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(54) **RNAI MODULATION OF THE RHO-A GENE
IN RESEARCH MODELS**

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(57) **ABSTRACT**

The invention relates to compositions and methods for
modulating the expression of the RhoA gene, and more
particularly to the downregulation of RhoA by chemically
modified oligonucleotides.

FIG. 1

Cholesterol-RNA 3'- conjugates

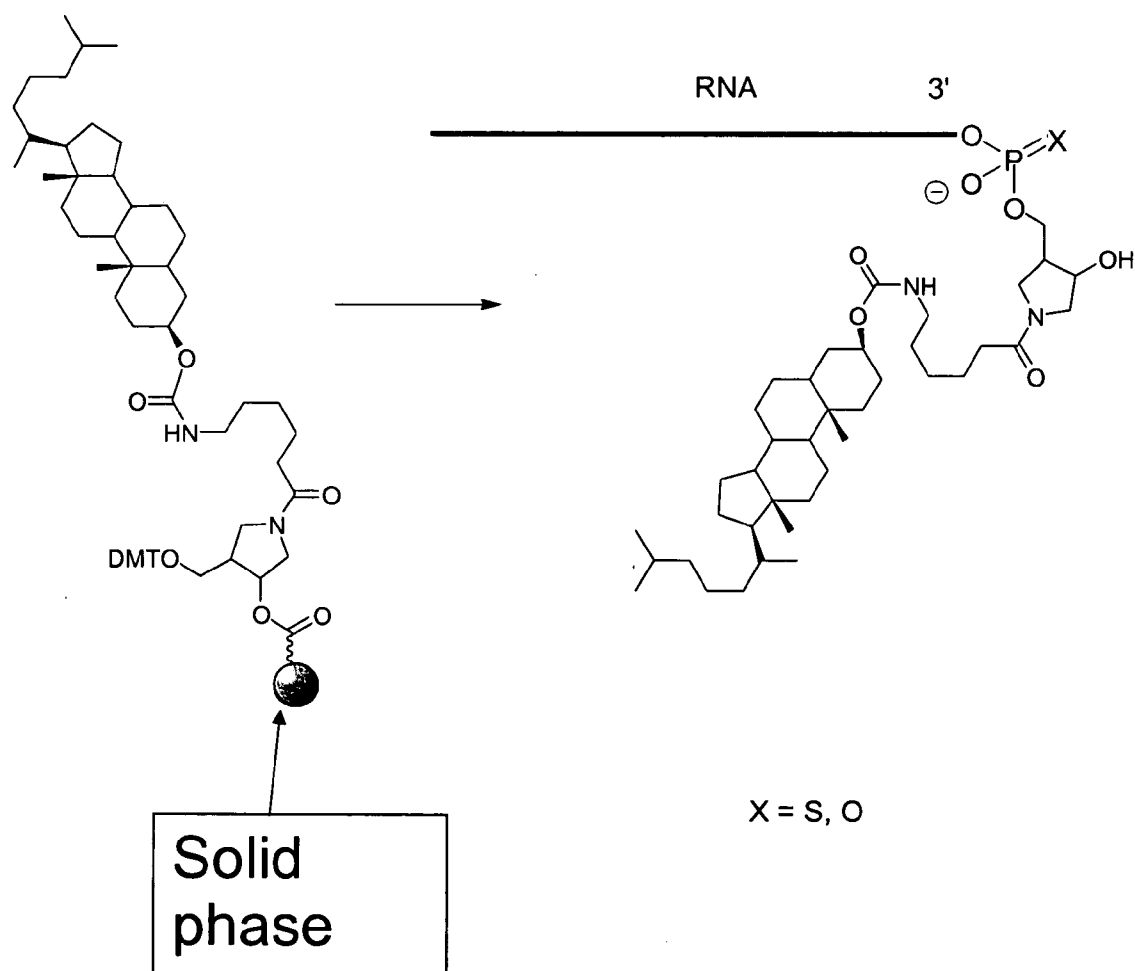
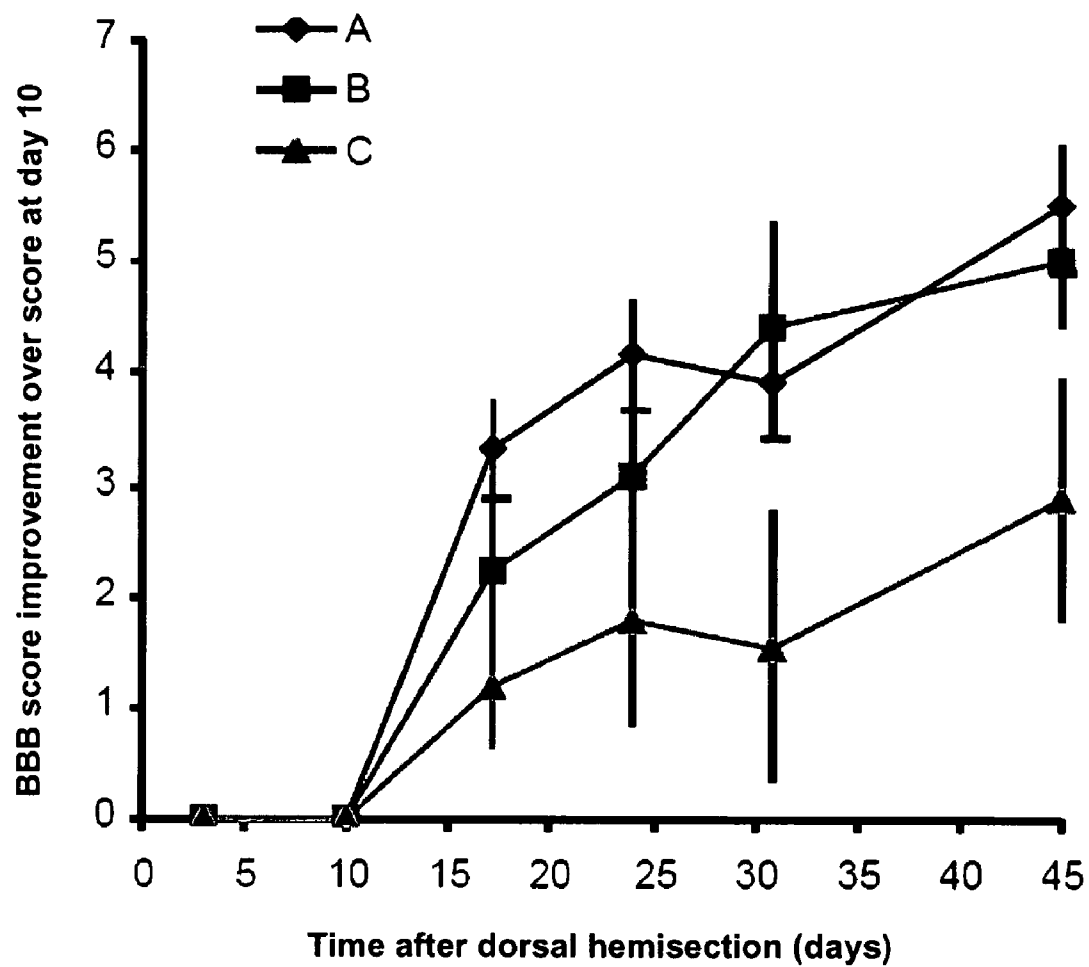


FIG. 2



RNAI MODULATION OF THE RHO-A GENE IN RESEARCH MODELS

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 60/701,470, filed Jul. 21, 2005, U.S. Provisional Application No. 60/726,838, filed Oct. 14, 2005, and U.S. Provisional Application No. 60/748,316, filed Dec. 7, 2005. The contents of each of these priority applications are incorporated herein by reference in their entirety.

TECHNICAL FIELD

[0002] The invention relates to compositions and methods for modulating the expression of RhoA, and more particularly to the downregulation of RhoA mRNA and RhoA protein levels by oligonucleotides via RNA interference, e.g., chemically modified oligonucleotides.

BACKGROUND

[0003] RNA interference or "RNAi" is a term initially coined by Fire and co-workers to describe the observation that double-stranded RNA (dsRNA) can block gene expression when it is introduced into worms (Fire et al., *Nature* 391:806-811, 1998). Short dsRNA directs gene-specific, post-transcriptional silencing in many organisms, including vertebrates, and has provided a new tool for studying gene function.

[0004] Numerous myelin-derived axon growth inhibitors have been characterized (see, for review, David et al., WO995394547, 1999; Bandman et al. U.S. Pat. No. 5,858,708, 1999; Schwab, *Neurochem. Res.* 21:755-761, 1996). Several components of CNS white matter, NI35, NI250 (Nogo) and Myelin-associated glycoprotein (MAG), which have inhibitory activity for axonal extension, have been described as well (Schwab et al., WO9005191, 1990; Schwab et al., U.S. Pat. No. 5,684,133, 1997). In particular, RhoA is a member of the large family of Rho (Ras homologue) GTPases, itself belonging to the superfamily of Ras GTPases. All eukaryotes contain at least one Rho GTPase. During the process of evolution the number of Rho GTPases increased from 5 to 6 per organism (yeast) to over 20 (mammals) (Karnoub, A. E., et al., *Breast Cancer Res. Treat.* 2004, 84:61). Like other GTPases, RhoA has intrinsic GTPase activity and shuttles between an inactive GDP-bound state and an active GTP-bound state. In vitro, the exchange of GDP to GTP occurs very slowly, and is catalyzed by guanine nucleotide exchange factors (GEFs), which exchange GDP for GTP. GTPase activating proteins (GAPs) catalyze hydrolysis of the γ -phosphate of GTP (Wheeler, A. P., Ridley, A. J., *Exp. Cell Res.* 2004, 301:43). A third set of regulatory proteins, the guanine nucleotide-dissociation inhibitors (GDIs), sequester GTPases in the cytosol in the inactive, GDP-bound state.

[0005] The N-terminal half of Rho GTPases contains the majority of the amino acids involved in GTP binding and hydrolysis, together with the Switch 1 and 2 regions that change conformation between the GTP-bound and GDP-bound states (Bishop, A. L., Hall, A., *Biochem. J.* 2000, 348 (Pt. 2):241). The C-terminus of Rho family GTPases is essential for correct localization of the proteins. It is post-translationally modified by prenylation of a conserved C-terminal cysteine followed by methylation and proteolytic

removal of the last three amino acids (Shao, F., Dixon, J. E., *Adv. Exp. Med. Biol.* 2003, 529:79). The prenyl group anchors the GTPases into membranes and this modification is essential for cell growth, transformation, and cytoskeleton organization (Allal, C., et al., *J. Biol. Chem.* 2000, 275:31001). Prenylation of Rho proteins appears to be important for their stability, inhibitors of enzymes that synthesize prenyl groups induce a decrease in Rho protein levels and their function (Stamatakis, K., et al., *J. Biol. Chem.* 2002, 277:49389). In the case of RhoA, prenylation adds a geranylgeranyl group. RhoA is mainly found in the cytoplasm or at the plasma membrane (Adamson, P., et al., *J. Cell Biol.* 1992, 119:617).

[0006] RhoA may bind to the intracellular portion of p75NTR and is activated by Nogo-R in a p75NTR-dependent manner (Wang, K. C., et al., *Nature* 2002, 420:74), which is how MAG, Nogo-66, and oligodendrocyte-myelin glycoprotein achieve RhoA activation. The central inhibitory domain of Nogo-A, NiG, distinct from Nogo-66, and Versican V2, a chondroitin-sulfate proteoglycan and another component of myelin, are able to activate RhoA in the absence of p75NTR, by an alternative pathway of RhoA activation remaining to be elucidated (Schweigreiter, R., et al., *Mol. Cell Neurosci.* 2004, 27:163). Further pathways of activation may exist.

[0007] RhoA is part of the growth inhibitory machinery present in the central nervous system (CNS), but not in peripheral nerves, which prevents the regeneration of CNS tissue after injury. Both the expression and the activation of RhoA is induced in brain and spinal cord injury (Mueller, K., et al., *Nature Reviews* 2005, 4:387). Activation of RhoA leads to neuronal growth cone collapse, retraction bulb formation and neurite withdrawal. Inactivation of RhoA leads to neurite outgrowth in primary neurons on otherwise inhibitory substrates in vitro, and promotes axon regeneration and functional recovery after spinal cord injury in rats and mice in vivo (Lehmann, M. A., et al., *J. Neurosci.* 1999, 19:7537; Hara, M., et al., *J. Neurosurg.* 2000, 93:94; Dergham, P., et al., *J. Neurosci.* 2002, 22:6570). Furthermore, inactivation of Rho has been shown to protect endogenous cells of the spinal cord from apoptosis induced by spinal cord injury (Dubreuil, C. I., et al., *J. Cell Biol.* 2003, 162:233). These findings have clinical relevance because neuroprotective treatments after spinal cord injury lead to improved functional recovery (Liu, X. Z., et al., *J. Neurosci.* 1997, 17:5395).

[0008] Evidently, RhoA is a potential target for therapeutic intervention strategies aimed at diseases and conditions involving, e.g., the destruction and/or impaired regeneration of cells of the CNS. The present invention advances the art by providing methods and medicaments encompassing short dsRNAs leading to the downregulation of RhoA mRNA and protein levels in cells expressing the RhoA gene. These methods and medicaments may be used in the treatment of disorders or pathological processes mediated, at least in part, by RhoA, e.g., by preventing the RhoA inhibition of axonal elongation and regeneration, and consequently stimulating nerve growth and proliferation.

SUMMARY

[0009] The present invention is based, at least in part, on an investigation of the RhoA gene using iRNA agents and

further testing of the iRNA agents that target the RhoA site. The present invention provides compositions and methods that are useful in reducing RhoA mRNA levels, RhoA protein levels and the treatment of pathological process mediated, at least in part, by RhoA, e.g. preventing RhoA inhibition of axonal elongation and regeneration, in a subject, e.g., a mammal, such as a human.

[0010] In one aspect, the invention provides iRNA agents comprising a sense strand, wherein the sense strand comprises at least 15 contiguous nucleotides that differ by no more than 1, 2, or 3 nucleotides from the sense strand sequences of any one agent selected from the group consisting of: agents number 6477 to 6836 as given in Table 1 below, and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides that differ by no more than 1, 2, or 3 nucleotides from the antisense sequences of any one agent selected from the group consisting of: agents number 6477 to 6836.

[0011] In a further aspect, the invention provides iRNA agents for inhibiting the expression of a rhoA gene in a cell comprising a sense strand, wherein the sense strand comprises at least 15 contiguous nucleotides that differ by no more than 1, 2, or 3 nucleotides from the sense strand sequences of any one agent selected from the group consisting of: agents number 6477 to 6836, and an antisense strand wherein the antisense strand comprises at least 15 contiguous nucleotides of the antisense sequences of any one agent selected from the group consisting of: agents number 6477 to 6836, and wherein the iRNA agent reduces the amount of RhoA MRNA present in cultured human cells after incubation with these agents by 40% or more compared to cells which have not been incubated with the agent.

[0012] In a further aspect, the invention provides iRNA agents for inhibiting the expression of a rhoA gene in a cell comprising a sense strand and an antisense strand each comprising a sequence of at least 16, 17 or 18 nucleotides which is essentially identical to one of the sequences of any one agent selected from the group consisting of: agents number 6477 to 6836, except that not more than 1, 2 or 3 nucleotides per strand, respectively, have been substituted by other nucleotides (e.g. adenosine replaced by uracil), while essentially retaining the ability to inhibit RhoA expression. Preferably, for such agents the sense and/or antisense strand sequence is chosen from the group consisting of: the sense and antisense strand sequences of agent numbers 6523, 6524, 6530, 6614, 6650, 6656, 6657, 6661, 6662, 6703, 6712, 6713, 6732, 6751, 6756, 6767, 6769, 6787, 6789, 6790, 6832.

[0013] Evidently, in the above embodiments, the sense strands and/or antisense strands of the iRNA agents of the invention can also be identical to the sense strands and antisense strands of the agents, agent numbers 6477 to 6836.

[0014] The iRNA agents of the invention may comprise a modification, e.g a modification that causes the iRNA agent to have increased stability in a biological sample. For example, they may comprise a phosphorothioate, a 2'-modified nucleotide, a locked nucleotide, an abasic nucleotide, morpholino nucleotide, a phosphoramidate, or a non-natural base comprising nucleotide. For purposes of the above embodiments, an iRNA agent is considered to comprise one of the sequences of the agents, agent numbers 6477 to 6836, irrespective of the potential presence of nucleotide modifi-

cations, i.e. a 2'-O-methyl guanosine would be considered a guanosine for such comparison. However, certain patterns of modifications are particularly preferred embodiments of the present invention. Consequently, in another embodiment, the invention provides iRNA agents for inhibiting the expression of a rhoA gene in a cell wherein the sense and/or antisense strand sequence is chosen from the group consisting of: the sense and antisense strand sequences of agent numbers AL-DP-5972, AL-DP-5973, AL-DP-5974, AL-DP-5975, AL-DP-5976, AL-DP-5978, AL-DP-5979, AL-DP-5981, AL-DP-5982, AL-DP-5983, AL-DP-5984, AL-DP-5986, AL-DP-5987, AL-DP-5988, AL-DP-5989, AL-DP-5990, AL-DP-5991, AL-DP-5992, AL-DP-5993, AL-DP-5994, AL-DP-5995, AL-DP-6176, AL-DP-6177.

[0015] In the iRNA agents of the present invention, the antisense RNA strand may be 30 or fewer nucleotides in length, and the duplex region of the iRNA agent may be 15-30 nucleotide pairs in length.

[0016] A 2'-modified nucleotide according to the instant invention may comprise at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide wherein the uridine is a 2'-modified nucleotide; at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide; or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[0017] The iRNA agents of the invention may be designed such that

[0018] every 5'-nucleotide in 5'-ua-3', 5'-uu-3', 5'-ca-3', and 5'-ug-3' motifs is a 2'-modified in sense strand, and every 5'-nucleotide in 5'-ua-3' and 5'-ca-3' motifs is 2'-modified in antisense strand, or

[0019] every 5'-nucleotide in 5'-ua-3', 5'-uu-3', 5'-ca-3', and 5'-ug-3' motifs is 2'-modified in the sense and antisense strand, or

[0020] every pyrimidine nucleotide is 2'-modified in the sense strand, and every 5'-nucleotide in 5'-ua-3' and 5'-ca-3' motifs is 2'-modified in the antisense strand, or

[0021] every pyrimidine nucleotide is 2'-modified in sense strand, and every 5'-nucleotide in 5'-ua-3', 5'-uu-3', 5'-ca-3', and 5'-ug-3' motifs is 2'-modified in the antisense strand, or

[0022] every pyrimidine nucleotide in the sense strand is 2'-modified, and no nucleotide is 2'-modified in the antisense strand.

[0023] The 2'-modification in the iRNA agents of the invention may be selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[0024] The iRNA agents of the invention may comprise a nucleotide overhang having 1 to 4 unpaired nucleotides, preferably 2 or 3 unpaired nucleotides. The nucleotide overhang may be at the 3'-end of the antisense strand of the iRNA agent. The iRNA agents may comprise a cholesterol moiety, which is preferably conjugated to the 3'-end of the

sense strand of the iRNA agent. In a preferred embodiment, the iRNA agent is targeted for uptake by nerve cells or nerve sheath cells.

[0025] The present invention further provides methods for reducing the level of RhoA mRNA in a cell. The present methods utilize the cellular mechanisms involved in RNA interference to selectively degrade RhoA mRNA in a cell and are comprised of the step of contacting a cell with one of the iRNA agents of the present invention. Such methods can be performed directly on a cell or can be performed on a mammalian subject by administering to a subject one of the iRNA agents of the present invention. Reduction of RhoA mRNA in a cell results in a reduction in the amount of RhoA protein produced, and in an organism, may result in a decrease in RhoA specific pathological/disease effects, e.g. preventing RhoA inhibition of axonal elongation and regeneration.

[0026] In another aspect of the invention, a method of treating a human subject having a pathological process mediated in part by RhoA is provided, comprising administering an iRNA agent of the invention, e.g. wherein the iRNA agent comprises a sense strand wherein the sense strand comprises at least 15 contiguous nucleotides that differ by no more than 1, 2, or 3 nucleotides from the sense strand sequences any one of the agents, agent numbers 6477 to 6836, and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides that differ by no more than 1, 2, or 3 nucleotides from the antisense strand sequences of any one of the agents, agent numbers 6477 to 6836.

[0027] In one embodiment of the above methods of the invention, the pathological process is the inhibition of nerve growth or elongation, preferably as a result of nerve injury or damage. In another preferred embodiment, the iRNA agent is administered in an amount sufficient to reduce the expression of RhoA in a cell or tissue of the subject. Preferably, the subject is a human.

[0028] In another aspect, the instant invention provides pharmaceutical compositions, comprising:

[0029] a.) an iRNA agent of the invention; and

[0030] b.) a pharmaceutically acceptable carrier

[0031] In another embodiment, the invention provides a cell comprising an iRNA agent of the invention.

[0032] In another embodiment, the invention provides a method for inhibiting the expression of a RhoA gene in a cell, the method comprising:

[0033] (a) introducing into the cell an iRNA agent of the invention; and

[0034] (b) maintaining the cell produced in step (a) for a time sufficient to obtain degradation of the mRNA transcript of the RhoA gene, thereby inhibiting expression of the RhoA gene in the cell.

[0035] In another embodiment, the invention provides a vector for inhibiting the expression of a RhoA gene in a cell, said vector comprising a regulatory sequence operably linked to a nucleotide sequence that encodes at least one strand of an iRNA agent of the invention.

[0036] In another embodiment, the invention provides a cell comprising the above vector.

[0037] The methods and compositions of the invention, e.g., the methods and iRNA compositions can be used with any dosage and/or formulation described herein, as well as with any route of administration described herein.

[0038] The details of one or more embodiments of the invention are set forth in the description below. Other features, objects, and advantages of the invention will be apparent from this description and from the claims. This application incorporates all cited references, patents, and patent applications by references in their entirety for all purposes.

BRIEF DESCRIPTION OF DRAWINGS

[0039] FIG. 1 is a schematic illustrating the synthesis and structure of cholesterol conjugated RNA strands. The sphere represents the solid phase (controlled pore glass, CPG).

[0040] FIG. 2 shows the effect of administration of iRNA agents of the invention, and of a control agent, respectively, to the site of injury in rats that have undergone partial dissection of the spinal cord; shown is the improvement in BBB locomotor score from day 10 after spinal cord injury, taking the BBB locomotor score of individual rats on day 10 as 0.

DETAILED DESCRIPTION

[0041] For ease of exposition the term “nucleotide” or “ribonucleotide” is sometimes used herein in reference to one or more monomeric subunits of an RNA agent. It will be understood that the usage of the term “ribonucleotide” or “nucleotide” herein can, in the case of a modified RNA or nucleotide surrogate, also refer to a modified nucleotide, or surrogate replacement moiety, as further described below, at one or more positions.

[0042] An “RNA agent” as used herein, is an unmodified RNA, modified RNA, or nucleoside surrogate, each of which is described herein or is well known in the RNA synthetic art. While numerous modified RNAs and nucleoside surrogates are described, preferred examples include those which have greater resistance to nuclease degradation than do unmodified RNAs. Preferred examples include those that have a 2' sugar modification, a modification in a single strand overhang, preferably a 3' single strand overhang, or, particularly if single stranded, a 5'-modification which includes one or more phosphate groups or one or more analogs of a phosphate group.

[0043] An “iRNA agent” (abbreviation for “interfering RNA agent”) as used herein, is an RNA agent, which can downregulate the expression of a target gene, e.g., RhoA. While not wishing to be bound by theory, an iRNA agent may act by one or more of a number of mechanisms, including post-transcriptional cleavage of a target mRNA sometimes referred to in the art as RNAi, or pre-transcriptional or pre-translational mechanisms. An iRNA agent can be a double stranded iRNA agent.

[0044] A “ds iRNA agent” (abbreviation for “double stranded iRNA agent”), as used herein, is an iRNA agent which includes more than one, and preferably two, strands in which interstrand hybridization can form a region of

duplex structure. A “strand” herein refers to a contiguous sequence of nucleotides (including non-naturally occurring or modified nucleotides). The two or more strands may be, or each form a part of, separate molecules, or they may be covalently interconnected, e.g., by a linker, e.g., a polyethyleneglycol linker, to form one molecule. At least one strand can include a region which is sufficiently complementary to a target RNA. Such strand is termed the “antisense strand.” A second strand of the dsRNA agent, which comprises a region complementary to the antisense strand, is termed the “sense strand.” However, a ds iRNA agent can also be formed from a single RNA molecule which is at least partly self-complementary, forming, e.g., a hairpin or panhandle structure, including a duplex region. In such case, the term “strand” refers to one of the regions of the RNA molecule that is complementary to another region of the same RNA molecule.

[0045] Although, in mammalian cells, long ds iRNA agents can induce the interferon response which is frequently deleterious, short ds iRNA agents do not trigger the interferon response, at least not to an extent that is deleterious to the cell and/or host (Manche et al., *Mol. Cell. Biol.* 12:5238, 1992; Lee et al., *Virology* 199:491, 1994; Castelli et al., *J. Exp. Med.* 186:967, 1997; Zheng et al., *RNA* 10:1934, 2004; Heideil et al., “Lack of interferon response in animals to naked siRNAs” *Nature Biotechnol. advance online publication* doi: 10.1038/nbt1038, Nov. 21, 2004). The iRNA agents of the present invention include molecules which are sufficiently short that they do not trigger a deleterious non-specific interferon response in normal mammalian cells. Thus, the administration of a composition including an iRNA agent (e.g., formulated as described herein) to a subject can be used to decreased expression of the RhoA genes in RhoA expressing cells in the subject, while circumventing an interferon response. Molecules that are short enough that they do not trigger a deleterious interferon response are termed siRNA agents or siRNAs herein. “siRNA agent” or “siRNA” as used herein, refers to an iRNA agent, e.g., a ds iRNA agent, that is sufficiently short that it does not induce a deleterious interferon response in a human cell, e.g., it has a duplexed region of less than 60 but preferably less than 50, 40, or 30 nucleotide pairs.

[0046] The isolated iRNA agents described herein, including ds iRNA agents and siRNA agents, can mediate the decreased expression of a RhoA nucleic acid, e.g., by RNA degradation. For convenience, such RNA is also referred to herein as the RNA to be silenced. Such a nucleic acid is also referred to as a target gene. Preferably, the RNA to be silenced is a gene product of an endogenous RhoA gene.

[0047] As used herein, the phrase “mediates RNAi” refers to the ability of an agent to silence, in a sequence specific manner, a target gene. “Silencing a target gene” means the process whereby a cell containing and/or expressing a certain product of the target gene when not in contact with the agent, will contain and/or express at least 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, or 90% less of such gene product when contacted with the agent, as compared to a similar cell which has not been contacted with the agent. Such product of the target gene can, for example, be a messenger RNA (mRNA), a protein, or a regulatory element.

[0048] As used herein, the term “complementary” is used to indicate a sufficient degree of complementarity such that

stable and specific binding occurs between a compound of the invention and a target RNA molecule, e.g., a RhoA mRNA. Specific binding requires a sufficient degree of complementarity to avoid non-specific binding of the oligomeric compound to non-target sequences under conditions in which specific binding is desired, i.e., under physiological conditions in the case of in vivo assays or therapeutic treatment, or in the case of in vitro assays, under conditions in which the assays are performed. The non-target sequences typically differ from the target sequences by at least 4 nucleotides.

