequence comprising at least 8 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598.

96. The compound of claim **95**, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides having a nucleobase sequence comprising any of the nucleobase sequences of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598.

97. The compound of claim **96**, wherein the modified oligonucleotide consists of linked nucleosides having a nucleobase sequence consisting of any of the nucleobase sequences of SEQ ID NOs: 198, 228, 237, 440, 444, 448, 450, 453, 455, 549, and 598.

98. The compound of claim **95**, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar, or at least one modified nucleobase.

99. The compound of claim **96**, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar, or at least one modified nucleobase.

100. The compound of claim **97**, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar, or at least one modified nucleobase.

101. The compound of claim **98**, wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage.

102. The compound of claim **99**, wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage.

103. The compound of claim **100**, wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage.

104. The compound of claim **98**, wherein the modified sugar is a bicyclic sugar.

105. The compound of claim **99**, wherein the modified sugar is a bicyclic sugar.

106. The compound of claim **100**, wherein the modified sugar is a bicyclic sugar.

107. The compound of claim **104**, wherein the bicyclic sugar is selected from the group consisting of: 4'-(CH_2)—O-2' (LNA); 4'-$(CH_2)_2$—O-2' (ENA); and 4'-$CH(CH_3)$—O-2' (cEt).

108. The compound of claim **105**, wherein the bicyclic sugar is selected from the group consisting of: 4'-(CH_2)—O-2' (LNA); 4'-$(CH_2)_2$—O-2' (ENA); and 4'-$CH(CH_3)$—O-2' (cEt).

109. The compound of claim **106**, wherein the bicyclic sugar is selected from the group consisting of: 4'-(CH_2)—O-2' (LNA); 4'-$(CH_2)_2$—O-2' (ENA); and 4'-$CH(CH_3)$—O-2' (cEt).

110. The compound of claim **98**, wherein the modified sugar is 2'-O-methoxyethyl.

111. The compound of claim **99**, wherein the modified sugar is 2'-O-methoxyethyl.

112. The compound of claim **100**, wherein the modified sugar is 2'-O-methoxyethyl.

113. The compound of claim **98**, wherein the modified nucleobase is a 5-methylcytosine.

114. The compound of claim **99**, wherein the modified nucleobase is a 5-methylcytosine.

115. The compound of claim **100**, wherein the modified nucleobase is a 5-methylcytosine.

116. The compound of claim **98**, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar, or at least one modified nucleobase; wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage; the modified sugar is 2'-O-methoxyethyl or a bicyclic sugar is selected from the group consisting of: 4'-(CH_2)—O-2' (LNA); 4'-$(CH_2)_2$—O-2' (ENA); and 4'-$CH(CH_3)$—O-2' (cEt); and the modified nucleobase is a 5-methylcytosine.

117. The compound of claim **99**, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar, or at least one modified nucleobase; wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage; the modified sugar is 2'-O-methoxyethyl or a bicyclic sugar is selected from the group consisting of: 4'-(CH_2)—O-2' (LNA); 4'-$(CH_2)_2$—O-2' (ENA); and 4'-$CH(CH_3)$—O-2' (cEt); and the modified nucleobase is a 5-methylcytosine.

118. The compound of claim **100**, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage, at least one modified sugar, or at least one modified nucleobase; wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage; the modified sugar is 2'-O-methoxyethyl or a bicyclic sugar is selected from the group consisting of: 4'-(CH_2)—O-2' (LNA); 4'-$(CH_2)_2$—O-2' (ENA); and 4'-$CH(CH_3)$—O-2' (cEt); and the modified nucleobase is a 5-methylcytosine.

119. The compound of claim **95**, wherein the modified oligonucleotide comprises:

a gap segment consisting of linked deoxynucleosides;

a 5' wing segment consisting of linked nucleosides; and

a 3' wing segment consisting of linked nucleosides;

wherein the gap segment is positioned immediately adjacent to and between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

120. The compound of claim **96**, wherein the modified oligonucleotide comprises:

a gap segment consisting of linked deoxynucleosides;

a 5' wing segment consisting of linked nucleosides; and

a 3' wing segment consisting of linked nucleosides;

wherein the gap segment is positioned immediately adjacent to and between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

121. The compound of claim **97**, wherein the modified oligonucleotide comprises:

a gap segment consisting of linked deoxynucleosides;

a 5' wing segment consisting of linked nucleosides; and

a 3' wing segment consisting of linked nucleosides;

wherein the gap segment is positioned immediately adjacent to and between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

122. The compound of claim **98**, wherein the compound is single-stranded.

123. The compound of claim **99**, wherein the compound is single-stranded.

124. The compound of claim **100**, wherein the compound is single-stranded.

125. The compound of claim **98**, wherein the compound is double-stranded.

126. The compound of claim **99**, wherein the compound is double-stranded.

127. The compound of claim **100**, wherein the compound is double-stranded.

128. The compound of claim **97**, wherein the modified oligonucleotide consists of 20 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 198, 228, 237, 444, 448, 450, 453, or 455, and comprises:

a gap segment consisting of ten linked deoxynucleosides;

a 5' wing segment consisting of five linked nucleosides; and

a 3' wing segment consisting of five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment,

wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; wherein each internucleoside linkage is a phosphorothioate linkage and wherein each cytosine is a 5-methylcytosine.