[0049] As used herein, an iRNA agent is “sufficiently complementary” to a target RNA, e.g., a target mRNA (e.g., a target RhoA mRNA) if the iRNA agent reduces the production of a protein encoded by the target RNA in a cell. The iRNA agent may also be “exactly complementary” to the target RNA, e.g., the target RNA and the iRNA agent anneal, preferably to form a hybrid made exclusively of Watson-Crick basepairs in the region of exact complementarity. A “sufficiently complementary” iRNA agent can include an internal region (e.g., of at least 10 nucleotides) that is exactly complementary to a target RhoA RNA. Moreover, in some embodiments, the iRNA agent specifically discriminates a single-nucleotide difference. In this case, the iRNA agent only mediates RNAi if exact complementarity is found in the region (e.g., within 7 nucleotides of) the single-nucleotide difference. Preferred iRNA agents will be based on or consist of or comprise the sense and antisense sequences provided in Table 1.

[0050] As used herein, “essentially identical” when used referring to a first nucleotide sequence in comparison to a second nucleotide sequence means that the first nucleotide sequence is identical to the second nucleotide sequence except for up to one, two or three nucleotide substitutions (e.g., adenosine replaced by uracil). “Essentially retaining the ability to inhibit RhoA expression in cultured human RhoA expressing cells,” as used herein referring to an iRNA agent not identical to but derived from one of the iRNA agents of Table 1 by deletion, addition or substitution of nucleotides, means that the derived iRNA agent possesses an inhibitory activity not more than 20% (in terms of remaining target mRNA) different from the inhibitory activity of the iRNA agent of Table 1 from which it was derived. For example, an iRNA agent derived from an iRNA agent of Table 1 which lowers the amount of RhoA mRNA present in cultured human RhoA expressing cells by 70% may itself lower the amount of RhoA mRNA present in cultured human RhoA expressing cells by at least 50% in order to be considered as essentially retaining the ability to inhibit RhoA expression in cultured human RhoA expressing cells. Optionally, an iRNA agent of the invention may lower the amount of RhoA mRNA present in cultured human RhoA expressing cells by at least 50%, or at least 40%.

[0051] As used herein, a “subject” refers to a mammalian organism undergoing treatment for a disorder mediated by RhoA protein expression. The subject can be any mammal, such as a cow, horse, mouse, rat, dog, pig, goat, or a primate. In the preferred embodiment, the subject is a human.

[0052] Design and Selection of iRNA Agents

[0053] As used herein, “disorders associated with RhoA expression” refers to any biological or pathological state that (1) is mediated in part by the presence of RhoA mRNA

and/or protein and (2) whose outcome can be affected by reducing the level of RhoA mRNA and/or protein present. Specific disorders associated with RhoA expression are noted below and are primarily based on the responsibility of RhoA action in inhibiting axonal elongation and regeneration.

[0054] The present invention is based on the design, synthesis and generation of iRNA agents that target RhoA and the demonstration of silencing of a RhoA gene in vitro in cultured cells after incubation with an iRNA agent, and the resulting RhoA-specific effect.

[0055] An iRNA agent can be rationally designed based on sequence information and desired characteristics. For example, an iRNA agent can be designed according to the relative melting temperature of the candidate duplex. Generally, the duplex should have a lower melting temperature at the 5' end of the antisense strand than at the 3' end of the antisense strand.

[0056] Candidate iRNA agents can also be designed by performing, for example, a gene walk analysis of the genes

that will serve as the target gene. Overlapping, adjacent, or closely spaced candidate agents corresponding to all or some of the transcribed region can be generated and tested. Each of the iRNA agents can be tested and evaluated for the ability to down regulate the target gene expression (see below, "Evaluation of Candidate iRNA agents").

[0057] Herein, potential iRNA agents targeting RhoA were designed using the known sequences of RhoA for human, rat and mouse and other known RhoA sequences. The target sequences shown in Table 1 hereinabove were selected from those regions of the human RhoA mRNA sequences that show complete homology with the corresponding sequences in rat and mouse. Therefore, the siRNA agents, agent numbers 6477-6836 should show cross reactivity between these three species. Based on the results provided, the present invention provides iRNA agents that silence RhoA in cultured human RhoA expressing cells and in a subject.

[0058] Table 1 provides exemplary iRNA agents targeting RhoA

TABLE 1

Exemplary iRNA agents for targeting RhoA mRNA										
Start			duplex		sense strand			antisense strand		
Agent number	pos. in RNA ^b	SEQ ID NO.	target sequence (5'-3')	design (overhang) ^a	SEQ ID NO.	sequence (5'-3')	SEQ ID NO.	sequence (5'-3')	SEQ ID NO.	sequence (5'-3')
6477	288	1	ccggaagaaacuggugauuguug	double	2	ggaagaaacuggugauuguTT	3	acaauaccaguuuuccTT		
6478	289	4	cggaagaaacuggugauuguugg	double	5	gaagaaacuggugauuguTT	6	aacaauaccaguuuuccTT		
6479	290	7	ggaagaaacuggugauuguuggu	double	8	aagaacuggugauuguugTT	9	caacaauaccaguuuuccTT		
6480	291	10	gaagaaacuggugauuguuggug	double	11	agaaacuggugauuguuggTT	12	ccaacaauaccaguuuuccTT		
6481	292	13	aagaacuggugauuguugguga	double	14	gaaacuggugauuguugguTT	15	accaacaauaccaguuuuccTT		
6482	293	16	agaaacuggugauuguuggugau	double	17	aaacuggugauuguuggugTT	18	caccaacaauaccaguuuTT		
6483	294	19	gaaacuggugauuguuggugaug	double	20	aacuggugauuguuggugaTT	21	ucaccaacaauaccaguuTT		
6484	295	22	aaacuggugauuguuggugaugg	double	23	acuggugauuguuggugaTT	24	aucaccaacaauaccaguuTT		
6485	296	25	aacuggugauuguuggugaugga	double	26	cuggugauuguuggugaugTT	27	cauccaccaacaauaccagTT		
6486	297	28	acuggugauuguuggugauggag	double	29	uggugauuguuggugauggTT	30	ccauccaccaacaauaccacTT		
6487	298	31	cuggugauuguuggugauggagc	double	32	ggugauuguuggugauggaTT	33	uccaucaccaacaauaccacTT		
6488	299	34	uggugauuguuggugauggagcc	double	35	gugauuguuggugauggagTT	36	cuccaucaccaacaauaccacTT		
6489	300	37	ggugauuguuggugauggagccu	double	38	ugauuguuggugauggagcTT	39	gcuccaucaccaacaauaccacTT		
6490	326	40	gaaagacaugcuugcucauaguc	double	41	aagacaugcuugcucauagTT	42	cuaugagcaagcaugucuTT		
6491	327	43	aaagacaugcuugcucauagucu	double	44	agacaugcuugcucauaguTT	45	acuagagcaagcaugucuTT		
6492	328	46	aagacaugcuugcucauagucuu	double	47	gacaugcuugcucauagucTT	48	gacuaugagcaagcaugucTT		
6493	329	49	agacaugcuugcucauagucuu	double	50	acaugcuugcucauagucuTT	SI	agacuaugagcaagcauguTT		
6494	330	52	gacaugcuugcucauagucuuca	double	53	caugcuugcucauagucuTT	54	aagacuaugagcaagcaugTT		
6495	331	55	acaugcuugcucauagucuuca	double	56	augcuugcucauagucuTT	57	gaagacuaugagcaagcauTT		
6496	332	58	caugcuugcucauagucuuca	double	59	ugcuugcucauagucuTT	60	ugaagacuaugagcaagcaTT		

TABLE 1-continued

Exemplary iRNA agents for targeting RhoA mRNA									
Agent number	Start		duplex	sense strand		antisense strand		SEQ ID NO.	sequence (5'-3')
	pos. in RNA ^b	SEQ ID NO.		design (over-hang) ^a	SEQ ID NO.	SEQ ID NO.	sequence (5'-3')		
6497	333	61	augcuugcuc	double	62	gcuugcuc	augcuucagTT	63	cugaagac
6498	334	64	ugcuugcuc	double	65	cuugcuc	augcuucagTT	66	gcugaagac
6499	335	67	gcuugcuc	double	68	uugcuc	augcuucagTT	69	ugcugaagac
6500	336	70	cuugcuc	double	71	ugcuc	augcuucagTT	72	uugcugaagac
6501	337	73	uugcuc	double	74	gcuc	augcuucagTT	75	cuugcugaagac
6502	338	76	ugcuc	double	77	cuc	augcuucagTT	78	ccuugcugaagac
6503	339	79	gcuc	double	80	uc	augcuucagTT	81	uccuugcugaagac
6504	340	82	cuc	double	83	cau	augcuucagTT	84	guccuugcugaagac
6505	341	85	ucau	double	86	au	augcuucagTT	87	gguccuugcugaagac
6506	342	88	cau	double	89	uag	cuucagcaTT	90	ugguccuugcugaagac
6507	343	91	au	double	92	ag	cuucagcaTT	93	cugguccuugcugaagac
6508	344	94	uag	double	95	guc	uucagcaTT	96	acugguccuugcugaagac
6509	345	97	ag	double	98	uc	uucagcaTT	99	aacugguccuugcugaagac
6510	346	100	guc	double	101	cu	uucagcaTT	102	gaacugguccuugcugaagac
6511	347	103	ucu	double	104	uuc	agcaagaccagTT	105	ggaacugguccuugcugaagac
6512	348	106	cu	double	107	uc	agcaagaccagTT	108	gggaacugguccuugcugaagac
6513	349	109	uuc	double	110	cag	caagaccagTT	111	ugggaacugguccuugcugaagac
6514	350	112	uc	double	113	ag	caagaccagTT	114	cugggaacugguccuugcugaagac
6515	351	115	cag	double	116	gca	agaccagTT	117	ucugggaacugguccuugcugaagac
6516	352	118	ag	double	119	ca	agaccagTT	120	cucugggaacugguccuugcugaagac
6517	353	121	gca	double	122	aag	accagTT	123	ccucugggaacugguccuugcugaagac
6518	354	124	ca	double	125	agg	accagTT	126	accucugggaacugguccuugcugaagac
6519	425	127	gaa	double	128	aag	cagguagagTT	129	aagccaacucuaaccugcTT
6520	426	130	aa	double	131	ag	cagguagagTT	132	aaagccaacucuaaccugcTT
6521	535	133	gac	double	134	cag	cccugauagTT	135	uucuaaaacuaucagggcTT
6522	536	136	ac	double	137	ag	cccugauagTT	138	uuucuaaaacuaucagggcTT
6523	537	139	cag	double	140	g	cccugauagTT	141	uuuucuaaaacuaucagggcTT
6524	538	142	ag	double	143	cc	cugauagTT	144	guuuucuaaaacuaucagggcTT
6525	539	145	g	double	146	cc	gauagTT	147	uguuuucuaaaacuaucagggcTT
6526	540	148	cc	double	149	c	gauagTT	150	auguuuucuaaaacuaucagggcTT
6527	541	151	cc	double	152	u	gauagTT	153	gauguuuucuaaaacuaucagggcTT
6528	542	154	c	double	155	g	auagTT	156	ggauguuuuucuaaaacuaucagggcTT
6529	543	157	u	double	158	a	guagTT	159	gggauguuuuucuaaaacuaucagggcTT
6530	544	160	g	double	161	u	guagTT	162	ugggauguuuuucuaaaacuaucagggcTT

TABLE 1-continued

Exemplary iRNA agents for targeting RhoA mRNA									
Agent number	Start		duplex	sense strand		antisense strand		SEQ ID NO.	sequence (5'-3')
	pos. in RNA ^b	SEQ ID NO.		design (over-hang) ^a	SEQ ID NO.	SEQ ID NO.			
6531	545	163	auaguuuagaaaacauccagaa	double	164	aguuuagaaaacaucccgATT	165	cugggauguuuuucuaaacuTT	
6532	546	166	uaguuuagaaaacauccagaaa	double	167	guuuagaaaacaucccgATT	168	ucugggauguuuuucuaaacTT	
6533	547	169	aguuuagaaaacauccagaaaa	double	170	uuuagaaaacaucccgaaTT	171	uucugggauguuuuucuaaaTT	
6534	548	172	guuuagaaaacauccagaaaag	double	173	uuagaaaacaucccgaaaTT	174	uuucugggauguuuuucuaaTT	
6535	549	175	uuuagaaaacauccagaaaagu	double	176	uagaaaacaucccgaaaaTT	177	uuuucugggauguuuuucuaTT	
6536	575	178	cccagaagucaagcauuucugu	double	179	ccagaagucaagcauuucTT	180	agaaugcuugacuucuggTT	
6537	576	181	cccagaagucaagcauuucuguc	double	182	cagaagucaagcauuucgTT	183	cagaaugcuugacuucugTT	
6538	577	184	ccagaagucaagcauuucugucc	double	185	agaagucaagcauuucgTT	186	acagaaugcuugacuucTT	
6539	578	187	cagaagucaagcauuucuguccc	double	188	gaagucaagcauuucgTT	189	gacagaaugcuugacuucTT	
6540	579	190	agaagucaagcauuucuguccca	double	191	aagucaagcauuucguccTT	192	ggacagaaugcuugacuTT	
6541	692	193	ugaaacccugaagaaggcagagau	double	194	aaaccugaagaaggcagagTT	195	cucugccuucucagguuTT	
6542	693	196	gaaaccugaagaaggcagagaua	double	197	aaccugaagaaggcagagaTT	198	ucucugccuucucagguTT	
6543	694	199	aaaccugaagaaggcagagauau	double	200	accugaagaaggcagagauTT	201	aucucugccuucucagguTT	
6544	695	202	aaccugaagaaggcagagauaug	double	203	ccugaagaaggcagagauaTT	204	uauccugccuucucagTT	
6545	696	205	accugaagaaggcagagauaugg	double	206	cugaagaaggcagagauauTT	207	auaucucugccuucucagTT	
6546	697	208	ccugaagaaggcagagauauggc	double	209	ugaagaaggcagagauaugTT	210	cauauccugccuucucTT	
6547	698	211	cugaagaaggcagagauauggca	double	212	gaagaaggcagagauaugTT	213	ccauauccugccuucucTT	
6548	699	214	ugaagaaggcagagauauggcaa	double	215	aagaaggcagagauaugcTT	216	gccauauccugccuucTT	
6549	700	217	gaagaaggcagagauaugycaa	double	218	agaaggcagagauaug9caTT	219	ugccauauccugccuucTT	
6550	701	220	aagaaggcagagauauggcaaac	double	221	gaaggcagagauauggcaaTT	222	uugccauauccugccuucTT	
6551	702	223	agaaggcagagauauggcaaaca	double	224	aaggcagagauauggcaaTT	225	uuugccauauccugccuTT	
6552	703	226	gaaggcagagauauggcaaacag	double	227	aggcagagauauggcaaacTT	228	guuugccauauccugccuTT	
6553	704	229	aaggcagagauauggcaaacagg	double	230	ggcagagauauggcaaacaTT	231	uguuugccauauccugccTT	
6554	705	232	aggcagagauauggcaaacagga	double	233	gcagagauauggcaaacagTT	234	cuguuugccauauccugcTT	
6555	706	235	ggcagagauauggcaaacaggau	double	236	cagagauauggcaaacaggTT	237	ccuguuugccauauccugTT	
6556	707	238	gcagagauauggcaaacaggauu	double	239	agagauauggcaaacaggTT	240	uccuguuugccauauccuTT	
6557	708	241	cagagauauggcaaacaggauug	double	242	gagauauggcaaacaggauTT	243	auccuguuugccauauccTT	
6558	709	244	agagauauggcaaacaggauugg	double	245	agauauggcaaacaggauTT	246	auccuguuugccauauccTT	
6559	710	247	gagauauggcaaacaggauuggc	double	248	gauauggcaaacaggauTT	249	caauccuguuugccauauccTT	
6560	711	250	agauauggcaaacaggauuggcg	double	251	auauggcaaacaggauTT	252	ccauuccuguuugccauauTT	
6561	712	253	gauauggcaaacaggauuggcgc	double	254	uauuggcaaacaggauTT	255	gccauuccuguuugccauTT	
6562	713	256	auauggcaaacaggauuggcgcu	double	257	auuggcaaacaggauTT	258	cgccauuccuguuugccauTT	
6563	714	259	uauuggcaaacaggauuggcgcuu	double	260	uggcaaacaggauTT	261	gcgccauuccuguuugccTT	
6564	715	262	auqgcaaacaggaauugcgcuu	double	263	qgcaaacaggaauugcgcuTT	264	agcgccauuccuguuugccTT	

TABLE 1-continued

<u>Exemplary iRNA agents for targeting RhoA mRNA</u>									
Agent number	Start		duplex	sense strand		antisense strand		SEQ ID NO.	sequence (5'-3')
	pos. in RNA ^b	SEQ ID NO.		design (over-hang) ^a	SEQ ID NO.	SEQ ID NO.	sequence (5'-3')		
6565	716	265	uggcaaacaggauuggcgcuuuu	double	266	gcaaacaggauuggcgcuuTT	267	aagcgccaauccuguuugcTT	
6566	717	268	ggcaaacaggauuggcgcuuuug	double	269	caaacaggauuggcgcuuTT	270	aaagcgccaauccuguuugTT	
6567	718	271	gcaaacaggauuggcgcuuuugg	double	272	aaacaggauuggcgcuuuuTT	273	aaaagcgccaauccuguuTT	
6568	719	274	caaacaggauuggcgcuuuuggg	double	275	aacaggauuggcgcuuuugTT	276	caaaagcgccaauccuguuTT	
6569	720	277	aaacaggauuggcgcuuuugggu	double	278	acaggauuggcgcuuuuggTT	279	ccaaaagcgccaauccuguTT	
6570	721	280	aacaggauuggcgcuuuugggua	double	281	caggauuggcgcuuuugggTT	282	cccaaaaagcgccaauccguTT	
6571	722	283	acaggauuggcgcuuuuggguac	double	284	aggauuggcgcuuuuggguTT	285	acccaaaagcgccaauccuTT	
6572	723	286	caggauuggcgcuuuuggguaca	double	287	ggauuggcgcuuuuggguacTT	288	uacccaaaagcgccaauccTT	
6573	724	289	aggauuggcgcuuuuggguacau	double	290	gauuggcgcuuuuggguacTT	291	guacccaaaagcgccaaucTT	
6574	725	292	ggauuggcgcuuuuggguacaug	double	293	auuggcgcuuuuggguacaTT	294	uguacccaaaagcgccaaTT	
6575	726	295	gauuggcgcuuuuggguacaugg	double	296	uuggcgcuuuuggguacauTT	297	auguacccaaaagcgccaaTT	
6576	727	298	auuggcgcuuuuggguacaugga	double	299	ugcgcuuuuggguacaugTT	300	cauguacccaaaagcgccaaTT	
6577	728	301	uuggcgcuuuuggguacauggag	double	302	ggcgcuuuuggguacauggTT	303	ccauguacccaaaagcgccTT	
6578	729	304	ugcgcuuuuggguacauggagu	double	305	cgcuuuuggguacauggaTT	306	uccauguacccaaaagcgccTT	
6579	730	307	ggcgcuuuuggguacauggagug	double	308	cgcuuuuggguacauggagTT	309	cuccauguacccaaaagcgTT	
6580	731	310	cgcuuuuggguacauggagugu	double	311	gcuuuuggguacauggaguTT	312	acuccauguacccaaaagcTT	
6581	732	313	cgcuuuuggguacauggaguguu	double	314	cuuuuggguacauggagugTT	315	cacuccauguacccaaaagTT	
6582	733	316	gcuuuuggguacauggaguguuc	double	317	uuuuggguacauggaguguTT	318	acacuccauguacccaaaTT	
6583	734	319	cuuuuggguacauggaguguuca	double	320	uuuggguacauggaguguuTT	321	aacacuccauguacccaaaTT	
6584	735	322	uuuuggguacauggaguguucag	double	323	uuggguacauggaguguucTT	324	gaacacuccauguacccaaTT	
6585	736	325	uuuggguacauggaguguucagc	double	326	uggguacauggaguguucaTT	327	ugaacacuccauguacccaaTT	
6586	737	328	uuggguacauggaguguucagca	double	329	ggguacauggaguguucagTT	330	cugaacacuccauguacccTT	
6587	738	331	uggguacauggaguguucagcaa	double	332	guacauggaguguucagcTT	333	gcugaacacuccauguaccTT	
6588	739	334	ggguacauggaguguucagcaaa	double	335	guacauggaguguucagcaTT	336	ugcugaacacuccauguacTT	
6589	740	337	guacauggaguguucagcaaaag	double	338	uacauggaguguucagcaaTT	339	uugcugaacacuccauguaTT	
6590	741	340	guacauggaguguucagcaaaaga	double	341	acauggaguguucagcaaaTT	342	uuugcugaacacuccauguTT	
6591	742	343	uacauggaguguucagcaaaagac	double	344	cauggaguguucagcaaaTT	345	cuuugcugaacacuccaugTT	
6592	743	346	acauggaguguucagcaaaagacc	double	347	auggaguguucagcaaaagaTT	348	ucuuugcugaacacuccauTT	
6593	744	349	cauggaguguucagcaaaagacca	double	350	uggaguguucagcaaaagacTT	351	gucuuugcugaacacuccaTT	
6594	745	352	auggaguguucagcaaaagaccaa	double	353	ggaguguucagcaaaagaccTT	354	ggucuugcugaacacuccTT	
6595	746	355	uggaguguucagcaaaagaccaaa	double	356	gaguguucagcaaaagaccaTT	357	uggucuugcugaacacuccTT	
6596	747	358	ggaguguucagcaaaagaccaaaag	double	359	aguguucagcaaaagaccaaTT	360	uuggucuugcugaacacucTT	
6597	748	361	gaguguucagcaaaagaccaaaaga	double	362	guguucagcaaaagaccaaaTT	363	uuuggucuugcugaacacTT	
6598	749	364	aguguucagcaaaagaccaaaagau	double	365	uguucagcaaaagaccaaaagTT	366	cuuuggucuugcugaacaTT	

TABLE 1-continued

Exemplary iRNA agents for targeting RhoA mRNA									
Agent number	Start		duplex	sense strand		antisense strand		SEQ ID NO.	sequence (5'-3')
	pos. in RNA ^b	SEQ ID NO.		design (over-hang) ^a	SEQ ID NO.	design (over-hang) ^a	SEQ ID NO.		
6599	750	367	guguucagcaaagaccaaagaug	double	368	guucagcaaagaccaaagaTT	369	ucuugggucuugcugaacTT	
6600	770	370	auggagugagagagguuuugaa	double	371	ggagugagagagguuuugTT	372	caaaaaccucucacacuccTT	
6601	771	373	uggagugagagagguuuugaaa	double	374	gagugagagagguuuugaTT	375	uaaaaaaccucucacacucTT	
6602	797	376	cuacgagagcugcucugcaagcu	double	377	acgagagcugcucugcaagTT	378	cuugcagagcagcucugcuTT	
6603	798	379	uacgagagcugcucugcaagcua	double	380	cgagagcugcucugcaagcTT	381	gcuugcagagcagcucugcTT	
6604	799	382	acgagagcugcucugcaagcuag	double	383	gagagcugcucugcaagcuTT	384	agcuugcagagcagcucucTT	
6605	800	385	cgagagcugcucugcaagcuaga	double	386	agagcugcucugcaagcuTT	387	uagcuugcagagcagcucuTT	
6606	801	388	gagagcugcucugcaagcuagac	double	389	gagcugcucugcaagcuagTT	390	cuagcuugcagagcagcucTT	
6607	802	391	agagcugcucugcaagcuagacg	double	392	agcugcucugcaagcuagaTT	393	ucuagcuugcagagcagcuTT	
6608	803	394	gagcugcucugcaagcuagacgu	double	395	gcugcucugcaagcuagacTT	396	gucuagcuugcagagcagcTT	
6609	804	397	agcugcucugcaagcuagacgug	double	398	cuyoucugcaagcuagacgTT	399	cgucuagcuugcagagcagTT	
6610	895	400	uugaagugcuguuuauuaucuu	double	401	gaagugcuguuuauuaucTT	402	gauuaauaaacagcacuucTT	
6611	896	403	ugaagugcuguuuauuaucua	double	404	aagugcuguuuauuaucTT	405	agauuaauaaacagcacuTT	
6612	897	406	gaagugcuguuuauuaucuuag	double	407	agugcuguuuauuaucuuTT	408	aagauuaauaaacagcacuTT	
6613	898	409	aagugcuguuuauuaucuuagu	double	410	gugcuguuuauuaucuuTT	411	uaagauuaauaaacagcacTT	
6614	899	412	agugcuguuuauuaucuuagug	double	413	ugcuguuuauuaucuuagTT	414	cuaagauuaauaaacagcaTT	
6615	900	415	gugcuguuuauuaucuuagugu	double	416	gcuguuuauuaucuuaguTT	417	acuaagauuaauaaacagcTT	
6616	901	418	ugcuguuuauuaucuuagugua	double	419	cuguuuauuaucuuagugTT	420	cacuaagauuaauaaacagTT	
6617	902	421	gcuguuuauuaucuuaguguau	double	422	uguuuauuaucuuaguguTT	423	acacuaagauuaauaaacaTT	
6618	903	424	cuguuuauuaucuuaguguaug	double	425	guuuauuaucuuaguguaTT	426	uacacuaagauuaauaaacTT	
6619	904	427	uguuuauuaucuuaguguauga	double	428	uuuauuaucuuaguguaTT	429	auacacuaagauuaauaaTT	
6620	905	430	guuuauuaucuuaguguaugau	double	431	uuauuaucuuaguguaugTT	432	cauacacuaagauuaauaaTT	
6621	906	433	uuuauuaucuuaguguaugauu	double	434	uauuaucuuaguguaugaTT	435	ucauacacuaagauuaauTT	
6622	907	436	uuauuaucuuaguguaugauua	double	437	auuaucuuaguguaugauTT	438	aucauacacuaagauuaauTT	
6623	908	439	uauuaucuuaguguaugauuac	double	440	uuaucuuaguguaugauuTT	441	aaucacacuaagauuaauTT	
6624	909	442	auuaucuuaguguaugauuacu	double	443	uaucuuaguguaugauuTT	444	uaucacacuaagauuaauTT	
6625	910	445	uuaucuuaguguaugauuacug	double	446	aaucuuaguguaugauuacTT	447	guaucauacacuaagauuTT	
6626	911	448	uaucuuaguguaugauuacugg	double	449	aucuuaguguaugauuacTT	450	aguaaucauacacuaagauTT	
6627	912	451	aaucuuaguguaugauuacuggc	double	452	ucuuaguguaugauuacugTT	453	caguaaucauacacuaagaTT	
6628	913	454	aucuuaguguaugauuacuggcc	double	455	cuuaguguaugauuacuggTT	456	ccaguaaucauacacuaagTT	
6629	914	457	ucuuaguguaugauuacuggccu	double	458	uuaguguaugauuacuggcTT	459	gccaguaaucauacacuaaTT	
6630	915	460	cuuaguguaugauuacuggccuu	double	461	uaguguaugauuacuggccTT	462	ggccaguaaucauacacuaTT	
6631	916	463	uuaguguaugauuacuggccuuu	double	464	aguguaugauuacuggccuTT	465	agccaguaaucauacacuuTT	
6632	917	466	uaguguaugauuacuggccuuuu	double	467	guguaugauuacuggccuuTT	468	aaggccaguaaucauacacTT	

TABLE 1-continued

Exemplary iRNA agents for targeting RhoA mRNA									
Agent number	Start		duplex	sense strand		antisense strand		SEQ ID NO.	sequence (5'-3')
	pos. in RNA ^b	SEQ ID NO.		design (over-hang) ^a	SEQ ID NO.	SEQ ID NO.	sequence (5'-3')		
6633	918	469	agugaugauuacugycuuuuu	double	470	uguugauuacuggccuuuTT	471	aaagccaguuaucauacATT	
6634	919	472	gugaugauuacuggccuuuuuc	double	473	guugauuacuggccuuuTT	474	aaaagccaguuaucauacATT	
6635	939	475	uucuuuuaucauaauuuaccua	double	476	cauuuaucauaauuuaccTT	477	gguaauuuauagauaaagTT	
6636	940	478	ucauuuaucauaauuuaccuaa	double	479	auuuaucauaauuuaccuTT	480	agguaaaauuagauaaauTT	
6637	941	481	cauuuaucauaauuuaccuaag	double	482	uuuaucauaauuuaccuaTT	483	uagguaaaauuagauaaaTT	
6638	942	484	auuuaucauaauuuaccuaaga	double	485	uuaucauaauuuaccuaaTT	486	uuagguaaaauuagauaaTT	
6639	943	487	uuuaucauaauuuaccuaagau	double	488	uaucauaauuuaccuaagTT	489	cuagguaaaauuagauaTT	
6640	944	490	uuaucauaauuuaccuaagauu	double	491	aucauaauuuaccuaagaTT	492	ucuuagguaaaauuagauTT	
6641	945	493	uaucauaauuuaccuaagauua	double	494	ucauaauuuaccuaagauTT	495	aucuuagguaaaauuagauTT	
6642	946	496	aucauaauuuaccuaagauuac	double	497	cuauauuuaccuaagauuTT	498	aaucuuagguaaaauuagTT	
6643	947	499	ucauaauuuaccuaagauuaca	double	500	uaauauuuaccuaagauuaTT	501	uaucuuagguaaaauuaTT	
6644	948	502	cuauauuuaccuaagauuacaa	double	503	auauuuuaccuaagauuacTT	504	guauauuagguaaaauuauTT	
6645	949	505	uaauauuuaccuaagauuacaaa	double	506	uaauuuaccuaagauuacaTT	507	uguaauuuagguaaaauaTT	
6646	950	508	auauuuuaccuaagauuacaaau	double	509	aaauuaccuaagauuacaaTT	510	uuguaauuuagguaaaauTT	
6647	951	511	uaauuuacauaagauuacaaauc	double	512	auuuuaccuaagauuacaaTT	513	uuuguaauuuagguaaaauTT	
6648	952	514	aaauuaccuaagauuacaaauca	double	515	uuuaccuaagauuacaaauTT	516	auuuguaauuuagguaaaTT	
6649	953	517	auuuaccuaagauuacaaucag	double	518	uuaccuaagauuacaaucTT	519	gauuuguaauuuagguaaTT	
6650	954	520	uuuaccuaagauuacaaucaga	double	521	uaccuaagauuacaaucattTT	522	ugauuuguaauuuagguattTT	
6651	974	523	agaagucauugcuaccagauu	double	524	aagucauugcuaccagauTT	525	acugguagcaagaugacuTT	
6652	975	526	gaagucauugcuaccagauuu	double	527	agucauugcuaccagauaTT	528	uacugguagcaagaugacuTT	
6653	976	529	aagucauugcuaccagauuuu	double	530	gucauugcuaccagauuTT	531	auacugguagcaagaugattTT	
6654	977	532	agucauugcuaccagauuuua	double	533	ucauugcuaccagauuTT	534	aaucugguagcaagaugaTT	
6655	978	535	gucauugcuaccagauuuuag	double	536	cauugcuaccagauuuuTT	537	aaauacugguagcaagaugTT	
6656	979	538	ucauugcuaccagauuuuaga	double	539	auuugcuaccagauuuuTT	540	uaauacugguagcaagaauTT	
6657	980	541	cauugcuaccagauuuuagaa	double	542	ucuugcuaccagauuuuagTT	543	cuauuacugguagcaagaTT	
6658	981	544	auuugcuaccagauuuuagaag	double	545	cuugcuaccagauuuuagattTT	546	ucuaauuacugguagcaagTT	
6659	982	547	ucuugcuaccagauuuuagaagc	double	548	uugcuaccagauuuuagattTT	549	uucuaauuacugguagcaattTT	
6660	983	550	cuugcuaccagauuuuagaagcc	double	551	ugcuaccagauuuuagaagTT	552	cuucuaauuacugguagcaTT	
6661	984	553	uugcuaccagauuuuagaagcca	double	554	gcuaccagauuuuagaagcTT	555	gcuucuaauuacugguagcTT	
6662	985	556	ugcuaccagauuuuagaagccaa	double	557	cuaccagauuuuagaagccTT	558	ggcuucuaauuacugguagTT	
6663	986	559	gcuaccagauuuuagaagccaac	double	560	uaccagauuuuagaagccaTT	561	uggcuucuaauuacugguaTT	
6664	987	562	cuaccagauuuuagaagccaacu	double	563	accagauuuuagaagccaattTT	564	uuggcuucuaauuacugguTT	
6665	988	565	uaccagauuuuagaagccaacua	double	566	ccagauuuuagaagccaattTT	567	guuggcuucuaauuacuggTT	
6666	1131	568	cuugcuucuuuagaaagagaa	double	569	ugcuucuuuagaaagagTT	570	cucuucuaagaaagacattTT	

TABLE 1-continued

Exemplary iRNA agents for targeting RhoA mRNA									
Agent number	Start		duplex	sense strand		antisense strand			
	pos. in RNA ^b	SEQ ID NO.		design (over-hang) ^a	SEQ ID NO.	SEQ ID NO.	sequence (5'-3')		
6667	1132	571	uugcuucuucuagaaagagaaa	double	572	gcuucuucuagaaagagaTT	573	ucucuucuagaaagaagcTT	
6668	1133	574	ugcuucuucuagaaagagaaac	double	575	cuucuucuagaaagagaaTT	576	uucucuucuagaaagaagTT	
6669	1134	577	gcuucuucuagaaagagaaaca	double	578	uucuucuagaaagagaaaTT	579	uuucuucuucuagaaagaTT	
6670	1135	580	cuucuucuagaaagagaaacag	double	581	ucuucuagaaagagaaacTT	582	guuucuucuagaaagaTT	
6671	1136	583	uucuucuagaaagagaaacagu	double	584	cuucuagaaagagaaacaTT	585	uguuucuucuucuagaaagTT	
6672	1137	586	ucuucuagaaagagaaacaguu	double	587	uuucuagaaagagaaacagTT	588	cuguuucuucuucuagaaTT	
6673	1138	589	cuucuagaaagagaaacaguug	double	590	uucuagaaagagaaacaguTT	591	acuguuucuucuucuagaaTT	
6674	1139	592	uuucuagaaagagaaacaguugg	double	593	ucuagaaagagaaacaguTT	594	aacuguuucuucuucuagaaTT	
6675	1140	595	uucuagaaagagaaacaguuggu	double	596	cuagaaagagaaacaguugTT	597	caacuguuucuucuucuagTT	
6676	1141	598	ucuagaaagagaaacaguuggua	double	599	uagaaagagaaacaguuggTT	600	ccaacuguuucuucuuaTT	
6677	1142	601	cuagaaagagaaacaguugguaa	double	602	agaaagagaaacaguugguTT	603	accaacuguuucuucuuaTT	
6678	1143	604	uagaaagagaaacaguugguaac	double	605	gaaagagaaacaguugguaTT	606	uaccaacuguuucuucuuaTT	
6679	1144	607	agaaagagaaacaguugguaacu	double	608	aaagagaaacaguugguaaTT	609	uuaccaacuguuucuucuTT	
6680	1145	610	gaaagagaaacaguugguaacuu	double	611	aagagaaacaguugguaacTT	612	guuaccaacuguuucuucuTT	
6681	1146	613	aaagagaaacaguugguaacuuu	double	614	agagaaacaguugguaacuTT	615	aguuaccaacuguuucuucuTT	
6682	1147	616	aagagaaacaguugguaacuuuu	double	617	gagaaacaguugguaacuuTT	618	aaguuaccaacuguuucucTT	
6683	1148	619	agagaaacaguugguaacuuuug	double	620	agaaacaguugguaacuuuTT	621	aaaguuaccaacuguuucTT	
6684	1149	622	gagaaacaguugguaacuuuugu	double	623	gaaacaguugguaacuuuTT	624	aaaaguuaccaacuguuucTT	
6685	1150	625	agaaacaguugguaacuuuugug	double	626	aaacaguugguaacuuuugTT	627	caaaaguuaccaacuguuTT	
6686	1151	628	gaaacaguugguaacuuuuguga	double	629	aacaguugguaacuuuuguTT	630	acaaaaguuaccaacuguuTT	
6687	1152	631	aaacaguugguaacuuuugugaa	double	632	acaguugguaacuuuugugTT	633	cacaaaaguuaccaacuguTT	
6688	1153	634	aacaguugguaacuuuugugaau	double	635	caguugguaacuuuugugaTT	636	ucacaaaaguuaccaacugTT	
6689	1154	637	acaguugguaacuuuugugaauu	double	638	aguugguaacuuuugugaaTT	639	uucacaaaaguuaccaacuTT	
6690	1155	640	caguugguaacuuuugugaauua	double	641	guugguaacuuuugugaauTT	642	auucacaaaaguuaccaacTT	
6691	1156	643	aguugguaacuuuugugaauuag	double	644	uugguaacuuuugugaauuTT	645	aaucacaaaaguuaccaaaTT	
6692	1157	646	guugguaacuuuugugaauuagg	double	647	ugguaacuuuugugaauuaTT	648	uaauucacaaaaguuaccaTT	
6693	1158	649	uugguaacuuuugugaauuaggc	double	650	gguaacuuuugugaauuagTT	651	cuaauucacaaaaguuaccTT	
6694	1159	652	ugguaacuuuugugaauuaggcu	double	653	guaacuuuugugaauuaggTT	654	ccuaauucacaaaaguuaccTT	
6695	1160	655	gguaacuuuugugaauuaggcug	double	656	uaacuuuugugaauuaggcTT	657	gccuaauucacaaaaguuaTT	
6696	1161	658	guaacuuuugugaauuaggcugu	double	659	aacuuuugugaauuaggcuTT	660	agccuaauucacaaaaguTT	
6697	1162	661	uaacuuuugugaauuaggcugua	double	662	acuuuugugaauuaggcugTT	663	cagccuaauucacaaaaguTT	
6698	1163	664	aacuuuugugaauuaggcuguaa	double	665	cuuuugugaauuaggcuguTT	666	acagccuaauucacaaaagTT	
6699	1164	667	acuuiuugugaauuaggcuguaac	double	668	uuuugugaauuaggcuguaTT	669	uacagccuaauucacaaaTT	
6700	1165	670	cuuuugugaauuaggcuguaacu	double	671	uuugugaauuaggcuguaaTT	672	uuacagccuaauucacaaaTT	

TABLE 1-continued

<u>Exemplary iRNA agents for targeting RhoA mRNA</u>									
Agent number	Start		duplex	sense strand		antisense strand		SEQ ID NO.	sequence (5'-3')
	pos. in RNA ^b	SEQ ID NO.		design (over-hang) ^a	SEQ ID NO.	SEQ ID NO.	sequence (5'-3')		
6701	1166	673	uuuugugaauuaggcuguaacua	double	674	uugugaauuaggcuguaacTT	675	guuacagccuaauucacaaTT	
6702	1167	676	uuugugaauuaggcuguaacuac	double	677	ugugaauuaggcuguaacuTT	678	aguacagccuaauucacaaTT	
6703	1168	679	uugugaauuaggcuguaacuacu	double	680	gugaauuaggcuguaacuacTT	681	uaguacagccuaauucacaaTT	
6704	1169	682	ugugaauuaggcuguaacuacu	double	683	ugaauuaggcuguaacuacTT	684	guaguacagccuaauucacaaTT	
6705	1170	685	gugaauuaggcuguaacuacu	double	686	gaauuaggcuguaacuacuTT	687	aguaguacagccuaauucacaaTT	
6706	1171	688	ugaauuaggcuguaacuacu	double	689	aaauaggcuguaacuacuTT	690	aaguaguacagccuaauucacaaTT	
6707	1172	691	gaauuaggcuguaacuacu	double	692	auuaggcuguaacuacuTT	693	aaaguaguacagccuaauucacaaTT	
6708	1173	694	aaauaggcuguaacuacu	double	695	uuaggcuguaacuacuTT	696	uaaguaguacagccuaauucacaaTT	
6709	1174	697	auuaggcuguaacuacu	double	698	uaggcuguaacuacuTT	699	auaaaguaguacagccuaauucacaaTT	
6710	1175	700	uuaggcuguaacuacu	double	701	aggcuguaacuacuTT	702	uaaaaguaguacagccuaauucacaaTT	
6711	1176	703	uaggcuguaacuacu	double	704	ggcuguaacuacuTT	705	uuauaaaguaguacagccuaauucacaaTT	
6712	1177	706	aggcuguaacuacu	double	707	gcuguaacuacuTT	708	guuauaaaguaguacagccuaauucacaaTT	
6713	1178	709	ggcuguaacuacu	double	710	cuguaacuacuTT	711	aguauaaaguaguacagccuaauucacaaTT	
6714	1179	712	gcuguaacuacu	double	713	uguacuacuTT	714	uaguauaaaguaguacagccuaauucacaaTT	
6715	1180	715	cuguaacuacu	double	716	guaacuacuTT	717	uuaguauaaaguaguacagccuaauucacaaTT	
6716	1181	718	uguacuacu	double	719	uaacuacuTT	720	guuaguauaaaguaguacagccuaauucacaaTT	
6717	1182	721	guaacuacu	double	722	aacuacuTT	723	uguuaguauaaaguaguacagccuaauucacaaTT	
6718	1183	724	uaacuacu	double	725	acuacuTT	726	auguaguauaaaguaguacagccuaauucacaaTT	
6719	1184	727	aacuacu	double	728	cuacuTT	729	cauguaguauaaaguaguacagccuaauucacaaTT	
6720	1185	730	acuacu	double	731	uacuTT	732	acauguaguauaaaguaguacagccuaauucacaaTT	
6721	1186	733	cuacu	double	734	acuTT	735	gacauguaguauaaaguaguacagccuaauucacaaTT	
6722	1187	736	uacu	double	737	cuuTT	738	ggacauguaguauaaaguaguacagccuaauucacaaTT	
6723	1188	739	acu	double	740	uuuTT	741	aggacauguaguauaaaguaguacagccuaauucacaaTT	
6724	1189	742	cuu	double	743	uuuTT	744	caggacauguaguauaaaguaguacagccuaauucacaaTT	
6725	1190	745	uuu	double	746	uuuTT	747	gcaggacauguaguauaaaguaguacagccuaauucacaaTT	
6726	1191	748	uuu	double	749	uuuTT	750	ggcaggacauguaguauaaaguaguacagccuaauucacaaTT	
6727	1192	751	uuu	double	752	uuuTT	753	aggcaggacauguaguauaaaguaguacagccuaauucacaaTT	
6728	1193	754	uuu	double	755	uuuTT	756	uaggcaggacauguaguauaaaguaguacagccuaauucacaaTT	
6729	1352	757	uggcagaguuacaguucuguggu	double	758	gcagaguuacaguucugugTT	759	cacagaacuguaacucugcTT	
6730	1353	760	ggcagaguuacaguucuguggu	double	761	cagaguuacaguucugugTT	762	ccacagaacuguaacucugcTT	
6731	1354	763	gcagaguuacaguucuguggu	double	764	agaguuacaguucugugTT	765	accacagaacuguaacucugcTT	
6732	1374	766	uuucauguuaguaccuuauagu	double	767	ucauguuaguaccuuauaTT	768	uauaagguaacuaacaugaTT	
6733	1375	769	uucauguuaguaccuuauagu	double	770	cauguuaguaccuuauagTT	771	cuauaagguaacuaacaugaTT	
6734	1376	772	ucauguuaguaccuuauagu	double	773	auguaguaccuuauaguTT	774	acuauaagguaacuaacaugaTT	

TABLE 1-continued

Exemplary iRNA agents for targeting RhoA mRNA									
Agent number	Start		duplex	sense strand		antisense strand			
	pos. in RNA ^b	SEQ ID NO.		design (over-hang) ^a	SEQ ID NO.	SEQ ID NO.	sequence (5'-3')		
6735	1377	775	cauguuaguuaaccuuauaguuaac	double	776	uguuaguuaaccuuauaguuaTT	777	aacuauaagguaacuaacATT	
6736	1378	778	auguuaguuaaccuuauaguuaacu	double	779	guuaguuaaccuuauaguuaTT	780	uaacuauaagguaacuaacATT	
6737	1379	781	uguuaguuaaccuuauaguuaacug	double	782	uuaguuaaccuuauaguuaacTT	783	guaacuauaagguaacuaaTT	
6738	1380	784	guuaguuaaccuuauaguuaacugu	double	785	uaguuaaccuuauaguuaacuTT	786	aguaacuauaagguaacuaTT	
6739	1381	787	uuaguuaaccuuauaguuaacugug	double	788	aguuaaccuuauaguuaacugTT	789	caguaacuauaagguaacuTT	
6740	1382	790	uaguuaaccuuauaguuaacugugu	double	791	guuaaccuuauaguuaacugTT	792	acaguaacuauaagguaacTT	
6741	1383	793	aguuaaccuuauaguuaacugugua	double	794	uuaccuuauaguuaacugugTT	795	cacaguaacuauaagguaaTT	
6742	1384	796	guuaaccuuauaguuaacuguguaa	double	797	uaccuuauaguuaacugugTT	798	acacaguaacuauaagguaTT	
6743	1385	799	uuaccuuauaguuaacuguguaau	double	800	accuuauaguuaacuguguaTT	801	uacacaguaacuauaagguaTT	
6744	1386	802	uaccuuauaguuaacuguguaauu	double	803	ccuuauaguuaacuguguaaTT	804	uuacacaguaacuauaaggTT	
6745	1387	805	accuuauaguuaacuguguaauua	double	806	cuuauaguuaacuguguaauTT	807	auuacacaguaacuauaagTT	
6746	1388	808	ccuuauaguuaacuguguaauuag	double	809	uuauaguuaacuguguaauuTT	810	aaauacacaguaacuauaTT	
6747	1389	811	cuuauaguuaacuguguaauuagu	double	812	uauaguuaacuguguaauuTT	813	uaauuacacaguaacuauaTT	
6748	1390	814	uuauaguuaacuguguaauuagug	double	815	auaguuaacuguguaauuagTT	816	cuaauuacacaguaacuauTT	
6749	1391	817	uauaguuaacuguguaauuagugc	double	818	uaguuaacuguguaauuaguTT	819	acuaauuacacaguaacuauTT	
6750	1392	820	auaguuaacuguguaauuagugcc	double	821	aguuaacuguguaauuagugTT	822	cacuaauuacacaguaacuTT	
6751	1393	823	uaguuaacuguguaauuagugcca	double	824	guuaacuguguaauuagugcTT	825	gcacuaauuacacaguaacTT	
6752	1394	826	aguuaacuguguaauuagugccac	double	827	uuacuguguaauuagugccTT	828	ggcacuaauuacacaguaaTT	
6753	1395	829	guuaacuguguaauuagugccacu	double	830	uacuguguaauuagugccaTT	831	uggcacuaauuacacaguaTT	
6754	1396	832	uuacuguguaauuagugccacuu	double	833	acuguguaauuagugccacTT	834	guggcacuaauuacacaguTT	
6755	1397	835	uacuguguaauuagugccacuua	double	836	cuguguaauuagugccacuTT	837	aguggcacuaauuacacagTT	
6756	1398	838	acuguguaauuagugccacuuua	double	839	uguguaauuagugccacuuTT	840	aaguggcacuaauuacacaTT	
6757	1399	841	cuguguaauuagugccacuuaau	double	842	guguaauuagugccacuuaTT	843	uaaguggcacuaauuacacTT	
6758	1400	844	uguguaauuagugccacuuaaag	double	845	uguuaauuagugccacuuaaTT	846	uuaguggcacuaauuacaTT	
6759	1401	847	guguaauuagugccacuuaaagu	double	848	guaauuagugccacuuaauTT	849	auuaaguggcacuaauuacTT	
6760	1402	850	uguuaauuagugccacuuaaugua	double	851	uaauuagugccacuuaaugTT	852	cauuuaguggcacuaauuTT	
6761	1403	853	guuaauuagugccacuuaauguau	double	854	aaauuagugccacuuaaugTT	855	acauuaguggcacuaauuTT	
6762	1404	856	uaauuagugccacuuaauguaug	double	857	auuagugccacuuaauguaTT	858	uacauuaguggcacuaauTT	
6763	1405	859	aaauuagugccacuuaauguaugu	double	860	uuagugccacuuaauguaTT	861	auacauuaguggcacuaaTT	
6764	1406	862	auuagugccacuuaauguauguu	double	863	uagugccacuuaauguaugTT	864	cauacauuaguggcacuaTT	
6765	1407	865	uuagugccacuuaauguauguua	double	866	agugccacuuaauguauguTT	867	acauacauuaguggcacuTT	
6766	1408	868	uagugccacuuaauguauguuac	double	869	gugccacuuaauguauguTT	870	aacauacauuagugggcacTT	
6767	1409	871	agugccacuuaauguauguuacc	double	872	ugccacuuaauguauguuaTT	873	uaacauacauuaguggcaTT	
6768	1410	874	gugccacuuaauguauguuacca	double	875	gccacuuaauguauguuacTT	876	guaacauacauuaguggcTT	

TABLE 1-continued

Exemplary iRNA agents for targeting RhoA mRNA										
Agent number	Start		duplex	sense strand		antisense strand				
	pos. in RNA ^b	SEQ ID NO.		design (over-hang) ^a	SEQ ID NO.	SEQ ID NO.				
			target sequence (5'-3')			sequence (5'-3')				sequence (5'-3')
6769	1411	877	ugccacuu	aauguauguuaccaa	double	878	ccacuua	aauguauguuaccTT	879	gguaacauacauuaaguggTT
6770	1412	880	gccacuu	aauguauguuacaaa	double	881	cacuu	aauguauguuaccaTT	882	ugguaacauacauuaagugTT
6771	1413	883	ccacuua	aauguauguuacaaaa	double	884	acuu	aauguauguuaccaaTT	885	uugguaacauacauuaaguTT
6772	1414	886	cacuu	aauguauguuacaaaaa	double	887	cuu	aauguauguuacaaaTT	888	uuugguaacauacauuaagTT
6773	1415	889	acuu	aauguauguuacaaaaau	double	890	uu	aauguauguuacaaaaaTT	891	uuuugguaacauacauuaaTT
6774	1416	892	cuu	aauguauguuacaaaaaua	double	893	ua	aauguauguuacaaaaaTT	894	uuuuugguaacauacauuaTT
6775	1435	895	aauaaa	uaauaucuaccccagacu	double	896	uaaa	uaauaucuaccccagacTT	897	ucuggggguagauauuuuaTT
6776	1436	898	auaaaa	uaauaucuaccccagacua	double	899	aaaa	uaauaucuaccccagacTT	900	gucuggggguagauauuuuTT
6777	1437	901	uaaa	uaauaucuaccccagacuag	double	902	aa	uaauaucuaccccagacuTT	903	agucuggggguagauauuuTT
6778	1438	904	aa	uaauaucuaccccagacuaga	double	905	au	uaauaucuaccccagacuTT	906	uagucuggggguagauauuTT
6779	1439	907	aa	uaauaucuaccccagacuagau	double	908	ua	uaauaucuaccccagacuagTT	909	cuagucuggggguagauuaTT
6780	1440	910	au	uaauaucuaccccagacuagau	double	911	au	uaauaucuaccccagacuagaTT	912	ucuagucuggggguagauuTT
6781	1441	913	ua	uaauaucuaccccagacuagau	double	914	ua	uaauaucuaccccagacuagaTT	915	aucuagucuggggguagauaTT
6782	1442	916	au	uaauaucuaccccagacuagau	double	917	au	uaauaucuaccccagacuagaTT	918	caucuagucuggggguagauTT
6783	1443	919	ua	uaauaucuaccccagacuagau	double	920	uc	uaauaucuaccccagacuagaTT	921	acaucuagucuggggguagaTT
6784	1444	922	au	uaauaucuaccccagacuagau	double	923	cu	uaauaucuaccccagacuagaTT	924	uacauacuagucuggggguagTT
6785	1445	925	uc	uaauaucuaccccagacuagau	double	926	ua	uaauaucuaccccagacuagaTT	927	cuacauacuagucuggggguaTT
6786	1446	928	cu	uaauaucuaccccagacuagau	double	929	ac	uaauaucuaccccagacuagaTT	930	acuacauacuagucuggggguTT
6787	1447	931	ua	uaauaucuaccccagacuagau	double	932	ccc	uaauaucuaccccagacuagaTT	933	uacuacauacuagucuggggTT
6788	1448	934	ac	uaauaucuaccccagacuagau	double	935	ccc	uaauaucuaccccagacuagaTT	936	auacuacauacuagucuggggTT
6789	1449	937	ccc	uaauaucuaccccagacuagau	double	938	cc	uaauaucuaccccagacuagaTT	939	aaacuacauacuagucuggTT
6790	1450	940	ccc	uaauaucuaccccagacuagau	double	941	c	uaauaucuaccccagacuagaTT	942	aaaacuacauacuagucugTT
6791	1451	943	cc	uaauaucuaccccagacuagau	double	944	ag	uaauaucuaccccagacuagaTT	945	aaaaacuacauacuagucuTT
6792	1452	946	c	uaauaucuaccccagacuagau	double	947	g	uaauaucuaccccagacuagaTT	948	aaaaauacuacauacuagucTT
6793	1453	949	ag	uaauaucuaccccagacuagau	double	950	ac	uaauaucuaccccagacuagaTT	951	aaaaaaacuacauacuaguTT
6794	1454	952	g	uaauaucuaccccagacuagau	double	953	cu	uaauaucuaccccagacuagaTT	954	caaaaaacuacauacuagTT
6795	1455	955	ac	uaauaucuaccccagacuagau	double	956	ua	uaauaucuaccccagacuagaTT	957	acaaaaaacuacauacuTT
6796	1456	958	cu	uaauaucuaccccagacuagau	double	959	aga	uaauaucuaccccagacuagaTT	960	uacaaaaaacuacauacuTT
6797	1457	961	ua	uaauaucuaccccagacuagau	double	962	ga	uaauaucuaccccagacuagaTT	963	auacaaaaaacuacauTT
6798	1458	964	aga	uaauaucuaccccagacuagau	double	965	au	uaauaucuaccccagacuagaTT	966	uaucaaaaaacuacauTT
6799	1459	967	ga	uaauaucuaccccagacuagau	double	968	ugu	uaauaucuaccccagacuagaTT	969	uuauacaaaaaacuacaTT
6800	1460	970	au	uaauaucuaccccagacuagau	double	971	gu	uaauaucuaccccagacuagaTT	972	auuuacaaaaaacuacTT
6801	1461	973	ugu	uaauaucuaccccagacuagau	double	974	ua	uaauaucuaccccagacuagaTT	975	auuuacaaaaaacuacTT
6802	1462	976	qua	uaauaucuaccccagacuagau	double	977	qua	uaauaucuaccccagacuagaTT	978	cauuuacaaaaaacuTT