129. The compound of claim **97**, wherein the modified oligonucleotide consists of 16 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 598, and comprises:

a gap segment consisting of ten linked deoxynucleosides;

a 5' wing segment consisting of three linked nucleosides; and

a 3' wing segment consisting of three linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment;

wherein the 5' wing segment comprises a 2'-O-methoxyethyl sugar, 2'-O-methoxyethyl sugar, and cEt sugar in the 5' to 3' direction; wherein the 3' wing segment comprises a cEt sugar, cEt sugar, and 2'-O-methoxyethyl sugar in the 5' to 3' direction; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

130. The compound of claim **97**, wherein the modified oligonucleotide consists of 16 linked nucleosides having a nucleobase sequence consisting of the sequence recited in SEQ ID NO: 549, and comprises:

a gap segment consisting of ten linked deoxynucleosides;

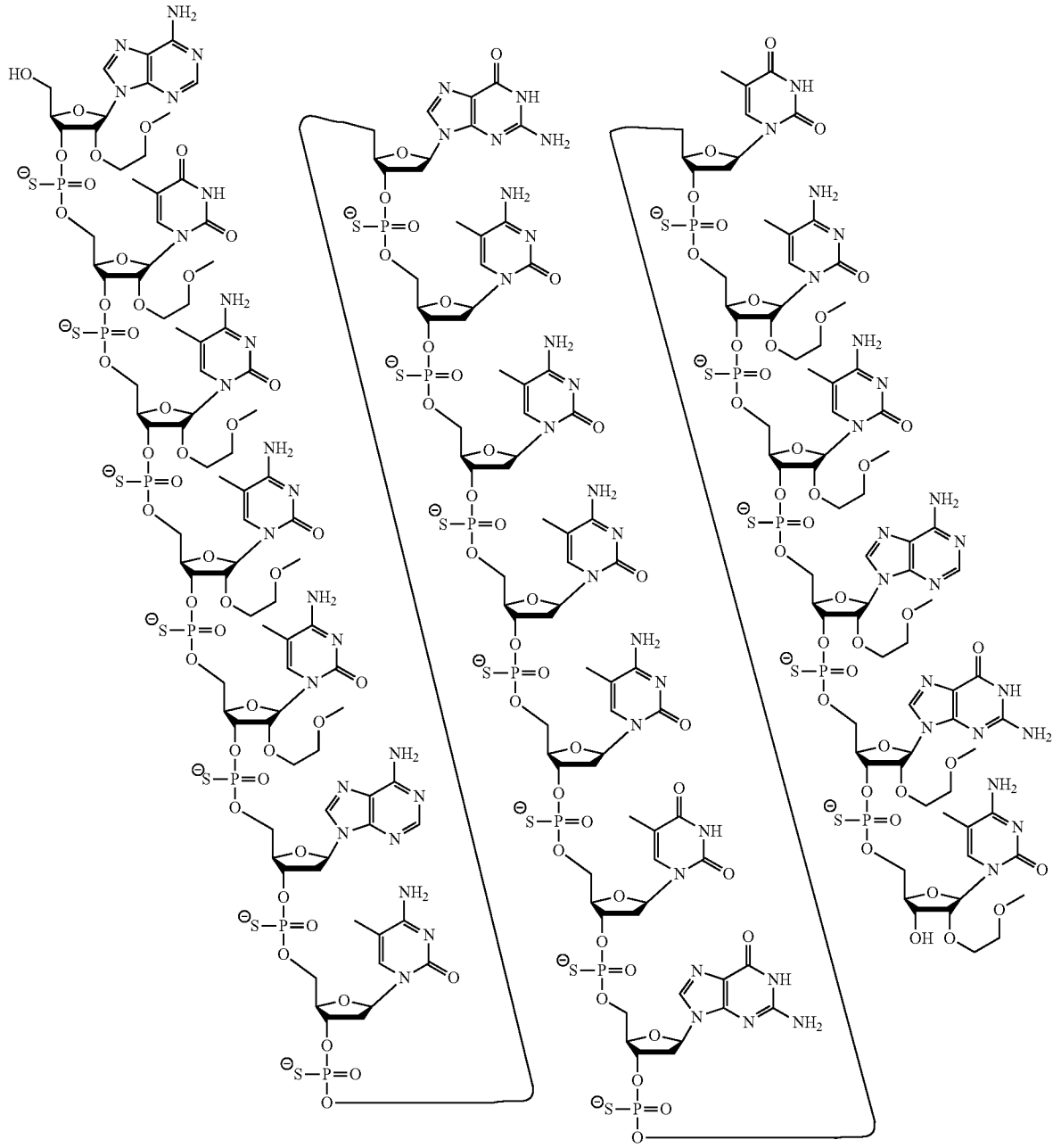
a 5' wing segment consisting of three linked nucleosides; and

a 3' wing segment consisting of three linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment;

wherein each nucleoside of each wing segment comprises a cEt sugar; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

131. A compound having the formula:



132. A compound consisting of a pharmaceutically acceptable salt of the compound of claim **131**.

133. The compound of claim **132**, wherein the pharmaceutically acceptable salt is sodium.

134. The compound of claim **132**, wherein the pharmaceutically acceptable salt is potassium.

135. A composition comprising the compound of claim **131** and a pharmaceutically acceptable carrier or diluent.

136. A composition comprising the compound of claim **133** and a pharmaceutically acceptable carrier or diluent.

137. A method of treating, preventing, or ameliorating a disease associated with dysregulation of the complement alternative pathway in a subject comprising administering to the subject the compound of claim **131**, thereby treating, preventing, or ameliorating the disease.

138. A method of treating, preventing, or ameliorating a disease associated with dysregulation of the complement alternative pathway in a subject comprising administering to the subject the compound of claim **133**, thereby treating, preventing, or ameliorating the disease.

139. The method of claim **137**, wherein the disease is macular degeneration, age related macular degeneration (AMD), wet AMD, dry AMD, or Geographic Atrophy.

140. The method of claim **138**, wherein the disease is macular degeneration, age related macular degeneration (AMD), wet AMD, dry AMD, or Geographic Atrophy.

* * * * *