TABLE 1-continued

Exemplary iRNA agents for targeting RhoA mRNA						
Agent number	Start		duplex design (over-hang) ^a	sense strand		antisense strand
	pos. in RNA ^b	SEQ ID NO. target sequence (5'-3')		SEQ ID NO. sequence (5'-3')	SEQ ID NO. sequence (5'-3')	
6803	1463	979 uaguauuuuuuguauaauggau	double	980 guauuuuuuguauaauggTT	981 ccauuuauacaaaaaacTT	
6804	1464	982 aguauuuuuuguauaauggauu	double	983 uauuuuuuguauaauggaTT	984 uccaauuuauacaaaaaTT	
6805	1465	985 guauuuuuuguauaauggauuu	double	986 auuuuuuguauaauggauTT	987 uccaauuuauacaaaaaTT	
6806	1466	988 uauuuuuuguauaauggauuuc	double	989 uuuuuuguauaauggauTT	990 aauccauuuauacaaaaaTT	
6807	1467	991 auuuuuuguauaauggauuucc	double	992 uuuuuguauaauggauuuTT	993 aaauccaauuuauacaaaaaTT	
6808	1468	994 uuuuuuguauaauggauuuccu	double	995 uuuguauaauggauuucTT	996 gaaauccaauuuauacaaaaaTT	
6809	1469	997 uuuguauaauggauuuuccua	double	998 uuuguauaauggauuucTT	999 ggaaauccaauuuauacaaaaaTT	
6810	1470	1000 uuuguauaauggauuuuccuaa	double	1001 uuguauaauggauuuccuTT	1002 aggaaauccaauuuauacaaTT	
6811	1471	1003 uuuguauaauggauuuuccaa	double	1004 uguauaauggauuuccuaTT	1005 uaggaaauccaauuuauacaTT	
6812	1472	1006 uuguauaauggauuuuccaa	double	1007 guauaauggauuuccuaTT	1008 uuaggaaauccaauuuauacTT	
6813	1473	1009 uguauaauggauuuuccaaac	double	1010 uauaauggauuuccaaTT	1011 auuaggaaauccaauuuauaTT	
6814	1540	1012 guauuuggaaaauaagucagaug	double	1013 auuuggaaaauaagucagaTT	1014 ucugacuuuuuuuccaaTT	
6815	1541	1015 uauuuggaaaauaagucagaug	double	1016 uuuggaaaauaagucagaTT	1017 aucugacuuuuuuuccaaTT	
6816	1542	1018 auuuggaaaauaagucagaugga	double	1019 uuggaaaauaagucagaTT	1020 aaucugacuuuuuuuccaaTT	
6817	1543	1021 uuuggaaaauaagucagauggaa	double	1022 uggaauaauaagucagaTT	1023 ccaucugacuuuuuuuccaaTT	
6818	1544	1024 uuggaaaauaagucagauggaaa	double	1025 ggaauaauaagucagaTT	1026 uccaucugacuuuuuuuccTT	
6819	1545	1027 uggaauaauaagucagauggaaaa	double	1028 gaaauaauaagucagaTT	1029 uccaucugacuuuuuuuccTT	
6820	1796	1030 ucccuccagaggagccaccagu	double	1031 ccuccagaggagccaccaTT	1032 ugguggcuccucugggagTT	
6821	1797	1033 cccuccagaggagccaccaguu	double	1034 cuccagaggagccaccagTT	1035 cugguggcuccucugggagTT	
6822	1798	1036 ccuccagaggagccaccaguuc	double	1037 uccagaggagccaccaguTT	1038 acugguggcuccucugggaTT	
6823	1799	1039 cuccagaggagccaccaguuc	double	1040 ccagaggagccaccaguTT	1041 aacugguggcuccucugggTT	
6824	1800	1042 uccagaggagccaccaguuc	double	1043 ccagaggagccaccaguTT	1044 gaacugguggcuccucuggTT	
6825	1801	1045 cccagaggagccaccaguuc	double	1046 cagaggagccaccaguTT	1047 agaacugguggcuccucugTT	
6826	1843	1048 cuucuccagcugacuaaacuu	double	1049 ucucuccagcugacuaacTT	1050 guuuagucagcuggagagaTT	
6827	1869	1051 uucuguaccaguuuuuuucca	double	1052 cuguaccaguuuuuuucTT	1053 gaaaaauaacugguacagTT	
6828	1870	1054 ucuguaccaguuuuuuuccaa	double	1055 uguaccaguuuuuuucTT	1056 ggaaaaauaacugguacaTT	
6829	1871	1057 cuguaccaguuuuuuuccaac	double	1058 guaccaguuuuuuuccaTT	1059 uggaaaaauaacugguacTT	
6830	1872	1060 uguaacaguuuuuuuccaacu	double	1061 uaccaguuuuuuuccaaTT	1062 uuggaaaaauaacugguacTT	
6831	1873	1063 guaccaguuuuuuuccaacua	double	1064 accaguuuuuuuccaacTT	1065 guuggaaaaauaacugguTT	
6832	1874	1066 uaccaguuuuuuuccaacuac	double	1067 ccaguuuuuuuccaacuTT	1068 aguuggaaaaauaacuggTT	
6833	1875	1069 accaguuuuuuuccaacuacu	double	1070 caguuuuuuuccaacuaTT	1071 uaguuggaaaaauaacugTT	
6834	1897	1072 uaaugaauaaaggcaguuuuc	double	1073 auagaauaaaggcaguuuTT	1074 aaaacugccuuuauucuaTT	

TABLE 1-continued

Exemplary iRNA agents for targeting RhoA mRNA							
Start			duplex		sense strand	antisense strand	
Agent number	pos. in RNA ^b	SEQ ID NO. target sequence (5'-3')	design (overhang) ^a	SEQ ID NO.	sequence (5'-3')	SEQ ID NO.	sequence (5'-3')
6835	1898	1075 aaagaauaaaggcaguuuucua	double	1076	uagaauaaaggcaguuuucTT	1077	gaaaacugccuuuauucuaTT
6836	1899	1078 auagaauaaaggcaguuuucuaa	double	1079	agaauaaaggcaguuuucTT	1080	agaaaacugccuuuauucTT

^aSingle: Single overhang design 21 mer sense, corresponding 23 mer antisense with 2 nucleotides overhang at 3' end; Double: double overhang design corresponding 19 mer sense and antisense strand each with 2 dT nucleotide overhang at 3' end

^b"Start position" corresponds to the position within the sequence of human RhoA (Genbank accession no. NM_001664) mRNA to which the 5'-most nucleotide of the sense strand corresponds for single overhang designs; for double overhang designs, the 5'-most ribonucleotide of the sense strand corresponds to (Start position + 2)

[0059] Based on these results, the invention specifically provides an iRNA agent that includes a sense strand having at least 15 contiguous nucleotides of the sense strand sequences of the agents provided in Table 1 under agent numbers 6477-6836, and an antisense strand having at least 15 contiguous nucleotides of the antisense sequences of the agents provided in Table 1 under agent numbers 6477 to 6836.

[0060] The iRNA agents shown in Table 1 are composed of two strands of 19 nucleotides in length which are complementary or identical to the target sequence, plus a 3'-TT overhang. The present invention provides agents that comprise 15 contiguous nucleotides from these agents. However, while these lengths may potentially be optimal, the iRNA agents are not meant to be limited to these lengths. The skilled person is well aware that shorter or longer iRNA agents may be similarly effective, since, within certain length ranges, the efficacy is rather a function of the nucleotide sequence than strand length. For example, Yang, et al., *PNAS* 99:9942-9947 (2002), demonstrated similar efficacies for iRNA agents of lengths between 21 and 30 base pairs. Others have shown effective silencing of genes by iRNA agents down to a length of approx. 15 base pairs (Byrom, et al., "Inducing RNAi with siRNA Cocktails Generated by RNase III" *Tech Notes* 10(1), Ambion, Inc., Austin, Tex.).

[0061] Therefore, it is possible and contemplated by the instant invention to select from the sequences provided in Table 1 under agent numbers 6477 to 6836 a partial sequence of between 15 to 22 nucleotides for the generation of an iRNA agent derived from one of the sequences provided in Table 1 under agent numbers 6477 to 6836. Alternatively, one may add one or several nucleotides to one of the sequences provided in Table 1 under agent numbers 6477 to 6836, or an agent comprising 15 contiguous nucleotides from one of these agents, preferably, but not necessarily, in such a fashion that the added nucleotides are complementary to the respective sequence of the target gene, e.g., RhoA. For example, the first 15 nucleotides from one of the agents can be combined with the 8 nucleotides found 5' to these sequence in the RhoA mRNA to obtain an agent with 23 nucleotides in the sense and antisense strands. All such derived iRNA agents are included in the iRNA agents

of the present invention, provided they essentially retain the ability to inhibit RhoA expression in cultured human RhoA expressing cells.

[0062] The antisense strand of an iRNA agent should be equal to or at least, 14, 15, 16 17, 18, 19, 25, 29, 40, or 50 nucleotides in length. It should be equal to or less than 60, 50, 40, or 30, nucleotides in length. Preferred ranges are 15-30, 17 to 25, 19 to 23, and 19 to 21 nucleotides in length.

[0063] The sense strand of an iRNA agent should be equal to or at least 14, 15, 16 17, 18, 19, 25, 29, 40, or 50 nucleotides in length. It should be equal to or less than 60, 50, 40, or 30 nucleotides in length. Preferred ranges are 15-30, 17 to 25, 19 to 23, and 19 to 21 nucleotides in length.

[0064] The double stranded portion of an iRNA agent should be equal to or at least, 15, 16 17, 18, 19, 20, 21, 22, 23, 24, 25, 29, 40, or 50 nucleotide pairs in length. It should be equal to or less than 60, 50, 40, or 30 nucleotides pairs in length. Preferred ranges are 15-30, 17 to 25, 19 to 23, and 19 to 21 nucleotides pairs in length.

[0065] Generally, the iRNA agents of the instant invention include a region of sufficient complementarity to the respective RhoA gene, and are of sufficient length in terms of nucleotides, that the iRNA agent, or a fragment thereof, can mediate down regulation of the RhoA gene. The ribonucleotide portions of the antisense strands of the iRNA agents of Table 1 under agent numbers 6477 to 6836 are fully complementary to the mRNA sequences of the RhoA gene, respectively, and ribonucleotide portion of their sense strands are fully complementary to the ribonucleotide portions of the respective antisense strands, except for the two 3'-terminal nucleotides on the antisense strand in single overhang design iRNA agents. However, it is not necessary that there be perfect complementarity between the iRNA agent and the target, but the correspondence must be sufficient to enable the iRNA agent, or a cleavage product thereof, to direct sequence specific silencing, e.g., by RNAi cleavage of a RhoA mRNA.

[0066] Therefore, the iRNA agents of the instant invention include agents comprising a sense strand and antisense strand each comprising a sequence of at least 16, 17 or 18 nucleotides which is essentially identical, as defined below, to one of the sequences of Table 1 under agent numbers 6477

to 6836, except that not more than 1, 2 or 3 nucleotides per strand, respectively, have been substituted by other nucleotides (e.g. adenosine replaced by uracil), while essentially retaining the ability to inhibit RhoA expression in cultured human RhoA expressing cells, respectively. These agents will therefore possess at least 15 nucleotides identical to one of the sequences of Table 1 under agent numbers 6477 to 6836, but 1, 2 or 3 base mismatches with respect to either the target RhoA mRNA sequence or between the sense and antisense strand are introduced. Mismatches to the target RhoA mRNA sequence, particularly in the antisense strand, are most tolerated in the terminal regions and if present are preferably in a terminal region or regions, e.g., within 6, 5, 4, or 3 nucleotides of a 5' and/or 3' terminus, most preferably within 6, 5, 4, or 3 nucleotides of the 5'-terminus of the sense strand or the 3'-terminus of the antisense strand. The sense strand need only be sufficiently complementary with the antisense strand to maintain the overall double stranded character of the molecule.

[0067] It is preferred that the sense and antisense strands be chosen such that the iRNA agent includes a single strand or unpaired region at one or both ends of the molecule. Thus, an iRNA agent contains sense and antisense strands, preferably paired to contain an overhang, e.g., one or two 5' or 3' overhangs but preferably a 3' overhang of 2-3 nucleotides. Most embodiments will have a 3' overhang. Preferred siRNA agents will have single-stranded overhangs, preferably 3' overhangs, of 1 to 4, or preferably 2 or 3 nucleotides, in length, at one or both ends of the iRNA agent. The overhangs can be the result of one strand being longer than the other, or the result of two strands of the same length being staggered. The unpaired nucleotides forming the overhang can be ribonucleotides, or they can be deoxyribonucleotides, preferably thymidine. 5'-ends are preferably phosphorylated.

[0068] Preferred lengths for the duplexed region are between 15 and 30, most preferably 18, 19, 20, 21, 22, and 23 nucleotides in length, e.g., in the siRNA agent range discussed above. siRNA agents can resemble in length and structure the natural Dicer processed products from long dsRNAs. Embodiments in which the two strands of the siRNA agent are linked, e.g., covalently linked, are also included. Hairpin, or other single strand structures which provide the required double stranded region, and preferably a 3' overhang are also within the invention.

[0069] Evaluation of Candidate iRNA Agents

[0070] A candidate iRNA agent can be evaluated for its ability to downregulate target gene expression. For example, a candidate iRNA agent can be provided, and contacted with a cell, that expresses the target gene, e.g., the RhoA gene, either endogenously or because it has been transfected with a construct from which a RhoA protein can be expressed. The level of target gene expression prior to and following contact with the candidate iRNA agent can be compared, e.g., on an mRNA or protein level. If it is determined that the amount of RNA or protein expressed from the target gene is lower following contact with the iRNA agent, then it can be concluded that the iRNA agent downregulates target gene expression. The level of target RhoA RNA or RhoA protein in the cell can be determined by any method desired. For example, the level of target RNA can be determined by Northern blot analysis, reverse transcription coupled with

polymerase chain reaction (RT-PCR), or RNase protection assay. The level of protein can be determined, for example, by Western blot analysis or immuno-fluorescence. Preferably, the assay also tests the ability of the iRNA agent to inhibit RhoA expression on a functional level, e.g. by assessing the ability of the iRNA agent to facilitate neuronal growth, e.g. the restoration of neurite outgrowth on an otherwise inhibitory substrate, e.g a substrate comprising myelin.

Stability Testing, Modification, and Retesting of iRNA Agents

[0071] A candidate iRNA agent can be evaluated with respect to stability, e.g., its susceptibility to cleavage by an endonuclease or exonuclease, such as when the iRNA agent is introduced into the body of a subject. Methods can be employed to identify sites that are susceptible to modification, particularly cleavage, e.g., cleavage by a component found in the body of a subject.

[0072] When sites susceptible to cleavage are identified, a further iRNA agent can be designed and/or synthesized wherein the potential cleavage site is made resistant to cleavage, e.g. by introduction of a 2'-modification on the site of cleavage, e.g. a 2'-O-methyl group. This further iRNA agent can be retested for stability, and this process may be iterated until an iRNA agent is found exhibiting the desired stability.

In Vivo Testing

[0073] An iRNA agent identified as being capable of inhibiting RhoA gene expression can be tested for functionality in vivo in an animal model (e.g., in a mammal, such as in mouse or rat). For example, the iRNA agent can be administered to an animal, and the iRNA agent evaluated with respect to its biodistribution, stability, and its ability to inhibit RhoA gene expression or reduce a biological or pathological process mediated at least in part by RhoA.

[0074] The iRNA agent can be administered directly to the target tissue, e.g. the spinal cord, and, in the case of a spinal cord injury model, to the site of spinal cord injury, such as by injection. Preferably, the iRNA agent is administered to the animal model in the same manner that it would be administered to a human.

[0075] The iRNA agent can also be evaluated for its intracellular distribution. The evaluation can include determining whether the iRNA agent was taken up into the cell. The evaluation can also include determining the stability (e.g., the half-life) of the iRNA agent. Evaluation of an iRNA agent in vivo can be facilitated by use of an iRNA agent conjugated to a traceable marker (e.g., a fluorescent marker such as fluorescein; a radioactive label, such as ³⁵S, ³²P, ³³P, or ³H; gold particles; or antigen particles for immunohistochemistry).

[0076] The iRNA agent can be evaluated with respect to its ability to down regulate RhoA gene expression. Levels of RhoA gene expression in vivo can be measured, for example, by in situ hybridization, or by the isolation of RNA from tissue prior to and following exposure to the iRNA agent. Where the animal needs to be sacrificed in order to harvest the tissue, an untreated control animal will serve for comparison. RhoA mRNA can be detected by any desired method, including but not limited to RT-PCR, Northern blot,

branched-DNA assay, or RNAase protection assay. Alternatively, or additionally, RhoA gene expression can be monitored by performing Western blot analysis on tissue extracts treated with the iRNA agent.

[0077] Animal models may be used to establish the concentration necessary to achieve a certain desired effect (e.g., EC_{50} or ED_{50}). Such animal models may include transgenic animals that express a human gene, e.g., a gene that produces a target human RhoA RNA. In another embodiment, the composition for testing includes an iRNA agent that is complementary, at least in an internal region, to a sequence that is conserved between the target RhoA RNA in the animal model and the target RhoA RNA in a human.

[0078] iRNA Chemistry

[0079] Described herein are isolated iRNA agents, e.g., ds RNA agents that mediate RNAi to inhibit expression of a RhoA gene.

[0080] RNA agents discussed herein include otherwise unmodified RNA as well as RNA which has been modified, e.g., to improve efficacy, and polymers of nucleoside surrogates. Unmodified RNA refers to a molecule in which the components of the nucleic acid, namely sugars, bases, and phosphate moieties, are the same or essentially the same as that which occur in nature, preferably as occur naturally in the human body. The art has referred to rare or unusual, but naturally occurring, RNAs as modified RNAs, see, e.g., Limbach et al. *Nucleic Acids Res.* 22: 2183-2196, 1994. Such rare or unusual RNAs, often termed modified RNAs (apparently because they are typically the result of a post-transcriptional modification) are within the term unmodified RNA, as used herein. Modified RNA as used herein refers to a molecule in which one or more of the components of the nucleic acid, namely sugars, bases, and phosphate moieties, are different from that which occurs in nature, preferably different from that which occurs in the human body. While they are referred to as modified "RNAs," they will of course, because of the modification, include molecules which are not RNAs. Nucleoside surrogates are molecules in which the ribophosphate backbone is replaced with a non-ribophosphate construct that allows the bases to be presented in the correct spatial relationship such that hybridization is substantially similar to what is seen with a ribophosphate backbone, e.g., non-charged mimics of the ribophosphate backbone. Examples of the above are discussed herein.

[0081] Modifications described herein can be incorporated into any double-stranded RNA and RNA-like molecule described herein, e.g., an iRNA agent. It may be desirable to modify one or both of the antisense and sense strands of an iRNA agent. As nucleic acids are polymers of subunits or monomers, many of the modifications described below occur at a position which is repeated within a nucleic acid, e.g., a modification of a base, or a phosphate moiety, or the non-linking O of a phosphate moiety. In some cases the modification will occur at all of the subject positions in the nucleic acid but in many, and in fact in most, cases it will not. By way of example, a modification may only occur at a 3' or 5' terminal position, may only occur in a terminal region, e.g. at a position on a terminal nucleotide or in the last 2, 3, 4, 5, or 10 nucleotides of a strand. A modification may occur in a double strand region, a single strand region, or in both. E.g., a phosphorothioate modification at a non-linking O position may only occur at one or both termini,

may only occur in a terminal regions, e.g., at a position on a terminal nucleotide or in the last 2, 3, 4, 5, or 10 nucleotides of a strand, or may occur in double strand and single strand regions, particularly at termini. Similarly, a modification may occur on the sense strand, antisense strand, or both. In some cases, the sense and antisense strand will have the same modifications or the same class of modifications, but in other cases the sense and antisense strand will have different modifications, e.g., in some cases it may be desirable to modify only one strand, e.g. the sense strand.

[0082] Two prime objectives for the introduction of modifications into iRNA agents is their stabilization towards degradation in biological environments and the improvement of pharmacological properties, e.g. pharmacodynamic properties, which are further discussed below. Other suitable modifications to a sugar, base, or backbone of an iRNA agent are described in co-owned PCT Application No. PCT/US2004/01193, filed Jan. 16, 2004. An iRNA agent can include a non-naturally occurring base, such as the bases described in co-owned PCT Application No. PCT/US2004/011822, filed Apr. 16, 2004. An iRNA agent can include a non-naturally occurring sugar, such as a non-carbohydrate cyclic carrier molecule. Exemplary features of non-naturally occurring sugars for use in iRNA agents are described in co-owned PCT Application No. PCT/US2004/11829, filed Apr. 16, 2003.

[0083] An iRNA agent can include an internucleotide linkage (e.g., the chiral phosphorothioate linkage) useful for increasing nuclease resistance. In addition, or in the alternative, an iRNA agent can include a ribose mimic for increased nuclease resistance. Exemplary internucleotide linkages and ribose mimics for increased nuclease resistance are described in co-owned PCT Application No. PCT/US2004/07070, filed on Mar. 8, 2004.

[0084] An iRNA agent can include ligand-conjugated monomer subunits and monomers for oligonucleotide synthesis. Exemplary monomers are described in co-owned U.S. application Ser. No. 10/916,185, filed on Aug. 10, 2004.

[0085] An iRNA agent can have a ZXY structure, such as is described in co-owned PCT Application No. PCT/US2004/07070, filed on Mar. 8, 2004.

[0086] An iRNA agent can be complexed with an amphipathic moiety. Exemplary amphipathic moieties for use with iRNA agents are described in co-owned PCT Application No. PCT/US2004/07070, filed on Mar. 8, 2004.

[0087] In another embodiment, the iRNA agent can be complexed to a delivery agent that features a modular complex. The complex can include a carrier agent linked to one or more of (preferably two or more, more preferably all three of): (a) a condensing agent (e.g., an agent capable of attracting, e.g., binding, a nucleic acid, e.g., through ionic or electrostatic interactions); (b) a fusogenic agent (e.g., an agent capable of fusing and/or being transported through a cell membrane); and (c) a targeting group, e.g., a cell or tissue targeting agent, e.g., a lectin, glycoprotein, lipid or protein, e.g., an antibody, that binds to a specified cell type. iRNA agents complexed to a delivery agent are described in co-owned PCT Application No. PCT/US2004/07070, filed on Mar. 8, 2004.

[0088] An iRNA agent can have non-canonical pairings, such as between the sense and antisense sequences of the

iRNA duplex. Exemplary features of non-canonical iRNA agents are described in co-owned PCT Application No. PCT/US2004/07070, filed on Mar. 8, 2004.

Enhanced Nuclease Resistance

[0089] An iRNA agent, e.g., an iRNA agent that targets RhoA, can have enhanced resistance to nucleases. Naked RNA is often an easy prey for nucleolytic enzymes, such as exonucleases and endonucleases, which are omnipresent in biological media, such as the cellular cytoplasm, blood, or cerebrospinal fluid (CSF). Quick degradation can severely hamper the ability of an siRNA to inhibit the expression of a target gene. The vulnerability towards nucleolytic degradation can be greatly reduced by chemically modifying certain nucleotides of an siRNA. However, adding modifications in order to stabilize an siRNA sometimes represents a trade-off with its activity, and stabilizing modifications may even introduce toxic effects. It is therefore desirable to introduce the minimum number of modifications that still imparts the desired level of stability. Modifications in the sense strand usually have less impact on the activity of an siRNA.

[0090] In order to increase the stability of an siRNA towards nucleolytic degradation by endonucleases, it is therefore advantageous to modify only a limited number of nucleotides in particularly degradation prone positions, as described in co-owned U.S. Application No. 60/559,917, filed on May 4, 2004, co-owned U.S. Application No. 60/574,744, filed on May 27, 2004, and co-owned international application PCT/US2005/018931, filed May 27, 2005. We have determined that pyrimidine nucleotides, and specifically the 5' nucleotide in a 5'-ua-3' sequence context, a 5'-ug-3' sequence context, a 5'-ca-3' sequence context, a 5'-uu-3' sequence context, or a 5'-cc-3' sequence context are particularly prone to degradative attack, in that approximate order. Sufficiently stable and highly active siRNAs have been obtained by our laboratory when the 5'-most pyrimidines in all occurrences of the sequence contexts 5'-ua-3' and 5'-ca-3', or in all occurrences of 5'-ua-3', 5'-ca-3', and 5'-uu-3', or in all occurrences of 5'-ua-3', 5'-ca-3', 5'-uu-3', and 5'-ug-3' were replaced by 2'-modified nucleotides, such as 2'-O-methyl nucleotides, in both strands. Alternatively, 2'-modifying all pyrimidine nucleotides in the sense strand and the 5'-most pyrimidines in all occurrences of the sequence contexts 5'-ua-3' and 5'-ca-3' in the antisense strand has given good results in terms of activity and stability. Sometimes, it has been necessary to 2'-modify all pyrimidine nucleotides in the sense strand and the 5'-most pyrimidines in all occurrences of the sequence contexts 5'-ua-3', 5'-ca-3', 5'-uu-3', and 5'-ug-3' in the antisense strand. The iRNA agent can include at least 2, at least 3, at least 4 or at least 5 of such dinucleotides.

[0091] Preferably, the 2'-modified nucleotides include, for example, a 2'-modified ribose unit, e.g., the 2'-hydroxyl group (OH) can be modified or replaced with a number of different "oxy" or "deoxy" substituents.

[0092] Examples of "oxy"-2' hydroxyl group modifications include alkoxy or aryloxy (OR, e.g., R=H, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or sugar); polyethylene glycols (PEG), $O(CH_2CH_2O)_nCH_2CH_2OR$; "locked" nucleic acids (LNA) in which the 2' hydroxyl is connected, e.g., by a methylene bridge, to the 4' carbon of the same ribose sugar; O-AMINE and aminoalkoxy,

$O(CH_2)_nAMINE$, (e.g., AMINE= NH_2 ; alkylamino, dialkylamino, heterocyclyl amino, arylamino, diaryl amino, heteroaryl amino, or diheteroaryl amino, ethylene diamine, polyamino). It is noteworthy that oligonucleotides containing only the methoxyethyl group (MOE), $(OCH_2CH_2OCH_3)_n$, a PEG derivative), exhibit nuclease stabilities comparable to those modified with the robust phosphorothioate modification.

[0093] "Deoxy" modifications include hydrogen (i.e. deoxyribose sugars, which are of particular relevance to the overhang portions of partially ds RNA); halo (e.g., fluoro); amino (e.g. NH_2 ; alkylamino, dialkylamino, heterocyclyl, arylamino, diaryl amino, heteroaryl amino, diheteroaryl amino, or amino acid); $NH(CH_2CH_2NH)_nCH_2CH_2-AMINE$ (AMINE= NH_2 ; alkylamino, dialkylamino, heterocyclyl amino, arylamino, diaryl amino, heteroaryl amino, or diheteroaryl amino), $-NHC(O)R$ (R=alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or sugar), cyano; mercapto; alkyl-thio-alkyl; thioalkoxy; and alkyl, cycloalkyl, aryl, alkenyl and alkynyl, which may be optionally substituted with e.g., an amino functionality.

[0094] Preferred substituents are 2'-methoxyethyl, 2'-OCH₃, 2'-O-allyl, 2'-C-allyl, and 2'-fluoro.

[0095] The inclusion of furanose sugars in the oligonucleotide backbone can also decrease endonucleolytic cleavage. An iRNA agent can be further modified by including a 3' cationic group, or by inverting the nucleoside at the 3'-terminus with a 3'-3' linkage. In another alternative, the 3'-terminus can be blocked with an aminoalkyl group, e.g., a 3' C5-aminoalkyl dT. Other 3' conjugates can inhibit 3'-5' exonucleolytic cleavage. While not being bound by theory, a 3' conjugate, such as naproxen or ibuprofen, may inhibit exonucleolytic cleavage by sterically blocking the exonuclease from binding to the 3'-end of oligonucleotide. Even small alkyl chains, aryl groups, or heterocyclic conjugates or modified sugars (D-ribose, deoxyribose, glucose etc.) can block 3'-5'-exonucleases.

[0096] Nucleolytic cleavage can also be inhibited by the introduction of phosphate linker modifications, e.g., phosphorothioate linkages. Thus, preferred iRNA agents include nucleotide dimers enriched or pure for a particular chiral form of a modified phosphate group containing a heteroatom at a nonbridging position normally occupied by oxygen. The heteroatom can be S, Se, Nr_2 , or Br_3 . When the heteroatom is S, enriched or chirally pure Sp linkage is preferred. Enriched means at least 70, 80, 90, 95, or 99% of the preferred form. Modified phosphate linkages are particularly efficient in inhibiting exonucleolytic cleavage when introduced near the 5'- or 3'-terminal positions, and preferably the 5'-terminal positions, of an iRNA agent.

[0097] 5' conjugates can also inhibit 5'-3' exonucleolytic cleavage. While not being bound by theory, a 5' conjugate, such as naproxen or ibuprofen, may inhibit exonucleolytic cleavage by sterically blocking the exonuclease from binding to the 5'-end of oligonucleotide. Even small alkyl chains, aryl groups, or heterocyclic conjugates or modified sugars (D-ribose, deoxyribose, glucose etc.) can block 3'-5'-exonucleases.

[0098] An iRNA agent can have increased resistance to nucleases when a duplexed iRNA agent includes a single-stranded nucleotide overhang on at least one end. In pre-

ferred embodiments, the nucleotide overhang includes 1 to 4, preferably 2 to 3, unpaired nucleotides. In a preferred embodiment, the unpaired nucleotide of the single-stranded overhang that is directly adjacent to the terminal nucleotide pair contains a purine base, and the terminal nucleotide pair is a G-C pair, or at least two of the last four complementary nucleotide pairs are G-C pairs. In further embodiments, the nucleotide overhang may have 1 or 2 unpaired nucleotides, and in an exemplary embodiment the nucleotide overhang is 5'-GC-3'. In preferred embodiments, the nucleotide overhang is on the 3'-end of the antisense strand. In one embodiment, the iRNA agent includes the motif 5'-CGC-3' on the 3'-end of the antisense strand, such that a 2-nt overhang 5'-GC-3' is formed.

[0099] Thus, an iRNA agent can include modifications so as to inhibit degradation, e.g., by nucleases, e.g., endonucleases or exonucleases, found in the body of a subject. These monomers are referred to herein as NRMs, or Nuclease Resistance promoting Monomers, the corresponding modifications as NRM modifications. In many cases these modifications will modulate other properties of the iRNA agent as well, e.g., the ability to interact with a protein, e.g., a transport protein, e.g., serum albumin, or a member of the RISC, or the ability of the first and second sequences to form a duplex with one another or to form a duplex with another sequence, e.g., a target molecule.

[0100] One or more different NRM modifications can be introduced into an iRNA agent or into a sequence of an iRNA agent. An NRM modification can be used more than once in a sequence or in an iRNA agent.

[0101] NRM modifications include some which can be placed only at the terminus and others which can go at any position. Some NRM modifications can inhibit hybridization so it is preferable to use them only in terminal regions, and preferable to not use them at the cleavage site or in the cleavage region of a sequence which targets a subject sequence or gene, particularly on the antisense strand. They can be used anywhere in a sense strand, provided that sufficient hybridization between the two strands of the ds iRNA agent is maintained. In some embodiments it is desirable to put the NRM at the cleavage site or in the cleavage region of a sense strand, as it can minimize off-target silencing.

[0102] In most cases, NRM modifications will be distributed differently depending on whether they are comprised on a sense or antisense strand. If on an antisense strand, modifications which interfere with or inhibit endonuclease cleavage should not be inserted in the region which is subject to RISC mediated cleavage, e.g., the cleavage site or the cleavage region (As described in Elbashir et al., 2001, *Genes and Dev.* 15: 188, hereby incorporated by reference). Cleavage of the target occurs about in the middle of a 20 or 21 nt antisense strand, or about 10 or 11 nucleotides upstream of the first nucleotide on the target mRNA which is complementary to the antisense strand. As used herein cleavage site refers to the nucleotides on either side of the cleavage site, on the target or on the iRNA agent strand which hybridizes to it. Cleavage region means the nucleotides within 1, 2, or 3 nucleotides of the cleavage site, in either direction.

[0103] Such modifications can be introduced into the terminal regions, e.g., at the terminal position or with 2, 3, 4, or 5 positions of the terminus, of a sense or antisense strand.

Tethered Ligands

[0104] The properties of an iRNA agent, including its pharmacological properties, can be influenced and tailored, for example, by the introduction of ligands, e.g. tethered ligands.

[0105] A wide variety of entities, e.g., ligands, can be tethered to an iRNA agent, e.g., to the carrier of a ligand-conjugated monomer subunit. Examples are described below in the context of a ligand-conjugated monomer subunit but that is only preferred, entities can be coupled at other points to an iRNA agent.

[0106] Preferred moieties are ligands, which are coupled, preferably covalently, either directly or indirectly via an intervening tether, to the carrier. In preferred embodiments, the ligand is attached to the carrier via an intervening tether. The ligand or tethered ligand may be present on the ligand-conjugated monomer when the ligand-conjugated monomer is incorporated into the growing strand. In some embodiments, the ligand may be incorporated into a "precursor" ligand-conjugated monomer subunit after a "precursor" ligand-conjugated monomer subunit has been incorporated into the growing strand. For example, a monomer having, e.g., an amino-terminated tether, e.g., TAP-(CH₂)_nNH₂ may be incorporated into a growing sense or antisense strand. In a subsequent operation, i.e., after incorporation of the precursor monomer subunit into the strand, a ligand having an electrophilic group, e.g., a pentafluorophenyl ester or aldehyde group, can subsequently be attached to the precursor ligand-conjugated monomer by coupling the electrophilic group of the ligand with the terminal nucleophilic group of the precursor ligand-conjugated monomer subunit tether.

[0107] In preferred embodiments, a ligand alters the distribution, targeting or lifetime of an iRNA agent into which it is incorporated. In preferred embodiments a ligand provides an enhanced affinity for a selected target, e.g., molecule, cell or cell type, compartment, e.g., a cellular or organ compartment, tissue, organ or region of the body, as, e.g., compared to a species absent such a ligand.

[0108] Preferred ligands can improve transport, hybridization, and specificity properties and may also improve nuclease resistance of the resultant natural or modified oligoribonucleotide, or a polymeric molecule comprising any combination of monomers described herein and/or natural or modified ribonucleotides.

[0109] Ligands in general can include therapeutic modifiers, e.g., for enhancing uptake; diagnostic compounds or reporter groups e.g., for monitoring distribution; cross-linking agents; nuclease-resistance conferring moieties; and natural or unusual nucleobases. General examples include lipophilic molecules, lipids, lectins, steroids (e.g., uvaol, hecigenin, diosgenin), terpenes (e.g., triterpenes, e.g., sarsasapogenin, Friedelin, epifriedelanol derivatized lithocholic acid), vitamins, carbohydrates (e.g., a dextran, pullulan, chitin, chitosan, inulin, cyclodextrin or hyaluronic acid), proteins, protein binding agents, integrin targeting molecules, polycationics, peptides, polyamines, and peptide mimics.

[0110] The ligand may be a naturally occurring or recombinant or synthetic molecule, such as a synthetic polymer, e.g., a synthetic polyamino acid. Examples of polyamino acids include polylysine (PLL), poly L-aspartic acid, poly L-glutamic acid, styrene-maleic acid anhydride copolymer, poly(L-lactide-co-glycolide) copolymer, divinyl ether-maleic anhydride copolymer, N-(2-hydroxypropyl) methacrylamide copolymer (HMPA), polyethylene glycol (PEG), polyvinyl alcohol (PVA), polyurethane, poly(2-ethylacrylic acid), N-isopropylacrylamide polymers, or polyphosphazine. Example of polyamines include: polyethylenimine, polylysine (PLL), spermine, spermidine, polyamine, pseudopeptide-polyamine, peptidomimetic polyamine, dendrimer polyamine, arginine, amidine, protamine, cationic moieties, e.g., cationic lipid, cationic porphyrin, quaternary salt of a polyamine, or an alpha helical peptide.

[0111] Ligands can also include targeting groups, e.g., a cell or tissue targeting agent, e.g., a thyrotropin, melanotropin, surfactant protein A, Mucin carbohydrate, a glycosylated polyamino acid, transferrin, bisphosphonate, polyglutamate, polyaspartate, or an RGD peptide or RGD peptide mimetic.

[0112] Ligands can be proteins, e.g., glycoproteins, lipoproteins, e.g. low density lipoprotein (LDL), or albumins, e.g. human serum albumin (HSA), or peptides, e.g., molecules having a specific affinity for a co-ligand, or antibodies e.g., an antibody, that binds to a specified cell type such as a cancer cell, endothelial cell, or bone cell. Ligands may also include hormones and hormone receptors. They can also include non-peptidic species, such as cofactors, multivalent lactose, multivalent galactose, N-acetyl-galactosamine, N-acetyl-glucosamine, multivalent mannose, or multivalent fucose. The ligand can be, for example, a lipopolysaccharide, an activator of p38 MAP kinase, or an activator of NF- κ B.

[0113] The ligand can be a substance, e.g. a drug, which can increase the uptake of the iRNA agent into the cell, for example, by disrupting the cell's cytoskeleton, e.g., by disrupting the cell's microtubules, microfilaments, and/or intermediate filaments. The drug can be, for example, taxon, vincristine, vinblastine, cytochalasin, nocodazole, japlakinolide, latrunculin A, phalloidin, swinholide A, indanocene, or myoservin.

[0114] In one aspect, the ligand is a lipid or lipid-based molecule. Such a lipid or lipid-based molecule preferably binds a serum protein, e.g., human serum albumin (HSA). An HSA binding ligand allows for distribution of the conjugate to a target tissue, e.g., liver tissue, including parenchymal cells of the liver. Other molecules that can bind HSA can also be used as ligands. For example, neproxin or aspirin can be used. A lipid or lipid-based ligand can (a) increase resistance to degradation of the conjugate, (b) increase targeting or transport into a target cell or cell membrane, and/or (c) can be used to adjust binding to a serum protein, e.g., HSA.

[0115] A lipid based ligand can be used to modulate, e.g., control the binding of the conjugate to a target tissue. For example, a lipid or lipid-based ligand that binds to HSA more strongly will be less likely to be targeted to the kidney and therefore less likely to be cleared from the body. A lipid or lipid-based ligand that binds to HSA less strongly can be used to target the conjugate to the kidney.

[0116] In a preferred embodiment, the lipid based ligand binds HSA. Preferably, it binds HSA with a sufficient affinity such that the conjugate will be preferably distributed to a non-kidney tissue. However, it is preferred that the affinity not be so strong that the HSA-ligand binding cannot be reversed.

[0117] In another aspect, the ligand is a moiety, e.g., a vitamin or nutrient, which is taken up by a target cell, e.g., a proliferating cell. These are particularly useful for treating disorders characterized by unwanted cell proliferation, e.g., of the malignant or non-malignant type, e.g., cancer cells. Exemplary vitamins include vitamin A, E, and K. Other exemplary vitamins include the B vitamins, e.g., folic acid, B12, riboflavin, biotin, pyridoxal or other vitamins or nutrients taken up by cancer cells.

[0118] In another aspect, the ligand is a cell-permeation agent, preferably a helical cell-permeation agent. Preferably, the agent is amphipathic. An exemplary agent is a peptide such as tat or antennapedia. If the agent is a peptide, it can be modified, including a peptidylmimetic, invertomers, non-peptide or pseudo-peptide linkages, and use of D-amino acids. The helical agent is preferably an alpha-helical agent, which preferably has a lipophilic and a lipophobic phase.

5'-Phosphate Modifications

[0119] In preferred embodiments, iRNA agents are 5' phosphorylated or include a phosphoryl analog at the 5' prime terminus. 5'-phosphate modifications of the antisense strand include those which are compatible with RISC mediated gene silencing. Suitable modifications include: 5'-monophosphate ((HO)2(O)P—O-5'); 5'-diphosphate ((HO)2(O)P—O—P(HO)(O)—O-5'); 5'-triphosphate ((HO)2(O)P—O—(HO)(O)P—O—P(HO)(O)—O-5'); 5'-guanosine cap (7-methylated or non-methylated) (7m-G-O-5'-(HO)(O)P—O—(HO)(O)P—O—P(HO)(O)—O-5'); 5'-adenosine cap (Appp), and any modified or unmodified nucleotide cap structure (N—O-5'-(HO)(O)P—O—(HO)(O)P—O—P(HO)(O)—O-5'); 5'-monothiophosphate (phosphorothioate; (HO)2(S)P—O-5'); 5'-monodithiophosphate (phosphorodithioate; (HO)(HS)(S)P—O-5'), 5'-phosphorothiolate ((HO)2(O)P—S-5'); any additional combination of oxygen/sulfur replaced monophosphate, diphosphate and triphosphates (e.g. 5'-alpha-thiotriphosphate, 5'-gamma-thiotriphosphate, etc.), 5'-phosphoramidates ((HO)2(O)P—NH-5', (HO)(NH2)(O)P—O-5'), 5'-alkylphosphonates (R=alkyl=methyl, ethyl, isopropyl, propyl, etc., e.g. RP(OH)(O)—O-5'-, (OH)2(O)P-5'-CH2-), 5'-alkyletherphosphonates (R=alkylether=methoxymethyl (MeOCH2-), ethoxymethyl, etc., e.g. RP(OH)(O)—O-5'-).

[0120] The sense strand can be modified in order to inactivate the sense strand and prevent formation of an active RISC, thereby potentially reducing off-target effects. This can be accomplished by a modification which prevents 5'-phosphorylation of the sense strand, e.g., by modification with a 5'-O-methyl ribonucleotide (see Nykänen et al., (2001) ATP requirements and small interfering RNA structure in the RNA interference pathway. Cell 107, 309-321.) Other modifications which prevent phosphorylation can also be used, e.g., simply substituting the 5'-OH by H rather than O-Me. Alternatively, a large bulky group may be added to the 5'-phosphate turning it into a phosphodiester linkage.

Transport of iRNA Agents into Cells

[0121] Not wishing to be bound by any theory, the chemical similarity between cholesterol-conjugated iRNA agents and certain constituents of lipoproteins (e.g. cholesterol, cholesteryl esters, phospholipids) may lead to the association of iRNA agents with lipoproteins (e.g. LDL, HDL) in blood and/or the interaction of the iRNA agent with cellular components having an affinity for cholesterol, e.g. components of the cholesterol transport pathway. Lipoproteins as well as their constituents are taken up and processed by cells by various active and passive transport mechanisms, for example, without limitation, endocytosis of LDL-receptor bound LDL, endocytosis of oxidized or otherwise modified LDLs through interaction with Scavenger receptor A, Scavenger receptor B1-mediated uptake of HDL cholesterol in the liver, pinocytosis, or transport of cholesterol across membranes by ABC (ATP-binding cassette) transporter proteins, e.g. ABC-A1, ABC-G1 or ABC-G4. Hence, cholesterol-conjugated iRNA agents could enjoy facilitated uptake by cells possessing such transport mechanisms, e.g. cells of the liver. As such, the present invention provides evidence and general methods for targeting iRNA agents to cells expressing certain cell surface components, e.g. receptors, by conjugating a natural ligand for such component (e.g. cholesterol) to the iRNA agent, or by conjugating a chemical moiety (e.g. cholesterol) to the iRNA agent which associates with or binds to a natural ligand for the component (e.g. LDL, HDL).

[0122] Other Embodiments

[0123] An RNA, e.g., an iRNA agent, can be produced in a cell in vivo, e.g., from exogenous DNA templates that are delivered into the cell. For example, the DNA templates can be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Pat. No. 5,328,470), or by stereotactic injection (see, e.g., Chen et al. *Proc. Natl. Acad. Sci. USA* 91:3054-3057, 1994). The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. The DNA templates, for example, can include two transcription units, one that produces a transcript that includes the top strand of an iRNA agent and one that produces a transcript that includes the bottom strand of an iRNA agent. When the templates are transcribed, the iRNA agent is produced, and processed into siRNA agent fragments that mediate gene silencing.

[0124] Formulation

[0125] The iRNA agents described herein can be formulated for administration to a subject.

[0126] For ease of exposition, the formulations, compositions, and methods in this section are discussed largely with regard to unmodified iRNA agents. It should be understood, however, that these formulations, compositions, and methods can be practiced with other iRNA agents, e.g., modified iRNA agents, and such practice is within the invention.

[0127] A formulated iRNA agent composition can assume a variety of states. In some examples, the composition is at least partially crystalline, uniformly crystalline, and/or anhydrous (e.g., less than 80, 50, 30, 20, or 10% water). In

another example, the iRNA agent is in an aqueous phase, e.g., in a solution that includes water.

[0128] The aqueous phase or the crystalline compositions can, e.g., be incorporated into a delivery vehicle, e.g., a liposome (particularly for the aqueous phase) or a particle (e.g., a microparticle as can be appropriate for a crystalline composition). Generally, the iRNA agent composition is formulated in a manner that is compatible with the intended method of administration.

[0129] An iRNA agent preparation can be formulated in combination with another agent, e.g., another therapeutic agent or an agent that stabilizes an iRNA agent, e.g., a protein that complexes with the iRNA agent to form an iRNP. Still other agents include chelators, e.g., EDTA (e.g., to remove divalent cations such as Mg^{2+}), salts, RNase inhibitors (e.g., a broad specificity RNase inhibitor such as RNasin) and so forth.

[0130] In one embodiment, the iRNA agent preparation includes two or more iRNA agent(s), e.g., two or more iRNA agents that can mediate RNAi with respect to the same gene, or different alleles of the gene, or with respect to different genes. Such preparations can include at least three, five, ten, twenty, fifty, or a hundred or more different iRNA agent species. Such iRNA agents can mediate RNAi with respect to a similar number of different genes.

[0131] Where the two or more iRNA agents in such preparation target the same gene, they can have target sequences that are non-overlapping and non-adjacent, or the target sequences may be overlapping or adjacent.

[0132] Disorders Associated with RhoA Expression

[0133] An iRNA agent that targets RhoA, e.g., an iRNA agent described herein, can be used to treat a subject, e.g., a human having or at risk for developing a disease or disorder associated with RhoA gene expression or treating a subject where a biological process mediated by RhoA is unwanted. Since Nogo-L, RhoA, and Nogo-R participate in inhibiting axonal growth and elongations, the iRNA agents of the present invention are used to reverse this inhibition leading to nerve/axonal growth and elongation. Such a treatment is useful in treating injuries to the nervous system such as spinal cord injury or peripheral nerve death (caused by, e.g., Metastatic cancers of the CNS, e.g., gliomas (such as glioblastomas, astrocytomas, oligodendrogliomas, ependymomas), meningiomas, medulloblastomas, neuroblastomas, choroid plexus papillomas, sarcomas can also be treated by the iRNA agents described herein. Other indications include diseases of the central nervous system, including but not limited to encephalomyelitis, ischemic stroke, Alzheimer's Disease, spongiform encephalopathy, Amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), multiple sclerosis, transverse myelitis, motor neuron disease, Guillan Barre, Anterior Spinal Artery Syndrome, and schizophrenia.

[0134] For example, an iRNA agent that targets RhoA mRNA can be used to treat a subject with a spinal cord injury or a subject having another pathological state which can be ameliorated, at least in part, by nerve growth and elongation. In such a use, an iRNA agent of the present invention is administered preferably locally at the site of nerve damage or the site at which the inhibitory effects of RhoA is desired to be reversed. Administration of the iRNA agent leads to

decrease in RhoA protein resulting in reversing Nogo mediated inhibition of axonal elongation and growth.

[0135] Treatment Methods and Routes of Delivery

[0136] A composition that includes an iRNA agent, e.g., an iRNA agent that targets RhoA, can be delivered to a subject by a variety of routes to achieve either local delivery to the site of action of systemic delivery to the subject. Exemplary routes include direct injection to the site of treatment, intrathecal, parenchymal, intravenous, nasal, oral, and ocular delivery. The preferred means of administering the iRNA agents of the present invention is through direct injection or infusion to the site of treatment.

[0137] An iRNA agent can be incorporated into pharmaceutical compositions suitable for administration. For example, compositions can include one or more species of an iRNA agent and a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

[0138] The pharmaceutical compositions of the present invention may be administered in a number of ways depending upon whether local or systemic treatment is desired and upon the area to be treated. Administration may be topical (including ophthalmic, intranasal, transdermal), oral or parenteral. Parenteral administration includes intravenous drip, subcutaneous, intraperitoneal or intramuscular injection, or intrathecal or intraventricular administration.

[0139] The route of delivery can be dependent on the disorder of the patient. In general, the delivery of the iRNA agents of the present invention is done to achieve systemic delivery into the subject. One preferred means of achieving this is through parenteral administration. In a particularly preferred embodiment, the application is achieved by direct application of the pharmaceutical composition to the site of nerve injury, such as the site of spinal cord injury. Formulations for parenteral administration may include sterile aqueous solutions which may also contain buffers, diluents and other suitable additives. For intravenous use, the total concentration of solutes should be controlled to render the preparation isotonic.

[0140] Using the small interfering RNA vectors previously described, the invention also provides devices, systems, and methods for delivery of small interfering RNA to target locations in the nervous system and/or the brain. The envisioned route of delivery is through the use of implanted, indwelling, intrathecal or intraparenchymal catheters that provide a means for injecting small volumes of fluid containing the dsRNA of the invention directly into local nerves or local brain tissue. The proximal end of these catheters may be connected to an implanted, intrathecal or intracerebral access port surgically affixed to the patient's body or cranium, or to an implanted drug pump located in the patient's torso.

[0141] Alternatively, implantable delivery devices, such as an implantable pump may be employed. Examples of the delivery devices within the scope of the invention include the Model 8506 investigational device (by Medtronic, Inc. of Minneapolis, Minn.), which can be implanted subcutaneously in the body or on the cranium, and provides an access port through which therapeutic agents may be delivered to the nerves or brain. Delivery occurs through a stereotactically implanted polyurethane catheter. Two models of catheters that can function with the Model 8506 access port include the Model 8770 ventricular catheter by Medtronic, Inc., for delivery to the intracerebral ventricles, which is disclosed in U.S. Pat. No. 6,093,180, incorporated herein by reference, and the IPA1 catheter by Medtronic, Inc., for delivery to the brain tissue itself (i.e., intraparenchymal delivery), disclosed in U.S. Ser. Nos. 09/540,444 and 09/625,751, which are incorporated herein by reference. The latter catheter has multiple outlets on its distal end to deliver the therapeutic agent to multiple sites along the catheter path. In addition to the aforementioned device, the delivery of the small interfering RNA vectors in accordance with the invention can be accomplished with a wide variety of devices, including but not limited to U.S. Pat. Nos. 5,735,814, 5,814,014, and 6,042,579, all of which are incorporated herein by reference. Using the teachings of the invention and those of skill in the art will recognize that these and other devices and systems may be suitable for delivery of small interfering RNA vectors for the treatment of pain in accordance with the invention.

[0142] In one such embodiment, the method further comprises the steps of implanting a pump outside the body or brain, the pump coupled to a proximal end of the catheter, and operating the pump to deliver the predetermined dosage of the at least one small interfering RNA or small interfering RNA vector through the discharge portion of the catheter. A further embodiment comprises the further step of periodically refreshing a supply of the at least one small interfering RNA or small interfering RNA vector to the pump outside said body or brain.

[0143] Thus, the invention includes the delivery of small interfering RNA vectors using an implantable pump and catheter, like that taught in U.S. Pat. Nos. 5,735,814 and 6,042,579, and further using a sensor as part of the infusion system to regulate the amount of small interfering RNA vectors delivered to the nerves or brain, like that taught in U.S. Pat. No. 5,814,014. Other devices and systems can be used in accordance with the method of the invention, for example, the devices and systems disclosed in U.S. Ser. No. 09/872,698 (filed Jun. 1, 2001) and Ser. No. 09/864,646 (filed May 23, 2001), which are incorporated herein by reference.

[0144] Preferably, the outlet of the pump or catheter is placed in close proximity of the desired site of action of the pharmaceutical composition, such as near the site of spinal cord, or other nerve, injury.

[0145] Administration can be provided by the subject or by another person, e.g., a caregiver. A caregiver can be any entity involved with providing care to the human: for example, a hospital, hospice, doctor's office, outpatient clinic; a healthcare worker such as a doctor, nurse, or other practitioner; or a spouse or guardian, such as a parent. The medication can be provided in measured doses or in a dispenser which delivers a metered dose.

[0146] The term “therapeutically effective amount” is the amount present in the composition that is needed to provide the desired level of drug in the subject to be treated to give the anticipated physiological response.

[0147] The term “physiologically effective amount” is that amount delivered to a subject to give the desired palliative or curative effect.

[0148] The term “pharmaceutically acceptable carrier” means that the carrier can be taken into the lungs with no significant adverse toxicological effects on the lungs.

[0149] The term “co-administration” refers to administering to a subject two or more agents, and in particular two or more iRNA agents. The agents can be contained in a single pharmaceutical composition and be administered at the same time, or the agents can be contained in separate formulation and administered serially to a subject. So long as the two agents can be detected in the subject at the same time, the two agents are said to be co-administered. In one embodiment, both Nogo-L, RhoA, and Nogo-R iRNA agents are co-administered.

[0150] The types of pharmaceutical excipients that are useful as carrier include stabilizers such as human serum albumin (HSA), bulking agents such as carbohydrates, amino acids and polypeptides; pH adjusters or buffers; salts such as sodium chloride; and the like. These carriers may be in a crystalline or amorphous form or may be a mixture of the two.

[0151] Bulking agents that are particularly valuable include compatible carbohydrates, polypeptides, amino acids or combinations thereof. Suitable carbohydrates include monosaccharides such as galactose, D-mannose, sorbose, and the like; disaccharides, such as lactose, trehalose, and the like; cyclodextrins, such as 2-hydroxypropyl- β -cyclodextrin; and polysaccharides, such as raffinose, maltodextrins, dextrans, and the like; alditols, such as mannitol, xylitol, and the like. A preferred group of carbohydrates includes lactose, threhalose, raffinose maltodextrins, and mannitol. Suitable polypeptides include aspartame. Amino acids include alanine and glycine, with glycine being preferred.

[0152] Suitable pH adjusters or buffers include organic salts prepared from organic acids and bases, such as sodium citrate, sodium ascorbate, and the like; sodium citrate is preferred.

[0153] Dosage. An iRNA agent can be administered at a unit dose less than about 75 mg per kg of bodyweight, or less than about 70, 60, 50, 40, 30, 20, 10, 5, 2, 1, 0.5, 0.1, 0.05, 0.01, 0.005, 0.001, or 0.0005 mg per kg of bodyweight, and less than 200 nmol of iRNA agent (e.g., about 4.4×10^{16} copies) per kg of bodyweight, or less than 1500, 750, 300, 150, 75, 15, 7.5, 1.5, 0.75, 0.15, 0.075, 0.015, 0.0075, 0.0015, 0.00075, 0.00015 nmol of iRNA agent per kg of bodyweight. The unit dose, for example, can be administered by injection (e.g., intravenous or intramuscular, intrathecally, or directly into an organ), an inhaled dose, or a topical application.

[0154] Delivery of an iRNA agent directly to an organ (e.g., directly to the liver) can be at a dosage on the order of about 0.00001 mg to about 3 mg per organ, or preferably

about 0.0001-0.001 mg per organ, about 0.03-3.0 mg per organ, about 0.1-3.0 mg per eye or about 0.3-3.0 mg per organ.

[0155] The dosage can be an amount effective to treat or prevent a disease or disorder.

[0156] In one embodiment, the unit dose is administered less frequently than once a day, e.g., less than every 2, 4, 8 or 30 days. In another embodiment, the unit dose is not administered with a frequency (e.g., not a regular frequency). For example, the unit dose may be administered a single time. Because iRNA agent mediated silencing can persist for several days after administering the iRNA agent composition, in many instances, it is possible to administer the composition with a frequency of less than once per day, or, for some instances, only once for the entire therapeutic regimen.

[0157] In one embodiment, a subject is administered an initial dose, and one or more maintenance doses of an iRNA agent, e.g., a double-stranded iRNA agent, or siRNA agent, (e.g., a precursor, e.g., a larger iRNA agent which can be processed into an siRNA agent, or a DNA which encodes an iRNA agent, e.g., a double-stranded iRNA agent, or siRNA agent, or precursor thereof). The maintenance dose or doses are generally lower than the initial dose, e.g., one-half less of the initial dose. A maintenance regimen can include treating the subject with a dose or doses ranging from 0.01 to 75 mg/kg of body weight per day, e.g., 70, 60, 50, 40, 30, 20, 10, 5, 2, 1, 0.5, 0.1, 0.05, 0.01, 0.005, 0.001, or 0.0005 mg per kg of body weight per day. The maintenance doses are preferably administered no more than once every 5, 10, or 30 days. Further, the treatment regimen may last for a period of time which will vary depending upon the nature of the particular disease, its severity and the overall condition of the patient. In preferred embodiments the dosage may be delivered no more than once per day, e.g., no more than once per 24, 36, 48, or more hours, e.g., no more than once every 5 or 8 days. Following treatment, the patient can be monitored for changes in his condition and for alleviation of the symptoms of the disease state. The dosage of the compound may either be increased in the event the patient does not respond significantly to current dosage levels, or the dose may be decreased if an alleviation of the symptoms of the disease state is observed, if the disease state has been ablated, or if undesired side-effects are observed.

[0158] The effective dose can be administered in a single dose or in two or more doses, as desired or considered appropriate under the specific circumstances. If desired to facilitate repeated or frequent infusions, implantation of a delivery device, e.g., a pump, semi-permanent stent (e.g., intravenous, intraperitoneal, intracisternal or intracapsular), or reservoir may be advisable.

[0159] Following successful treatment, it may be desirable to have the patient undergo maintenance therapy to prevent the recurrence of the disease state, wherein the compound of the invention is administered in maintenance doses, ranging from 0.001 g to 100 g per kg of body weight (see U.S. Pat. No. 6,107,094).

[0160] The concentration of the iRNA agent composition is an amount sufficient to be effective in treating or preventing a disorder or to regulate a physiological condition in humans. The concentration or amount of iRNA agent administered will depend on the parameters determined for the agent and the method of administration, e.g. nasal, buccal, pulmonary, or topical, such as intrathecal or at the site of

nerve injury. For example, topical formulations tend to require much lower concentrations of some ingredients in order to avoid irritation or burning.

[0161] Certain factors may influence the dosage required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. It will also be appreciated that the effective dosage of an iRNA agent such as an siRNA used for treatment may increase or decrease over the course of a particular treatment. Changes in dosage may result and become apparent from the results of diagnostic assays. For example, the subject can be monitored after administering an iRNA agent composition. Based on information from the monitoring, an additional amount of the iRNA agent composition can be administered.

[0162] Dosing is dependent on severity and responsiveness of the disease condition to be treated, with the course of treatment lasting from several days to several months, or until a cure is effected or a diminution of disease state is achieved. Optimal dosing schedules can be calculated from measurements of drug accumulation in the body of the patient, or of drug accumulation at the site of application when delivering locally, e.g. at the site of nerve injury, e.g. at the site of spinal cord injury. Persons of ordinary skill can easily determine optimum dosages, dosing methodologies and repetition rates.

[0163] Optimum dosages may vary depending on the relative potency of individual compounds, and can generally be estimated based on EC₅₀s found to be effective in vitro and in vivo animal models as described above.

[0164] The invention is further illustrated by the following examples, which should not be construed as further limiting.

EXAMPLES

[0165] Nucleic acid sequences are represented below using standard nomenclature, and specifically the abbreviations of Table 2.

TABLE 2

Abbreviations of nucleotide monomers used in nucleic acid sequence representation. It will be understood that these monomers, when present in an oligonucleotide, are mutually linked by 5'-3'-phosphodiester bonds.	
Abbreviation ^a	Nucleotide(s)
A, a	2'-deoxy-adenosine-5'-phosphate, adenosine-5'-phosphate
C, c	2'-deoxy-cytidine-5'-phosphate, cytidine-5'-phosphate
G, g	2'-deoxy-guanosine-5'-phosphate, guanosine-5'-phosphate
T, t	2'-deoxy-thymidine-5'-phosphate, thymidine-5'-phosphate
U, u	2'-deoxy-uridine-5'-phosphate, uridine-5'-phosphate
N, n	any 2'-deoxy-nucleotide/nucleotide (G, A, C, or T, g, a, c or u)
am	2'-O-methyladenosine-5'-phosphate
cm	2'-O-methylcytidine-5'-phosphate
gm	2'-O-methylguanosine-5'-phosphate
tm	2'-O-methyl-thymidine-5'-phosphate
um	2'-O-methyluridine-5'-phosphate

TABLE 2-continued

Abbreviations of nucleotide monomers used in nucleic acid sequence representation. It will be understood that these monomers, when present in an oligonucleotide, are mutually linked by 5'-3'-phosphodiester bonds.	
Abbreviation ^a	Nucleotide(s)
<u>A</u> , <u>C</u> , <u>G</u> , <u>T</u> , <u>a</u> , <u>c</u> , <u>g</u> , <u>t</u> , <u>u</u>	underlined: nucleoside-5'-phosphorothioate
-Chol	1-{6-[cholester-3-yloxy-carbonylamino]-hexanoyl}-4-hydroxy-pyrrolidin-3-phosphorothioate diester

^acapital letters represent 2'-deoxyribonucleotides (DNA), lower case letters represent ribonucleotides (RNA)

Source of Reagents

[0166] Where the source of a reagent is not specifically given herein, such reagent may be obtained from any supplier of reagents for molecular biology at a quality/purity standard for application in molecular biology.

Example 1

Selection of Sequences

[0167] Sequence alignment was performed to identify regions within the sequence of human RhoA mRNA with full homology to the respective sequences in both mouse and rat RhoA mRNA (human RhoA mRNA: Genbank accession no. NM_001664; mouse RhoA mRNA: Genbank accession no. NM_016802; rat RhoA mRNA: Genbank accession no. NM_057132). Within the regions of homology thus identified, all possible contiguous sequences of 19 nucleotides were examined by further BLAST comparison for potential cross-reactivity of an siRNA comprising such sequence to other mRNA sequences present in humans. Only sequences with 3 or more mismatches to any other human mRNA or genomic sequence were chosen. The resulting set of 19 nt sequences is represented in the sense strand ribonucleotide sequences of the double-overhang iRNA agents given in Table 1.

[0168] In order to maximise the stability of the siRNAs for testing in biological media, particularly towards nucleolytic attack by endo- and exonucleases, the siRNAs were synthesized such that in the sense strands, all cytidine and uridine nucleotides comprise a 2'-O-methyl group, and in the antisense strand, all cytidines and uridines appearing in a sequence context of 5'-ca-3' or 5'-ua-3' comprise a 2'-O-methyl group.

[0169] To the same end, phosphorothioate linkages were introduced between 3'-terminal 5'-TT-3'-group thymidines. It has been our experience that the most active exonucleases in serum and other biological media relevant for the in vivo activity of siRNAs act by degrading siRNA strands 3'-5'. It has proven advantageous, and often sufficient, to replace the 2 penultimate nucleotides in the antisense strand by 2'-O-methyl-5'-phosphorothioate-modified nucleotides (e.g. the nucleotides in positions 21 and 22, counting 5' to 3', of a 23-nucleotide antisense strand); sometimes it is sufficient to modify only the penultimate nucleotide, or to use only 5'-phosphorothioate-modified nucleotides, or both. The sense strand may be protected in a similar fashion, and/or it may be 3'-conjugated to a tethered ligand via a phosphodiester or a phosphorothioate diester.

[0170] In addition to the sequences selected as described above, four siRNAs were synthesized which corresponded to four of those utilized by the authors of Ahmed, Z., et al, Mol Cell Neurosci. 2005, 28:509-23. AL-DP-5850 corresponds to RHO-A1 of Ahmed et al., supra, AL-DP-5851 to RHO-A2, AL-DP-5852 to RHO-A5 and AL-DP-5853 to RHO-A4 of Ahmed et al., supra.

Example 2

siRNA Synthesis

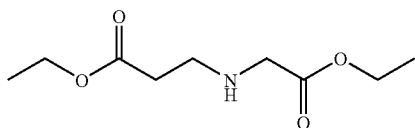
[0171] Single-stranded RNAs were produced by solid phase synthesis on a scale of 1 μ mole using an Expedite 8909 synthesizer (Applied Biosystems, Applied Deutschland GmbH, Darmstadt, Germany) and controlled pore glass (CPG, 500 Å, Glen Research, Sterling Va.) as solid support. RNA and RNA containing 2'-O-methyl nucleotides were 30 generated by solid phase synthesis employing the corresponding phosphoramidites and 2'-O-methyl phosphoramidites, respectively (Proligo Biochemie GmbH, Hamburg, Germany). These building blocks were incorporated at selected sites within the sequence of the oligoribonucleotide chain using standard nucleoside phosphoramidite chemistry such as described in Current protocols in nucleic acid chemistry, Beaucage, S. L. et al. (Edrs.), John Wiley & Sons, Inc., New York, N.Y., USA. Phosphorothioate linkages were introduced by replacement of the iodine oxidizer solution with a solution of the Beaucage reagent (Chromachem Ltd, Glasgow, UK) in acetonitrile (1%). Further ancillary reagents were obtained from Mallinckrodt Baker (Griesheim, Germany).

[0172] Deprotection and purification by anion exchange HPLC of the crude oligoribonucleotides were carried out according to established procedures. Yields and concentrations were determined by UV absorption of a solution of the respective RNA at a wavelength of 260 nm using a spectral photometer (DU 640B, Beckman Coulter GmbH, Unterschleißheim, Germany). Double stranded RNA was generated by mixing an equimolar solution of complementary strands in annealing buffer (20 mM sodium phosphate, pH 6.8; 100 mM sodium chloride), heated in a water bath at 85-90° C. for 3 minutes and cooled to room temperature over a period of 3-4 hours. The purified RNA solution was stored at -20° C. until use.

[0173] As a result of the synthesis strategy described above, all oligonucleotides synthesized as described above do not comprise a phosphate group on their 5'-most nucleotide.

[0174] Cholesterol was 3'-conjugated to siRNA as illustrated in FIG. 1. For the synthesis of these 3'-cholesterol-conjugated siRNAs, an appropriately modified solid support was used for RNA synthesis. The modified solid support was prepared as follows:

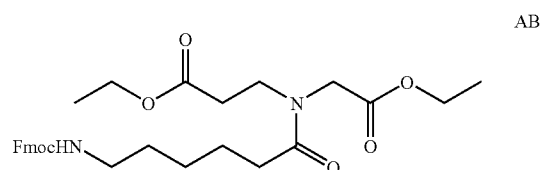
Diethyl-2-azabutane-1,4-dicarboxylate AA



AA

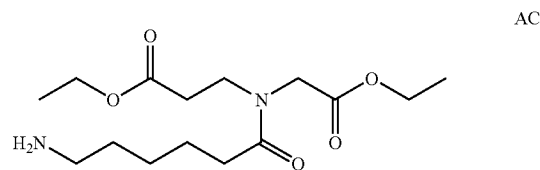
[0175] A 4.7 M aqueous solution of sodium hydroxide (50 mL) was added into a stirred, ice-cooled solution of ethyl glycinate hydrochloride (32.19 g, 0.23 mole) in water (50 mL). Then, ethyl acrylate (23.1 g, 0.23 mole) was added and the mixture was stirred at room temperature until the completion of reaction was ascertained by TLC (19 h). After 19 h which it was partitioned with dichloromethane (3×100 mL). The organic layer was dried with anhydrous sodium sulfate, filtered and evaporated. The residue was distilled to afford AA (28.8 g, 61%).

3-{[Ethoxycarbonylmethyl-[6-(9H-fluoren-9-ylmethoxycarbonyl-amino)-hexanoyl]-amino]-propionic acid ethyl ester AB



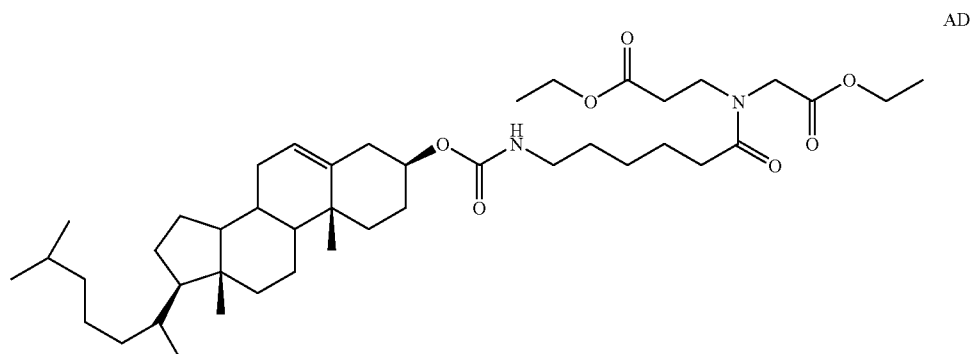
[0176] Fmoc-6-amino-hexanoic acid (9.12 g, 25.83 mmol) was dissolved in dichloromethane (50 mL) and cooled with ice. Diisopropylcarbodiimide (3.25 g, 3.99 mL, 25.83 mmol) was added to the solution at 0° C. It was then followed by the addition of Diethyl-azabutane-1,4-dicarboxylate (5 g, 24.6 mmol) and dimethylamino pyridine (0.305 g, 2.5 mmol). The solution was brought to room temperature and stirred further for 6 h. the completion of the reaction was ascertained by TLC. The reaction mixture 1 5 was concentrated in vacuum and to the ethylacetate was added to precipitate diisopropyl urea. The suspension was filtered. The filtrate was washed with 5% aqueous hydrochloric acid, 5% sodium bicarbonate and water. The combined organic layer was dried over sodium sulfate and concentrated to give the crude product which was purified by column chromatography (50% EtOAC/Hexanes) to yield 11.87 g (88%) of AB.

3-{[6-Amino-hexanoyl]-ethoxycarbonylmethyl-amino]-propionic acid ethyl ester AC



[0177] 3-{[Ethoxycarbonylmethyl-[6-(9H-fluoren-9-ylmethoxycarbonylamino)-hexanoyl]-amino]-propionic acid ethyl ester AB (11.5 g, 21.3 mmol) was dissolved in 20% piperidine in dimethylformamide at 0° C. The solution was continued stirring for 1 h. The reaction mixture was concentrated in vacuum and the residue water was added and the product was extracted with ethyl acetate. The crude product was purified by converting into hydrochloride salt.

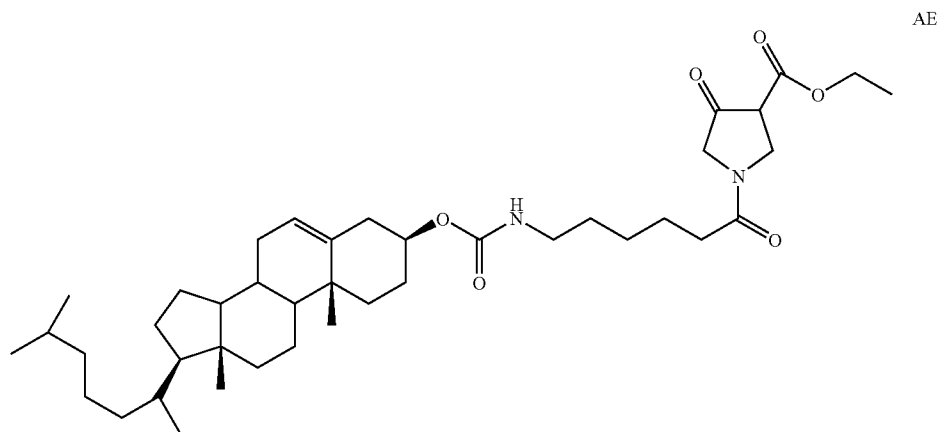
3-{[6-[17-(1,5-Dimethyl-hexyl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yloxy carbonylamino]-hexanoyl]ethoxycarbonylmethyl-amino)-propionic acid ethyl ester AD



[0178] The hydrochloride salt of 3-[(6-Amino-hexanoyl)-ethoxycarbonylmethyl-amino]-propionic acid ethyl ester AC (4.7 g, 14.8 mmol) was taken up in dichloromethane. The suspension was cooled to 0° C. on ice. To the suspension diisopropylethylamine (3.87 g, 5.2 mL, 30 mmol) was added. To the resulting solution cholesteryl chloroformate (6.675 g, 14.8 mmol) was added. The reaction mixture was stirred overnight. The reaction mixture was diluted with dichloromethane and washed with 10% hydrochloric acid. The product was purified by flash chromatography (10.3 g, 92%).

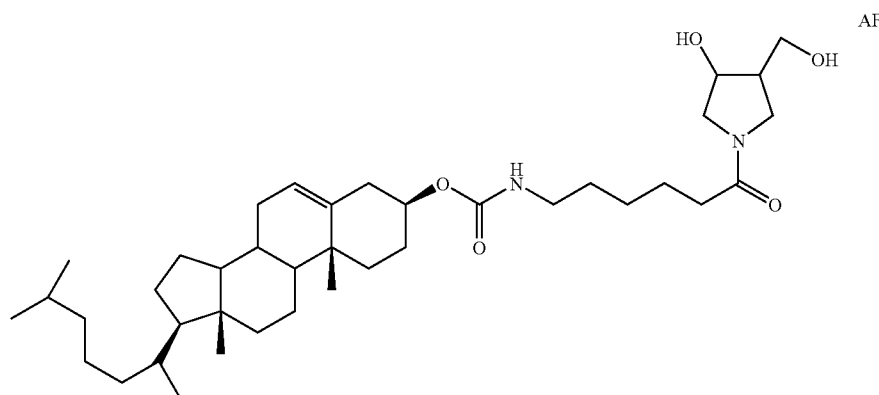
1-{6-[17-(1,5-Dimethyl-hexyl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yloxy-carbonylamino]-hexanoyl}-4-oxo-pyrrolidine-3-carboxylic acid ethyl ester AE

below 5° C. during the addition. The stirring was continued for 30 mins at 0° C. and 1 mL of glacial acetic acid was added, immediately followed by 4 g of NaH₂PO₄·H₂O in 40 mL of water. The resultant mixture was extracted twice with 100 mL of dichloromethane each and the combined organic extracts were washed twice with 10 mL of phosphate buffer each, dried, and evaporated to dryness. The residue was dissolved in 60 mL of toluene, cooled to 0° C. and extracted with three 50 mL portions of cold pH 9.5 carbonate buffer. The aqueous extracts were adjusted to pH 3 with phosphoric acid, and extracted with five 40 mL portions of chloroform which were combined, dried and evaporated to a residue. The residue was purified by column chromatography using 25% ethylacetate/hexane to afford 1.9 g of b-ketoester (39%).



[0179] Potassium t-butoxide (1.1 g, 9.8 mmol) was slurried in 30 mL of dry toluene. The mixture was cooled to 0° C. on ice and 5 g (6.6 mmol) of diester AD was added slowly with stirring within 20 mins. The temperature was kept

[6-(3-Hydroxy-4-hydroxymethyl-pyrrolidin-1-yl)-6-oxo-hexyl]-carbamic acid 17-(1,5-dimethyl-hexyl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl ester AF

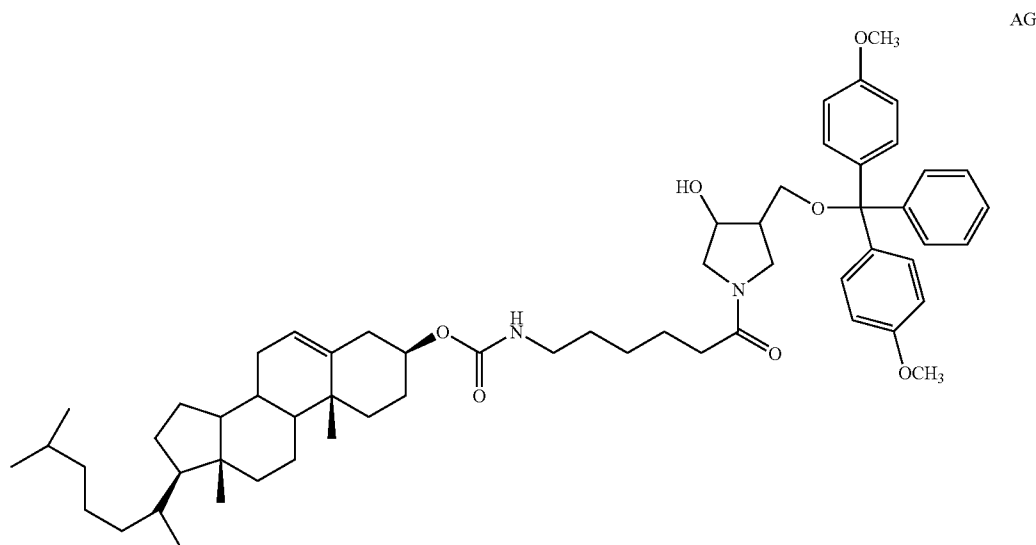


[0180] Methanol (2 mL) was added dropwise over a period of 1 h to a refluxing mixture of b-ketoester AE (1.5 g, 2.2 mmol) and sodium borohydride (0.226 g, 6 mmol) in tetrahydrofuran (10 mL). Stirring was continued at reflux temperature for 1 h. After cooling to room temperature, 1 N HCl (12.5 mL) was added, the mixture was extracted with ethylacetate (3×40 mL). The combined ethylacetate layer was dried over anhydrous sodium sulfate and concentrated in vacuum to yield the product which was purified by column chromatography (10% MeOH/CHCl₃) (89%).

(6-{3-[Bis-(4-methoxy-phenyl)-phenyl-methoxymethyl]-4-hydroxy-pyrrolidin-1-yl}-6-oxo-hexyl)-carbamic acid 17-(1,5-dimethyl-hexyl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl ester AG

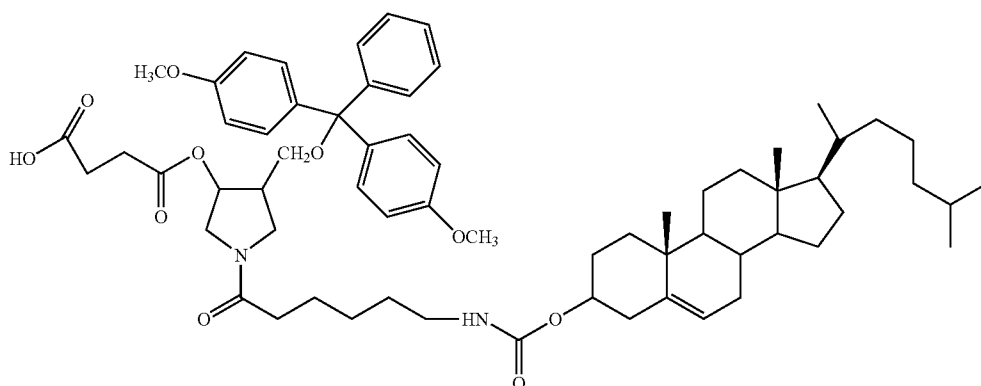
pyridine (10 mL) and 4,4'-dimethoxytritylchloride (0.724 g, 2.13 mmol) were added with stirring. The reaction was carried out at room temperature overnight. The reaction was quenched by the addition of methanol. The reaction mixture was concentrated in vacuum and to the residue dichloromethane (50 mL) was added. The organic layer was washed with 1M aqueous sodium bicarbonate. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated. The residual pyridine was removed by evaporating with toluene. The crude product was purified by column chromatography (2% MeOH/Chloroform, R_f=0.5 in 5% MeOH/CHCl₃) (1.75 g, 95%).

Succinic acid mono-(4-[bis-(4-methoxy-phenyl)-phenyl-methoxymethyl]-1-{6-[17-(1,5-dimethyl-hexyl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-



[0181] Diol AF (1.25 gm 1.994 mmol) was dried by evaporating with pyridine (2×5 mL) in vacuo. Anhydrous

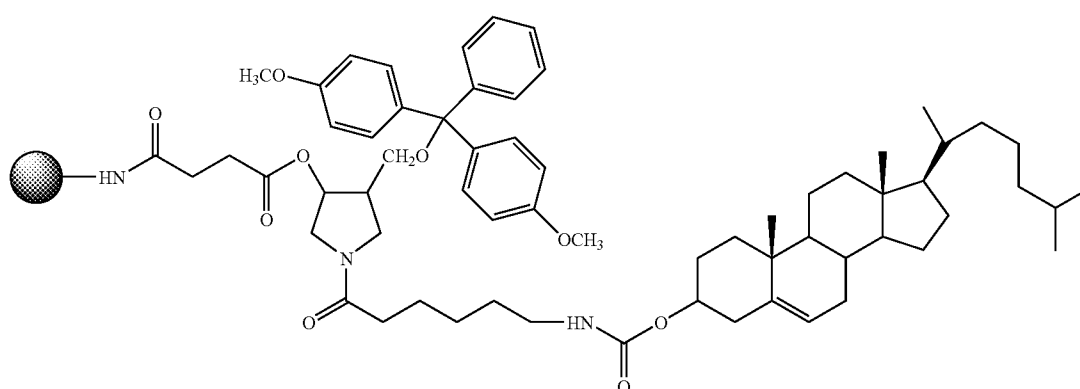
1H cyclopenta[a]phenanthren-3-yloxy carbonylamino}-hexanoyl}-pyrrolidin-3-yl) ester AH



[0182] Compound AG (1.0 g, 1.05 mmol) was mixed with succinic anhydride (0.150 g, 1.5 mmol) and DMAP (0.073 g, 0.6 mmol) and dried in a vacuum at 40° C. overnight. The mixture was dissolved in anhydrous dichloroethane (3 mL), triethylamine (0.318 g, 0.440 mL, 3.15 mmol) was added and the solution was stirred at room temperature under argon atmosphere for 16 h. It was then diluted with dichloromethane (40 mL) and washed with ice cold aqueous citric acid (5 wt %, 30 mL) and water (2×20 mL). The organic phase was dried over anhydrous sodium sulfate and concentrated to dryness. The residue was used as such for the next step.

Cholesterol Derivatised CPG AI

mmol) in acetonitrile/dichloroethane (3:1, 1.25 mL) were added successively. To the resulting solution triphenylphosphine (0.064 g, 0.242 mmol) in acetonitrile (0.6 mL) was added. The reaction mixture turned bright orange in color. The solution was agitated briefly using wrist-action shaker (5 mins). Long chain alkyl amine-CPG (LCAA-CPG) (1.5 g, 61 mm/g) was added. The suspension was agitated for 2 h. The CPG was filtered through a sintered funnel and washed with acetonitrile, dichloromethane and ether successively. Unreacted amino groups were masked using acetic anhydride/pyridine. The loading capacity of the CPG was measured by taking UV measurement (37 mM/g).



[0183] Succinate AH (0.254 g, 0.242 mmol) was dissolved in a mixture of dichloromethane/acetonitrile (3:2, 3 mL). To that solution DMAP (0.0296 g, 0.242 mmol) in acetonitrile (1.25 mL), 2,2'-Dithio-bis(5-nitropyridine) (0.075 g, 0.242

[0184] The synthesis and structure of cholesterol conjugated RNA strands is illustrated in FIG. 1.

[0185] The siRNAs listed Table 3 were synthesized for activity screening.

TABLE 3

<u>siRNAs specific for RhoA</u>				
Agent number	Sense strand	SEQ ID NO.	Antisense strand	SEQ ID NO. C. a. # ¹
AL-DP-5850	gauuugaccgucugaggcTT	1081	gccucagucggucuaaauTT	1082 n.a.
AL-DP-5851	ggauucuuggaugaugagTT	1083	cucaucauuccgaagauTT	1084 n.a.
AL-DP-5852	agaccaaagacggagugagTT	1085	cucacuccgucuuuggucTT	1086 na.
AL-DP-5853	ugaagcaggagccgguaaaTT	1087	uuuaccggcuccgcucaTT	1088 na.
AL-DP-5972	gcmumacmumagumumumagaagcmTT	1089	gcuucumaaumacuggumagTT	1090 6661
AL-DP-5973	cmumacmumagumumumagaagcmTT	1091	ggcuucumaaumacuggumagTT	1092 6662
AL-DP-5974	gcmumgumaaumacmumumumaacmTT	1093	guumumaaumagumumacmagTT	1094 6712
AL-DP-5975	gumumacmumgumumaaumumagumcmTT	1095	gcmumaaumacmumagumaaTT	1096 6751
AL-DP-5976	cmumacmumumaaumumumumumacmTT	1097	ggumaaumacmumumaaugggTT	1098 6769
AL-DP-5977	cmagcmumumumagumumumagaTT	1099	uucumaaumacmumagggcTT	1100 6521
AL-DP-5978	gcmumumumumumumumumagaaaTT	1101	uuuucumaaumacmumagggTT	1102 6523
AL-DP-5979	cmumumumumumumumumumagaaacmTT	1103	guuucumaaumacmumagggTT	1104 6524
AL-DP-5980	gaumumumumumumumumumumcmTT	1105	ggauuuucumaaumumumTT	1106 6528
AL-DP-5981	umumumumumumumumumumumcmTT	1107	ugggauguuuucumumumTT	1108 6530
AL-DP-5982	cmumumumumumumumumumumTT	1109	aaumumumumumumumumTT	1110 6790
AL-DP-5983	cmumumumumumumumumumumTT	1111	umumumumumumumumumTT	1112 6787
AL-DP-5984	cmumumumumumumumumumumTT	1113	aaumumumumumumumumTT	1114 6789
AL-DP-5985	cmumumumumumumumumumumTT	1115	umumumumumumumumumTT	1116 6788
AL-DP-5986	umumumumumumumumumumumTT	1117	umumumumumumumumumTT	1118 6767
AL-DP-5987	umumumumumumumumumumumTT	1119	cumumumumumumumumumTT	1120 6614
AL-DP-5988	umumumumumumumumumumumTT	1121	umumumumumumumumumTT	1122 6732
AL-DP-5989	cmumumumumumumumumumumTT	1123	agumumumumumumumumTT	1124 6832
AL-DP-5990	umumumumumumumumumumumTT	1125	ugumumumumumumumumTT	1126 6650
AL-DP-5991	umumumumumumumumumumumTT	1127	cumumumumumumumumumTT	1128 6657
AL-DP-5992	umumumumumumumumumumumTT	1129	agumumumumumumumumTT	1130 6756
AL-DP-5993	umumumumumumumumumumumTT	1131	umumumumumumumumumTT	1132 6656
AL-DP-5994	umumumumumumumumumumumTT	1133	agumumumumumumumumTT	1134 6713
AL-DP-5995	umumumumumumumumumumumTT	1135	umumumumumumumumumTT	1136 6703
AL-DP-6176	cmumumumumumumumumumumTT-Chol	1137	ggcuucumaaumacuggumagTT	1138 6662
AL-DP-6177	umumumumumumumumumumumTT-Chol	1139	cumumumumumumumumumTT	1140 6614

¹C. a. # = corresponding agent # in Table 2. The agent given under this agent number in Table 3 possesses the same core nucleotide sequence when nucleotide modifications, e.g. 2'-O-methyl modifications and phosphorothioate linkages, are disregarded

Example 3

siRNA Activity Testing

[0186] The ability of the iRNA agents represented in Table 3 to inhibit the expression of human RhoA was tested in

human cell lines expressing the respective gene product from an expression construct, or in cell lines constitutively expressing the respective gene product. The iRNA agent is transfected into the cells, e.g., by transfection or electroporation, allowed to act on the cells for a certain time, e.g., 24

hours, and levels of RhoA expression were determined by measurement of RhoA mRNA concentrations in cell lysates. These expression levels were then compared to RhoA expression levels in cells treated equivalently but without addition of the iRNA agent, or to expression levels of housekeeping genes (e.g. GAPDH), and the ability of the iRNA agents representend in Table 3 to inhibit the expression of human RhoA thereby assessed.

Screening for Inhibition of RhoA Expression

[0187] One day before transfection, Neuroscreen-1 cells (Cellomics Inc., Pittsburgh, USA) were seeded at 1.5×10^4 cells/well on 96-well collagen-coated plates (Greiner Bio-One GmbH, Frickenhausen, Germany) in 100 μ l of growth medium (RPMI 1640, 10% horse serum, 5% fetal calf serum, 100 u penicillin/100 μ g/ml streptomycin, 2 mM L-glutamine, Biochrom AG, Berlin, Germany). Transfections were performed in triplicates. For each well 0.5 μ l Lipofectamine2000 (Invitrogen GmbH, Karlsruhe, Germany) were mixed with 12 μ l Opti-MEM (Invitrogen) and incubated for 15 min at room temperature. 2 μ l of a 5 μ M solution of siRNA in annealing buffer (20 mM sodium phosphate, pH 6.8; 100 mM sodium chloride) were mixed with 10.5 μ l Opti-MEM per well, combined with the Lipofectamine2000-Opti-MEM mixture and again incubated for 15 minutes at room temperature. During this incubation, growth medium was removed from cells and replaced by 75 μ l/well of fresh medium. The 25 μ l solution of siRNA-Lipofectamine2000-complex were added, resulting in an overall 100 nM siRNA concentration in the 100 μ l incubation volume, and the cells were incubated for 24 h at 37° C. and 5% CO₂ in a humidified incubator (Heraeus GmbH, Hanau).

[0188] mRNA levels in cell lysates were quantitated by a commercially available branched DNA hybridization assay (QuantiGene bDNA-kit, Genospectra, Fremont, USA). Cells were harvested by applying 50 μ l additional growth medium and 75 μ l of Lysis Mixture (from QuantiGene bDNA-kit) to each well and were lysed at 53° C. for 30 min. 50 μ l of the lysates were incubated with probes specific to rat RhoA and rGAPDH (sequence of probes given in Table 4 and Table 5) according to the manufacturer's protocol for the QuantiGene bDNA kit assay. Finally, chemoluminescence was measured in a Victor2-Light (Perkin Elmer, Wiesbaden, Germany) as RLUs (relative light units) and values obtained with RhoA probes were normalized to the respective GAPDH values for each well. Mock transfected cells (following the same protocol except that no siRNA was added) served as controls and for comparison of mRNA levels.

[0189] Effective siRNAs from the screen were further characterized by establishment of dose response curves and calculation of IC₅₀ concentrations (the concentration at which 50% inhibition of gene expression would be observed). For dose response assessment, transfections were performed at the following concentrations: 100 nM, 33.3 nM, 11.1 nM, 3.7 nM, 1.2 nM, 0.4 nM, 137 pM, 46 pM, 15 pM, 5 pM and mock (no siRNA) by serially diluting the 5 μ M siRNA stock solution with annealing buffer and using 2 μ l of the diluted stock according to the above protocol. The IC₅₀ was determined by curve fitting using the computer software Xlfit using the following parameters: Dose Response One Site, 4 Parameter Logistic Model, fit=(A+((B-A)/(1+(((10⁻⁵ AC)/x)^D))))), inv=((10⁻⁵ C)/((((B-A)/(y-A))-1)^(1/D))), res=(y-fit).

TABLE 4

Rat RhoA probes		
Probe type ¹	Nucleotide sequence	SEQ ID NO.
CE	CCATTTTCTGGGATGTTTCTAAATTTTCTCTTGGAAGAAAGT	1141
CE	ACAGAAATGCTTGACTTCTGGAGTTTTTCTCTTGGAAGAAAGT	1142
CE	CTTCAGGTTTACC GGCTCCTTTTCTCTTGGAAGAAAGT	1143
CE	CTGTTTGCCATATCTCTGCCTTTTTCTCTTGGAAGAAAGT	1144
CE	TTGGTCTTTGCTGAACACTCCATTTTCTCTTGGAAGAAAGT	1145
CE	CCCGCGTCTAGCTTGCAGATTTTCTCTTGGAAGAAAGT	1146
LE	AGGATGATGGGCACATTTGGTTTTTAGGCATAGGACCCGTGTCT	1147
LE	GCCTTGCTGTGCTCATTCCTTTTAGGCATAGGACCCGTGTCT	1148
LE	TGCTTCATTTTGGCTAACTCCCTTTTAGGCATAGGACCCGTGTCT	1149
LE	TGTACCCAAAGCGCCAATCTTTTAGGCATAGGACCCGTGTCT	1150
LE	GCAGCTCTCGTGGCCATCTTTTAGGCATAGGACCCGTGTCT	1151
LE	AGGCACCCCGACTTTTCTTTTAGGCATAGGACCCGTGTCT	1152
BL	CTATCAGGGCTGTGATGGAA	1153
BL	GAAGATCCTTCTTGTCCCAACT	1154
BL	CAAAAACCTCTCTCACTCCGTCT	1155

¹CE = Capture Extender probe; LE = Label Extender probe; BL = blocking probe

[0190]

TABLE 5

Rat GAPDH probes		
Probe type ¹	Nucleotide sequence	SEQ ID NO.
CE	CCAGCTTCCCATTTCTAGCCTTTTCTCTTGGAAGAAAGT	1156
CE	TCTCGCTCCTGGAAGATGGTTTTTCTCTTGGAAGAAAGT	1157
CE	CCCATTGTGTTAGCGGATTTTCTCTTGGAAGAAAGT	1158
CE	CGGAGATGATGACCCTTTTGGTTTTTCTCTTGGAAGAAAGT	1159

TABLE 5-continued

Rat GAPDH probes		
Probe type ¹	Nucleotide sequence	SEQ ID NO.
LE	GATGGGTTTCCCGTTGATGATTTT TAGGCATAGGACCCG TGTCT	1160
LE	GACATACTCAGCACCAGCATCACTTTT TAGGCATAGGAC CCGTGTCT	1161
LE	CCCAGCCTTCTCCATGGTGGTTT TAGGCATAGGACCCG TGTCT	1162
BL	TTGACTGTGCCGTTGAACCTTG	1163
BL	CCCCACCCCTTCAGGTGAGC	1164
BL	GGCATCAGCGGAAGGGG	1165

¹CE = Capture Extender probe; LE = Label Extender probe; BL = blocking probe

[0191] Table 6 lists the agent number, the position of the nucleotide within the human RhoA mRNA sequence (Genbank accession number NM_001664) corresponding to the 5'-most nucleotide of the sense strand of the agent, the amount of total RhoA mRNA remaining in cells treated with the agent at 100 nM concentration in % of controls, and the IC₅₀ value for selected agents.

TABLE 6

Ability of siRNAs specific for RhoA to reduce RhoA mRNA levels in cultured cells				
Agent number	Pos. in mRNA ¹	Rem. RhoA mRNA at 100 nM agent, first screen	Rem. RhoA mRNA at 100 nM agent, second screen	IC ₅₀ RhoA [nM]
AL-DP-5850			73 ± 8%	142
AL-DP-5852			17 ± 4%	3.1
AL-DP-5853			18 ± 3%	2.8
AL-DP-5854			17 ± 1%	4.2
AL-DP-5972	986	30 ± 9%	17 ± 2%	0.003
AL-DP-5973	987	21 ± 2%	15 ± 1%	
AL-DP-5974	1179	44 ± 12%	48 ± 2%	
AL-DP-5975	1395	33 ± 4%	27 ± 10%	0.13
AL-DP-5976	1413	26 ± 3%	17 ± 2%	
AL-DP-5977	537	n.d.	30 ± 1%	
AL-DP-5978	539	58 ± 4%	51 ± 1%	0.06
AL-DP-5979	540	12 ± 2%	15 ± 2%	
AL-DP-5980	544	75 ± 3%	95 ± 3%	
AL-DP-5981	546	17 ± 2%	16 ± 1%	0.13
AL-DP-5982	1452	18 ± 2%	22 ± 2%	0.13
AL-DP-5983	1449	37 ± 4%	29 ± 3%	0.37
AL-DP-5984	1451	26 ± 1%	33 ± 4%	
AL-DP-5985	1450	n.d.	33 ± 1%	
AL-DP-5986	1411	18 ± 1%	22 ± 1%	0.4
AL-DP-5987	901	22 ± 5%	10 ± 0%	0.01
AL-DP-5988	1376	17 ± 1%	16 ± 1%	0.34
AL-DP-5989	1876	20 ± 1%	25 ± 3%	3.1
AL-DP-5990	956	16 ± 2%	17 ± 1%	0.36
AL-DP-5991	982	55 ± 5%	33 ± 5%	0.24
AL-DP-5992	1400	55 ± 6%	55 ± 6%	
AL-DP-5993	981	32 ± 2%	33 ± 3%	
AL-DP-5994	1180	23 ± 2%	20 ± 1%	6.0
AL-DP-5995	1170	25 ± 2%	26 ± 2%	

TABLE 6-continued

Ability of siRNAs specific for RhoA to reduce RhoA mRNA levels in cultured cells				
Agent number	Pos. in mRNA ¹	Rem. RhoA mRNA at 100 nM agent, first screen	Rem. RhoA mRNA at 100 nM agent, second screen	IC ₅₀ RhoA [nM]
AL-DP-6176	987		14 ± 2%	1.17
AL-DP-6177	901		19 ± 5%	0.005

¹Position of nucleotide within human Nogo-R mRNA corresponding to the 5'-most nucleotide of the sense strand of the agent

[0192] In summary, agents AL-DP-5979, AL-DP-5990, AL-DP-5988, AL-DP-5981, AL-DP-5982, AL-DP-5986, AL-DP-5989, AL-DP-6176, and AL-DP-6177 were able to reduce the expression of RhoA mRNA by 80% or more, AL-DP-5973, AL-DP-5987, AL-DP-5994, AL-DP-5995, AL-DP-5976, AL-DP-5984, and AL-DP-5972 were able to reduce the expression of RhoA mRNA by 70% or more, AL-DP-5993, AL-DP-5975, and AL-DP-5983 were able to reduce the expression of RhoA mRNA by 60% or more, AL-DP-5974 was able to reduce the expression of RhoA mRNA by 50% or more, and AL-DP-5991, AL-DP-5992, and AL-DP-5978 were able to reduce the expression of RhoA mRNA by 40% or more. The high activity of AL-DP-6176 and AL-DP-6177 shows that a cholesteryl moiety may be conjugated to the 3'-end of the sense strand of an siRNA without significant loss of activity. AL-DP-6176 and AL-DP-6177 are identical to AL-DP-5973 and AL-DP-5987, respectively, except for the 3'-conjugated cholesteryl moiety on the sense strand.

Example 4

Stability Testing

[0193] In order to verify the stability of siRNAs in the biological matrix most relevant to their intended physiological application, cerebrospinal fluid (CSF), we established a method for determining the degradation half life of siRNAs in this medium. This method comprises the incubation of siRNAs with CSF followed by Proteinase K treatment of the CSF sample and the separation of CSF sample constituents on an HPLC.

[0194] The example below shows the analyses of CSF samples which were contacted with siRNAs in vitro. However, this method can equally be applied to biological samples ex vivo, i.e. obtained from a subject which was contacted with an siRNA in vivo.

[0195] Bovine CSF was obtained from a calf (Bos bovis), age 6 months (Prof. Dr. J. Rehage, University of Veterinary Medicine Hannover, Foundation, Hannover, Germany). Porcine CSF was pooled from 3 healthy weaner pigs (Sus scrofa domestica), age 3-4 months (Prof. Dr. M. Wendt, University of Veterinary Medicine Hannover, Foundation, Hannover, Germany). Rat CSF was pooled from 20 male Sprague Dawley rats (Rattus norvegicus), 175-200 g in weight (Charles River Laboratories, L'Arbresle Cedex, France). Proteinase K (20 mg/ml) was obtained from peQLab (Erlangen, Germany; Cat.-No. 04-1075) and diluted 1:1 with deionized water (18.2 mΩ) to a final concentration of 10 mg/ml Proteinase K. Proteinase K Buffer (4.0 ml TRIS-HCl 1M pH 7.5, 1.0 ml EDTA 0.5M, 1.2 ml NaCl 5M, 4.0 ml SDS 10%) was prepared fresh and kept at 50° C. until use to avoid precipitation.

[0196] A 40 mer of poly(L-dT), (L-dT)₄₀ was obtained from Noxxon Pharma AG (Berlin, Germany) and used as an internal standard. Polymers of the L-enantiomers of nucleic acids show an extraordinary stability towards nucleolytic degradation (Klussman S, et al., Nature Biotechn. 1996, 14:1112) but otherwise very similar properties when compared to naturally occurring nucleic acids consisting of R-enantiomers.

Proteinase K Treatment of siRNA Incubation Samples

[0197] 6 µl of a 50 µM solution of the respective siRNA in phosphate buffered saline (PBS, Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) was incubated with 54 µl CSF at 37° C. for 30 min, 1, 2, 4, 8, 16, 24 or 48 hours. To terminate the siRNA-degradation, 25 µl of Proteinase K buffer were added to incubation samples immediately after expiry of the respective incubation period, the mixture vortexed at highest speed for 5 s (Vortex Genie 2, Scientific Industries, Inc., Bohemia, N.Y., USA, cat. no. SI 0256), 8 µl Proteinase K (10 mg/ml) were added followed by vortexing for 5 s, and finally the mixture was incubated for 20 min in a thermomixer at 42° C. and 1050 rpm.

[0198] 5 µl of a 50 µM solution (250 pmole) of (L-dT)₄₀ were added as an internal standard to each well, the solution was vortexed for 5 s, and the tube centrifuged for 1 min in a tabletop centrifuge to collect all droplets clinging to the inner surfaces of the wells at the bottom. The solution was transferred to a 96 well Captiva 0.2 µm filter plate (Varian, Germany, Cat. No. A5960002) and filtered by centrifugation at 21900 rcf for 45 min.

[0199] The incubation wells were washed with 47.5 µl deionized water (18.2 mΩ), the wash filtered through the Captiva Filter Unit at 21900 rcf for 15 min, and the wash step repeated. Approximately 180 µl of the theoretical total volume of 200 µl are on average recovered after the second washing step.

Ion exchange chromatographic separation of siRNA single strands from each other and from degradation products:

[0200] A Dionex BioLC HPLC-system equipped with inline-degasser, autosampler, column oven and fixed wavelength UV-detector (Dionex GmbH, Idstein, Germany) was used under denaturing conditions. Standard run parameters were:

Column:	Dionex DNA-Pac100; 4 × 250 mm	
Temperature:	75° C.	
Eluent A:	10 mM NaClO ₄ , 20 mM TRIS-HCl, 1 mM EDTA; 10% acetonitrile, pH = 8.0	
Eluent B:	800 mM NaClO ₄ , 20 mM TRIS-HCl, 1 mM EDTA; 10% acetonitrile, pH = 8.0	
Detection:	@ 260 nm	
Gradient:	0–1 min:	10% B
	1–11 min:	10% → 35% B
	11–12 min:	35% B → 100% B
	12–14 min:	100% B → 10% B
	14–16 min:	10% B for column reequilibration
Injection volume:	20 µl	

[0201] Where separation between the two strands of an siRNA was not satisfactory or a degradation fragment co-eluted with one strand, the chromatographic parameters were adjusted by changing temperature, pH, replacement of NaClO₄ by NaBr, the concentration of acetonitrile, and/or

adjusting the slope of the eluent gradient until separation was achieved which allowed separate quantitation of the peaks from sense and antisense strand.

[0202] Peak areas for full length strands were obtained by integration of the UV detector signal using software supplied by the manufacturer of the instrument (Chromeleon 6.6; Dionex GmbH, Idstein, Germany).

Data Analysis:

[0203] Integrated sense strand, antisense strand, and internal standard peak areas were obtained for all samples and the normalization control.

[0204] A correction factor CF, accounting for liquid losses in the filtration and washing steps, was determined for every sample by calculating the ratio of experimental to theoretical internal standard peak area. The theoretical internal standard peak area is obtained, e.g. from a calibration curve of the internal standard obtained by injecting 50 µl each of a serial dilution of the 50 µM solution of (L-dT)₄₀ onto the HPLC column, and calculation of the theoretical peak area corresponding to 25 pmole (L-dT)₄₀ with the equation obtained by linear least square fit to the peak areas from the dilution series. The correction factor CF to be applied to the peak areas of the sense and antisense strand is the obtained as:

$$CF = \frac{\text{PeakArea}_{\text{intStd}}(\text{theoretical})}{\text{PeakArea}_{\text{intStd}}(\text{Sample})}$$

[0205] This treatment assumes that, by virtue of washing the filter twice, virtually complete recovery is achieved in the combined filtrates, and corrects for the variable volume of wash water retained in the filter, such that peak areas from different samples can be compared.

[0206] The peak areas obtained for the sense and antisense strand peaks for each time point are then multiplied with the correction factor CF to obtain Normalized Peak Areas (NPA_{sense,t}, NPA_{antisense,t}):

$$NPA_{\text{sense or antisense,t}} = (\text{Peak Area}_{\text{sense or antisense,t}}) \times CF$$

[0207] To obtain the relative amount of remaining Full Length Product (% FLP) for the sense and antisense strands at time t, the Normalized Peak Area for each strand at time

t=0 min (NPA_{sense,t=0}, NPA_{antisense,t=0}) is set as 100%, and the NPAs from other time points are divided by these values.

$$\% FLP_{t=1, 2, 3 \dots n} = (NPA_{t=1, 2, 3 \dots n} / NPA_{t=0}) * 100$$

[0208] The value obtained from the control sample, where the siRNA was incubated with annealing buffer only, may

serve as a control of the accuracy of the method. The % FLP for both strands should lie near 100%, within error margins, regardless of time of incubation.

[0209] The degradation half life $t_{1/2}$ may then be calculated for each strand, assuming first order kinetics, from the slope of a linear least square fit to a plot of $\ln(\% \text{ FLP})$ versus time as:

$$t_{1/2} = \ln(0.5) / \text{slope}$$

Stability of siRNAs Specific for NogoL and RhoA in Rat, Bovine and Porcine CSF

[0210] Table 7 shows the results for select siRNAs of the determination of the relative amount of full length dsRNA present in porcine, rat, and bovine CSF, and PBS, after 48 h of incubation in the respective medium. In addition, the degradation half life was determined for the sense and antisense strands separately for some siRNAs.

TABLE 7

Stability of various siRNAs specific for NogoL and RhoA in rat, bovine and porcine CSF							
Agent number	% full length duplex present after 48 h in				Specific for	Modification ¹	C.a. # ²
	Porcine CSF	Rat CSF	Bovine CSF	PBS			
AL-DP-5973	95	3	95	100	RhoA	3/TTs	6662
AL-DP-5979	99			108	RhoA	3/TTs	6524
AL-DP-5981	96			103	RhoA	3/TTs	6530
AL-DP-5982	56			98	RhoA	3/TTs	6790
AL-DP-5986	100			105	RhoA	3/TTs	6767
AL-DP-5987	87			97	RhoA	3/TTs	6614
AL-DP-5988	41			99	RhoA	3/TTs	6732
AL-DP-5989	87			101	RhoA	3/TTs	6832
AL-DP-5990	76			92	RhoA	3/TTs	6650

¹0 = no 2'-modifications; 1 = 5'-nucleotide in 5'-ua-3', 5'-uu-3', 5'-ca-3', and 5'-ug-3' motifs is 2'-modified in sense strand, 5'-nucleotide in 5'-ua-3' and 5'-ca-3' motifs is 2'-modified in antisense strand; 2 = 5'-nucleotide in 5'-ua-3', 5'-uu-3', 5'-ca-3', and 5'-ug-3' motifs is 2'-modified in sense and antisense strand; 3 = all pyrimidine nucleotides are 2'-modified in sense strand, 5'-nucleotide in 5'-ua-3' and 5'-ca-3' motifs is 2'-modified in antisense strand; 4 = all pyrimidine nucleotides are 2'-modified in sense strand, 5'-nucleotide in 5'-ua-3', 5'-uu-3', 5'-ca-3', and 5'-ug-3' motifs is 2'-modified in antisense strand; 5 = all pyrimidine nucleotides are 2'-modified in sense strand, no 2'-modifications in antisense strand; TT = 21 nucleotides and 3'-terminal TT single strand overhangs in sense and antisense strands; TTs = 21 nucleotides and 3'-terminal TT single strand overhangs in sense and antisense strands; 23 = 21 nucleotide sense, 23 nucleotide antisense strand, 2 nucleotide single strand overhang on 3'-end of antisense strand; 23s = 21 nucleotide sense, 23 nucleotide antisense strand, 2 nucleotide single strand overhang on 3'-end of antisense strand, nucleotides comprise 5'-phosphorothioate groups in positions 21 and 22 of antisense strand

²C.a. # = corresponding agent # in Table 2. The agent given under this agent number in Table 2 possesses the same core nucleotide sequence when nucleotide modifications, e.g. 2'-O-methyl modifications and phosphorothioate linkages, are disregarded

[0211] As is evident from Table 7, the modification of siRNAs in select sites vulnerable to degradation can lead to agents with excellent properties in terms of activity and stability. For example, AL-DP-5871, AL-DP-5938, AL-DP-5963, AL-DP-5973, AL-DP-5979, AL-DP-5981, AL-DP-5986, AL-DP-5987, AL-DP-5989, and AL-DP-5990 all inhibit their respective target gene by more than 70% in the in vitro assays described above, and more than 70% full length duplex remain after incubation with porcine CSF for 48 h. However, there is some indication that rat CSF is more aggressive towards siRNAs than porcine or bovine CSF.

Example 5

Inhibition of RhoA Expression in Rat Primary Dorsal Root Ganglia (DRG) Cells in Culture

[0212] The inhibition of RhoA expression was assessed in rat primary dorsal root ganglia (DRG) cells in culture in order to validate results obtained using Neuroscreen 1 cells as described above.

[0213] DRG cells were isolated from Sprague-Dawley rats at postnatal day 3 to 6. Rats were dissected and cells dissociated into single cells by addition of 1.3 ml (0.28 Wunsch units/ml) Liberase Blendzyme (Roche) in S-MEM (Invitrogen Gibco, Carlsbad Calif., USA) and incubated for 35 min at 37° C. The cell suspension was pre-plated on tissue-culture plates to remove non-neuronal cells. Neurons were then plated onto tissue-culture Biocoat™ PDL Poly-D-Lysine/Laminin 96 well plates (BD Biosciences, Bedford Mass., USA) in F12-HAM's Medium containing glutamine (Invitrogen Gibco, Carlsbad Calif., USA) with 5% fetal bovine serum (FBS, heat inactivated) and 5% horse serum (heat inactivated) (both Invitrogen Gibco, Carlsbad Calif., USA) supplemented with 50 ng/ml mouse nerve growth factor 2.5S (NGF; Promega Corp., Madison Wis., USA) and kept at 37° C., 5% CO₂ in a humidified incubator until transfection.

[0214] A rhoA-specific siRNA, agent number AL-DP-5987, was tested in DRG cultures at 200 nM concentration using TransMessenger™ Transfection reagent (Qiagen GmbH, Hilden, Germany, cat. no. 301525) which is based on a lipid formulation, specific RNA-condensing reagent (Enhancer R™) and an RNA-condensing buffer (Buffer EC-R™) keeping siRNA:Enhancer R™ ratio (μg:μl) constant at 1:2, and siRNA:TransMessenger™ ratio (μg:μl) constant at 1:12.

[0215] DRG neurons were transfected 24 h post-plating. For each well 0.52 μl Enhancer R™ were first mixed with 13.68 μl Buffer EC-R™. 0.8 μl of a 25 μM solution of AL-DP-5987 (0.26 μg) in annealing buffer (20 mM sodium phosphate, pH 6.8; 100 mM sodium chloride), or 0.8 μl of annealing buffer (siRNA-free control) were added and the mixture incubated for 5 min at RT. 3.12 μl TransMessenger™ Transfection Reagent were diluted with 6.88 μl Buffer EC-R™, added to the mixture, and the mixture incubated for another 10 min at room temperature to allow transfection-complex formation. 75 μl serum free F12-HAM's Medium containing glutamine (Invitrogen Gibco, Carlsbad Calif., USA) supplemented with 50 ng/ml NGF 2.5S (Promega Corp., Madison Wis., USA) and 1:50 B27 supplement (Invitrogen Gibco, Carlsbad Calif., USA) were added to the transfection complexes and complete mixing achieved by gently pipetting up and down. The growth medium was removed from the DRG cells, and 90 μl of the above transfection complex mixture were added onto the cells. After 8 h of incubation at 37° C., 5% CO₂ in a humidified incubator supernatant was removed from the cells, fresh F12-HAM's medium containing glutamine supplemented with 5% FBS, 5% horse serum (both Invitrogen Gibco, Carlsbad Calif., USA), 50 ng/ml mouse NGF 2.5S (Promega Corp., Madison Wis., USA) and 1:100 Penicillin/Streptomycin (Invitrogen Gibco, Carlsbad Calif., USA) was added, the cells were incubated for another 16 h at 37° C., 5% CO₂ in a humidified incubator, and rhoA mRNA was quantified.

[0216] RhoA mRNA levels were measured using the QuantiGene™ bDNA kit (Genospectra, Fremont, USA) according to manufacturer's protocol. Briefly, the supernatant was removed from the DRG cells, and the cells were lysed by addition of 150 μ l of Lysis Working Reagent (1 volume of Lysis Mixture plus 2 volumes of medium) and incubation at 52° C. for 30min. 40 μ l of the lysates were incubated at 52° C. for 40 min with the probe sets specific to rat RhoA and rat GAPDH given above in Table 4 and Table 5. Chemoluminescence was read on a Victor²-Light™ (PerkinElmer Life And Analytical Sciences, Inc., Boston Mass., USA) as Relative Light Units (RLU). RLU for RhoA were normalized to GAPDH RLU for each well. Normalized RhoA/GAPDH ratios were then compared to the siRNA-free control, which was set as 100%.

[0217] In several independent experiments, rhoA mRNA was reduced in primary DRG cells treated with AL-DP-5987 in culture consistently to 20-25% of rhoA mRNA levels found in the siRNA free controls.

Example 6

Neurite Outgrowth Assessment in Primary DRG Transfected with Selected iRNA Agents of the Invention

Neuron Dissection

[0218] Dorsal root ganglia (DRG) were isolated from Sprague-Dawley rats at postnatal day 7-12. DRG were dissected into the culture medium (Neurobasal-A supplemented with 1:50 B27, Glutamine, and Pen/Strep; Invitrogen Gibco, Carlsbad Calif., USA), blood was rinsed off with PBS and neurons were dissociated by incubation with 1 mL DMEM/collagenase (0.5%) for 90 minutes at 37° C., inverting the tube every 30 minutes. The collagenase was washed off by serial dilution and the isolated DRG were resuspended in 500 μ l of culture medium. The suspension was then triturated 15-20 times with a fire-polished pipette until a homogeneous cell suspension was achieved. Cells were spun down three times for 3 minutes at 1500 RPM, and the cell debris aspirated off. Cells were then resuspended in 500 μ l of culture media and passed through a 70 μ m strainer (Falcon, 352350). The cell suspension was pre-plated on a 24 well tissue-culture plate in 300 μ l of culture media for 24 hours at 37° C., 5% CO₂ in a humidified incubator. Neurons were then transfected with appropriate siRNA as follows:

Transfection of siRNA

[0219] For each well, Lipofectamine™ 2000 was used and transfections were performed according to the manufacturer's protocol. The appropriate amount of siRNA was diluted into Opti-MEM I Reduced Serum Medium and mixed

gently. The Lipofectamine™ 2000 was vortexed before use. For each well of a 24 well plate, 1.5 μ l was diluted in 25 μ l of Opti-MEM I Reduced Serum Medium, mixed gently and incubated for 5 minutes at room temperature. After the 5 minute incubation, 3 μ l of the diluted siRNA was combined with the diluted Lipofectamine™ 2000 (total volume is 29.5 μ l). The complex was mixed gently and incubated for 20 minutes at room temperature to allow the siRNA: Lipofectamine™ 2000 complexes to form. 300 μ l of Media were added to the transfection complexes and complete mixing was achieved by gently pipetting up and down (total volume: 600 μ l). The cells were incubated for another 20-24 h at 37° C., 5% CO₂ in a humidified incubator

Outgrowth Assay Plate Preparation

[0220] Chondroitin sulfate proteoglycan (CSPG) or myelin was dried down overnight in 50 μ l in individual wells of a biocoat Poly-D-Lysine plate (BD Biosciences, Bedford Mass., USA). The plate was rinsed once with water to remove salt deposits. laminin (Invitrogen, CA; 1 μ g/ml) was then coated for 1 h at room temperature.

Replating of the Neurons

[0221] Neurons were resuspended from the 24 well plate by gently pipetting up and down, spun down at 1500 RPM for 3 minutes and resuspended in the appropriate volume. Neurons were replated at a concentration of 3000 neurons/well onto the prepared Poly-D-Lysine/Laminin 96-well plates in culture medium. The neurons were allowed to grow for 16-24 hours at 37° C., 5% CO₂ in a humidified incubator and subjected to neurite quantification as follows.

Neurite Quantification

[0222] The cells were fixed in 4% formaldehyde, 20% sucrose in PBS for 15 minutes. The cells were rinsed once with PBS, permeabilized and blocked for an hour at room temperature using 0.1% Triton, 10% Goat serum in PBS. The cells were stained with a beta-III tubulin, polyclonal rabbit antibody (Covance, 1:500) diluted in PBS and incubated overnight at 4° C. After three 5 minutes rinses in PBS, the secondary Alexa-Fluor 488 goat anti-rabbit IgG antibody (Molecular Probes, 1:500 filtered through 0.22 μ m) was incubated overnight at 4° C. Following 3 rinses in PBS, neurite outgrowth was quantified using an automated cellular imaging and analysis system (Axon Instrument, Union City, Calif.).

Results

[0223] Two iRNA agents specific for the green fluorescent protein gene (AL-DP 5549, AL-DP 5266; nucleic acid sequences in Table 8) were used as controls.

TABLE 8

Nucleic acid sequences of control iRNA agents specific for the green fluorescent protein gene			
Agent number	Sense strand	SEQ ID NO.	Antisense strand
AL-DP-5549	ccacaugaagcagcagcagcuu-Chol	1166	aagucgugcugcucucauguggmumc
AL-DP-5266	ccacaugaagcagcagcagcuu	1168	aagucgugcugcucucauguggmumc

[0224] The iRNA agent of the invention AL-DP-6176 was tested at a concentration of 250 nM at transfection for its effect on neurite outgrowth on growth substrate supplemented with 0, 40, or 200 ng myelin, and compared to the effect of AL-DP-5266. In Table 9, neurite outgrowth is expressed as percent of neurite outgrowth seen without myelin. Evidently, the green fluorescent protein-specific iRNA agent has no effect on neurite outgrowth of DRG on the inhibitory substrate, while the RhoA-specific iRNA agent strongly counters the growth inhibitory effect of myelin.

TABLE 9

Inhibition of neurite outgrowth by myelin in DRG in the absence or presence of iRNA agents specific for green fluorescent protein (GFP) or RhoA			
Myelin (ng)	no siRNA	AL-DP 5266 (GFP)	AL-DP 6176 (RhoA)
0	100%	100%	100%
40	82%	75%	183%
200	3%	6%	19%

[0225] Furthermore, the iRNA agents of the invention AL-DP 5973, AL-DP 5987, AL-DP 6176, and AL-DP 6177 were tested at a concentration of 250 nM at transfection for its effect on neurite outgrowth on growth substrate supplemented with 30 ng CSPG, and compared to the effect of AL-DP-5549 and AL-DP-5266. In Table 10, neurite outgrowth is expressed as percent of neurite outgrowth seen without CSPG. Evidently, the green fluorescent protein-specific iRNA agent has no effect on neurite outgrowth of DRG on the inhibitory substrate, while the RhoA-specific iRNA agents counter the growth inhibitory effect of CSPG.

TABLE 10

Inhibition of neurite outgrowth by CSPG in DRG in the absence or presence of iRNA agents specific for green fluorescent protein (GFP) or RhoA	
	Relative outgrowth
AL-DP-5549	3 ± 2%
AL-DP-5266	2 ± 1%
AL-DP 5266	6 ± 2%
AL-DP 5973	5 ± 2%

TABLE 10-continued

Inhibition of neurite outgrowth by CSPG in DRG in the absence or presence of iRNA agents specific for green fluorescent protein (GFP) or RhoA	
	Relative outgrowth
AL-DP 6176	8 ± 4%
AL-DP 5987	10 ± 5%

Example 7

Assessing Behavioural Improvement by Intrathecal Administration of iRNA Agents of the Invention Following Hemisection Injury

Animals and iRNA Agent Administration

[0226] Thirty adult female Sprague-Dawley rats (Charles River Laboratories, Wilmington, Mass., USA; weight 200-230 grams) were randomly divided into 3 groups. One day before the spinal cord lesion surgery, all the animals were trained for locomotor BBB score in an open field. 3 iRNA agents were administered in blinded fashion to the three different groups. Group A being administered a first rhoA-specific iRNA agent (AL-DP-6177), group B receiving a second rhoA-specific iRNA agent (AL-DP-6176), group C as a control group getting the unrelated control iRNA agent, directed against Luciferase (AL-DP-1956, for nucleic acid sequence see Table 11). The iRNA agents were delivered through an osmotic minipump (Alzet 2004, 0.25 µl/hr, 28 day delivery), which was filled with appropriate drug for the groups A, B, C, and pre-incubated overnight at 37° C. before implantation to the animals (described below). The siRNA was released at a dose of 0.4 mg per day for 28 days.

TABLE 11

Nucleic acid sequences of control iRNA agent specific for luciferase			
Agent number	Sense strand	SEQ ID NO.	SEQ ID NO.
		Antisense strand	
AL-DP-5549	cmumumacmgcmungagumacmumumcmgaTT-Chol	1170 ucgaagumacucmaggcumaagTT	1171

Microsurgery

[0227] For the microsurgery procedure generating the hemisection injury the rats were deeply anesthetized with ketamine (60 mg/kg) and xylazine (10 mg/kg). A complete laminectomy was conducted at spinal level T6-7 under a surgical microscope. The dorsal part of spinal cord was transected with the sharp tip of a 30 gauge needle and a pair of microscissors. The depth of transection (1.85 mm) was confirmed by passing the sharp part of number 11 blade across the dorsal spinal cord for several times with the aid of a stereotaxic (David Kopf Instruments, Tujunga, Calif.). Routinely, the spinal cord was severed past the central canal area (GrandPre, T., et al., Nature 2002, 417:547-551; Li, S., et al., J Neurosci 2004, 24:10511-10520). Rats with an

incomplete lesion documented by uninjured dorsal or dorsolateral corticospinal fibers in caudal spinal cord or a less degree of disability (BBB score ≥ 5) at two days after injury were excluded.

[0228] For intrathecal administration of the siRNA solutions with the osmotic pumps the dura over the dorsal spinal cord was gently lifted with a pair of microforceps and a small hole was made in the midline with a pair of microscissors at T7 level. The minipump was sutured to the muscles under the skin on the back of the animals. The outlet of the minipump was connected to one end of an intrathecal catheter (PE-60, MS-0040, Marsil Scientific). The other end of the catheter with a small diameter of PE-5 was inserted into the subdura space of spinal cord at T7 level through the small opening made for drug infusion. After pump and catheter implantation, muscle and connective tissue layers were sutured with 4.0 silk. The skin incision was closed with sterile animal clips. The animals received a subcutaneous injection of lactated Ringer's solutions (5% of body weight) immediately after surgery and two times per day for the first two days after injury. Postoperative antibiotics and analgesics were given during the first two days post injury. Bladder expression was performed manually three times per day during the survival period of the animal.

Behavioral Tests

[0229] To monitor the recovery of locomotor functions during and after siRNA treatment after spinal cord hemisection, we used a standard behavioral test, the Basso, Beattie, and Bresnahan (BBB) locomotor rating scale (GrandPre, T., et al., *Nature* 2002, 417:547-551; Li, S., et al., *J Neurosci* 2004, 24:10511-10520; Basso, D. M., et al., *J Neurotrauma* 1995, 12:1-21) to analyze individual components of limb movements, weight support, plantar and dorsal stepping, forelimb-hindlimb coordination, paw rotation, toe clearance, trunk stability, and tail placement. Scores from 0-21 were given based on these observations. The BBB score was evaluated by two individuals unaware of experimental treatments at several time points (Li, S., et al., *J Neurosci* 2004, 24:10511-10520). In particular, the locomotion was analyzed on day 3, 10, 17, 24, 31 and 45 post hemisection of the spinal cord.

Results

[0230] The obtained BBB score data were plotted by normalizing all the single day score data of the animals to the score at day 10. The group averages of those normalized scores were charted including the error representing the calculated standard error. By this procedure improvements in locomotion from day 10 onwards are shown in FIG. 2. As evident, a significant improvement was obtained by virtue of the treatment with the inventive RhoA-specific iRNA agents over the unrelated control iRNA agent.

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 60

ugaagacuau gagcaagcan n 21

<210> SEQ ID NO 61
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 61

augcuugcuc auagucuca gca 23

<210> SEQ ID NO 62
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 62

gcuugcucau agucuucagn n 21

<210> SEQ ID NO 63
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 63

cugaagacua ugagcaagcn n 21

<210> SEQ ID NO 64
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 64

ugcuugcuca uagucuucag caa 23

<210> SEQ ID NO 65
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 65

cuugcucaua gucuucagcn n 21

<210> SEQ ID NO 66
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 66

gcugaagacu augagcaagn n 21

<210> SEQ ID NO 67
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 67

gcuugcucau agucuucagc aag 23

<210> SEQ ID NO 68
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 68

uugcucauag ucuucagcan n 21

<210> SEQ ID NO 69
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 69

ugcugaagac uaugagcaan n 21

<210> SEQ ID NO 70
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 70

cuugcucaua gucuucagca agg 23

<210> SEQ ID NO 71

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 71

ugcucauagu cuucagcaan n 21

<210> SEQ ID NO 72

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 72

uugcugaaga cuaugagcan n 21

<210> SEQ ID NO 73

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 73

uugcucauag ucuucagcaa gga 23

<210> SEQ ID NO 74

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 74

gcucuauaguc uucagcaagn n 21

<210> SEQ ID NO 75

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 75

cuugcugaag acuaugagcn n 21

<210> SEQ ID NO 76

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 76

ugcucauagu cuucagcaag gac 23

<210> SEQ ID NO 77

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 77

cucauagucu ucagcaaggn n 21

<210> SEQ ID NO 78

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 78

ccuugcugaa gacuaugagn n 21

<210> SEQ ID NO 79

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 79

gcucauaguc uucagcaagg acc 23

<210> SEQ ID NO 80

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 80

ucauagucuu cagcaaggan n 21

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<210> SEQ ID NO 81
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 81

uccuugcuga agacuaugan n 21

<210> SEQ ID NO 82
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 82

cucauagucu ucagcaagga cca 23

<210> SEQ ID NO 83
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 83

cauagucuuc agcaaggacn n 21

<210> SEQ ID NO 84
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 84

guccuugcug aagacuaugn n 21

<210> SEQ ID NO 85
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 85

ucauagucuu cagcaaggac cag 23

<210> SEQ ID NO 86
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 86

auagucuuca gcaaggaccn n 21

<210> SEQ ID NO 87
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 87

gguccuugcu gaagacuaun n 21

<210> SEQ ID NO 88
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 88

cauagucuuc agcaaggacc agu 23

<210> SEQ ID NO 89
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 89

uagucuucag caaggaccan n 21

<210> SEQ ID NO 90
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 90

ugguccuugc ugaagacuan n 21

<210> SEQ ID NO 91
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 91

auagucuuca gcaaggacca guu 23

<210> SEQ ID NO 92
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 92

agucuucagc aaggaccagn n 21

<210> SEQ ID NO 93
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 93

cugguccuug cugaagacun n 21

<210> SEQ ID NO 94
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 94

uagucuucag caaggaccag uuc 23

<210> SEQ ID NO 95
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 95

gucuucagca aggaccagun n 21

<210> SEQ ID NO 96
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 96

acugguccuu gcugaagacn n 21

<210> SEQ ID NO 97
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 97

agucuucagc aaggaccagu ucc 23

<210> SEQ ID NO 98
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 98

ucuucagcaa ggaccaguun n 21

<210> SEQ ID NO 99
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 99

aacugguccu ugcugaagan n 21

<210> SEQ ID NO 100
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 100

gucuucagca aggaccagu ccc 23

<210> SEQ ID NO 101
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 101

cuucagcaag gaccaguucn n

21

<210> SEQ ID NO 102

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 102

gaacuggucc uugcugaagn n

21

<210> SEQ ID NO 103

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 103

ucuucagcaa ggaccaguuc cca

23

<210> SEQ ID NO 104

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 104

uucagcaagg accaguuccn n

21

<210> SEQ ID NO 105

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 105

ggaacugguc cuugcugaan n

21

<210> SEQ ID NO 106

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 106

cuucagcaag gaccaguucc cag

23

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<210> SEQ ID NO 107
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 107

ucagcaagga ccaguucccn n 21

<210> SEQ ID NO 108
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 108

gggaacuggu ccuugcugan n 21

<210> SEQ ID NO 109
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 109

uucagcaagg accaguuccc aga 23

<210> SEQ ID NO 110
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 110

cagcaaggac caguucccn n 21

<210> SEQ ID NO 111
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 111

ugggaacugg uccuugcugn n 21

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<210> SEQ ID NO 112
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 112

ucagcaagga ccaguuccca gag 23

<210> SEQ ID NO 113
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 113

agcaaggacc aguucccagn n 21

<210> SEQ ID NO 114
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 114

cugggaacug guccuugcun n 21

<210> SEQ ID NO 115
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 115

cagcaaggac caguucccag agg 23

<210> SEQ ID NO 116
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 116

gcaaggacca guucccagan n 21

<210> SEQ ID NO 117
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 117

ucugggaacu gguccuugcn n 21

<210> SEQ ID NO 118
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 118

agcaaggacc aguucccaga ggu 23

<210> SEQ ID NO 119
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 119

caaggaccag uucccagagn n 21

<210> SEQ ID NO 120
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 120

cucugggaac ugguccuugn n 21

<210> SEQ ID NO 121
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 121

gcaaggacca guucccagag gug 23

<210> SEQ ID NO 122
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 122
aaggaccagu ucccagaggn n 21

<210> SEQ ID NO 123
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 123
ccucugggaa cugguccuun n 21

<210> SEQ ID NO 124
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 124
caaggaccag uucccagagg ugu 23

<210> SEQ ID NO 125
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 125
aggaccaguu cccagaggun n 21

<210> SEQ ID NO 126
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 126
accucuggga acugguccun n 21

<210> SEQ ID NO 127
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 127

gaaagcaggu agaguuggcu uug 23

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

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<400> SEQUENCE: 128

aagcagguag aguuggcuun n 21

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aagccaacuc uaccugcuun n 21

<210> SEQ ID NO 130

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aaagcaggua gaguuggcuu ugu 23

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agcagguaga guuggcuun n 21

<210> SEQ ID NO 132

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aaagccaacu cuaccugcun n 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

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gacagcccug auaguuuaga aaa 23

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<213> ORGANISM: Artificial Sequence

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<400> SEQUENCE: 134

cagcccugau aguuaagaan n 21

<210> SEQ ID NO 135

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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uucuaaacua ucagggcugn n 21

<210> SEQ ID NO 136

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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acagcccuga uaguuuagaa aac 23

<210> SEQ ID NO 137

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<222> LOCATION: 20, 21

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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uuucuaaacu aucagggcun n 21

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cagcccugau aguuuagaaa aca 23

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gcccugauag uuuagaaaa n 21

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uuuucuaaac uaucaggcn n 21

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<400> SEQUENCE: 142

agcccugaua guuuagaaaa cau 23

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cccugauagu uuagaaaacn n 21

<210> SEQ ID NO 144
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 144

guuuucuaaa cuaucagggn n 21

<210> SEQ ID NO 145
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 145

gcccgauag uuuagaaaac auc 23

<210> SEQ ID NO 146
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ccugauaguu uagaaaacan n 21

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<400> SEQUENCE: 147

uguuuucuaa acuaucagggn n 21

<210> SEQ ID NO 148
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<212> TYPE: RNA

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cccugauagu uuagaaaaca ucc 23

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<400> SEQUENCE: 149

cugauaguuu agaaaacaun n 21

<210> SEQ ID NO 150
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<400> SEQUENCE: 150

auguuuucua aacuaucagn n 21

<210> SEQ ID NO 151
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<212> TYPE: RNA
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<400> SEQUENCE: 151

ccugauagu uagaaaacau ccc 23

<210> SEQ ID NO 152
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<400> SEQUENCE: 152

ugauaguua gaaaacaun n 21

<210> SEQ ID NO 153
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 153
gauguuuuucu aaacuaucan n 21

<210> SEQ ID NO 154
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<400> SEQUENCE: 154
cugauaguuu agaaaacauc cca 23

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 155
gauaguuuag aaaacaucn n 21

<210> SEQ ID NO 156
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 156
ggauguuuuc uaaacuaucn n 21

<210> SEQ ID NO 157
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<212> TYPE: RNA
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<220> FEATURE:
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<400> SEQUENCE: 157
ugauaguuaa gaaaacauc cag 23

<210> SEQ ID NO 158
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 158

auaguuuaga aaacauccon n

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<210> SEQ ID NO 159

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 159

gggauguuuu cuaaacuaun n

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<210> SEQ ID NO 160

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 160

gauaguuuag aaaacaucac aga

23

<210> SEQ ID NO 161

<211> LENGTH: 21

<212> TYPE: DNA

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<220> FEATURE:

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<222> LOCATION: 20, 21

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<400> SEQUENCE: 161

uaguuuagaa aacaucacn n

21

<210> SEQ ID NO 162

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 162

ugggauguuu ucuaaacuan n

21

<210> SEQ ID NO 163

<211> LENGTH: 23

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 163

auaguuuaga aaacaucaca gaa

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 164

aguuuagaaa acaucccagn n 21

<210> SEQ ID NO 165
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 165

cugggauguu uucuaaacun n 21

<210> SEQ ID NO 166
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 166

uaguuuagaa aacaucccag aaa 23

<210> SEQ ID NO 167
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 167

guuuagaaaa caucccagan n 21

<210> SEQ ID NO 168
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 168

ucugggaugu uuucuaaacn n 21

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<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 169

aguuuagaaa acaucccaga aaa 23

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<400> SEQUENCE: 170

uuuagaaaac aucccgaaan n 21

<210> SEQ ID NO 171
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 171

uucugggaug uuuucuaaan n 21

<210> SEQ ID NO 172
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 172

guuuagaaaa caucccagaa aag 23

<210> SEQ ID NO 173
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 173

uuagaaaaca ucccagaaan n 21

<210> SEQ ID NO 174
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 174

uuucugggau guuuucuaan n 21

<210> SEQ ID NO 175
<211> LENGTH: 23
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 175

uuuagaaaac aucccagaaa agu 23

<210> SEQ ID NO 176
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<212> TYPE: DNA
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 176

uagaaaacau cccagaaaan n 21

<210> SEQ ID NO 177
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<212> TYPE: DNA
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 177

uuuucuggga uguuuucuan n 21

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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 178

ccccagaagu caagcauuuc ugu 23

<210> SEQ ID NO 179
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<212> TYPE: DNA
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
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<400> SEQUENCE: 179

ccagaaguca agcauuucun n 21

<210> SEQ ID NO 180
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<400> SEQUENCE: 180

agaaaugcuu gacuucuggn n 21

<210> SEQ ID NO 181
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 181

cccagaaguc aagcauuucu guc 23

<210> SEQ ID NO 182
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 182

cagaagucaa gcauuucugn n 21

<210> SEQ ID NO 183
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<212> TYPE: DNA
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<400> SEQUENCE: 183

cagaaaugcu ugacuucugn n 21

<210> SEQ ID NO 184
<211> LENGTH: 23
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<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 184

ccagaaguca agcauuucug ucc 23

<210> SEQ ID NO 185

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 185

agaagucaag cauuucugun n 21

<210> SEQ ID NO 186

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 186

acagaaaugc uugacuucun n 21

<210> SEQ ID NO 187

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 187

cagaagucaa gcauuucugu ccc 23

<210> SEQ ID NO 188

<211> LENGTH: 21

<212> TYPE: DNA

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 188

gaagucaagc auuucugun n 21

<210> SEQ ID NO 189

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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gacagaaaug cuugacuucn n 21

<210> SEQ ID NO 190

<211> LENGTH: 23

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 191

aagucaagca uuucuguccn n 21

<210> SEQ ID NO 192

<211> LENGTH: 21

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 192

ggacagaaau gcuugacuun n 21

<210> SEQ ID NO 193

<211> LENGTH: 23

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ugaaaccuga agaaggcaga gau 23

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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aaaccugaag aaggcagagn n 21

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<210> SEQ ID NO 195
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<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 195

cucugccuuc uucagguuun n 21

<210> SEQ ID NO 196
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 196

gaaaccugaa gaaggcagag aua 23

<210> SEQ ID NO 197
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 197

aaccugaaga aggcagagan n 21

<210> SEQ ID NO 198
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 198

ucucugccuu cuucagguun n 21

<210> SEQ ID NO 199
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 199

aaaccugaag aaggcagaga uau 23

<210> SEQ ID NO 200
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 200

accugaagaa ggcagagaun n 21

<210> SEQ ID NO 201
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 201

aucucugccu ucuucaggun n 21

<210> SEQ ID NO 202
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 202

aaccugaaga aggcagagau aug 23

<210> SEQ ID NO 203
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 203

ccugaagaag gcagagauan n 21

<210> SEQ ID NO 204
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 204

uauucucugcc uucuucaggn n 21

<210> SEQ ID NO 205
<211> LENGTH: 23
<212> TYPE: RNA

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<223> OTHER INFORMATION: Exemplary iRNA agents

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accugaagaa ggcagagaua ugg 23

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 206
cugaagaagg cagagauaun n 21

<210> SEQ ID NO 207
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 207
auaucucugc cuucucagn n 21

<210> SEQ ID NO 208
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 208
ccugaagaag gcagagauau ggc 23

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<400> SEQUENCE: 209
ugaagaaggc agagauaun n 21

<210> SEQ ID NO 210
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 210

cauaucucug ccuucuucan n 21

<210> SEQ ID NO 211
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cugaagaagg cagagauaug gca 23

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<400> SEQUENCE: 212

gaagaaggca gagauaugn n 21

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<400> SEQUENCE: 213

ccaauaucucu gccuucuucn n 21

<210> SEQ ID NO 214
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 214

ugaagaaggc agagauaugg caa 23

<210> SEQ ID NO 215
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 215

aagaaggcag agauauggc n 21

<210> SEQ ID NO 216

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 216

gccauaucuc ugccuucun n 21

<210> SEQ ID NO 217

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 217

gaagaaggca gagauauggc aaa 23

<210> SEQ ID NO 218

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 218

agaaggcaga gauauggc n 21

<210> SEQ ID NO 219

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 219

ugccauaucu cugccuucun n 21

<210> SEQ ID NO 220

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 220

aagaaggcag agauauggca aac 23

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<210> SEQ ID NO 221
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
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<400> SEQUENCE: 221

gaaggcagag auauggcaan n 21

<210> SEQ ID NO 222
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 222

uugccauauc ucugccuucn n 21

<210> SEQ ID NO 223
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 223

agaaggcaga gauauggcaa aca 23

<210> SEQ ID NO 224
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 224

aaggcagaga uauggcaaan n 21

<210> SEQ ID NO 225
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 225

uuugccauau cucugccuun n 21

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<210> SEQ ID NO 226
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<212> TYPE: RNA
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 226

gaaggcagag auauggcaaa cag 23

<210> SEQ ID NO 227
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 227

aggcagagau auggcaaacn n 21

<210> SEQ ID NO 228
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 228

guuugccaau ucucugccun n 21

<210> SEQ ID NO 229
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 229

aaggcagaga uauggcaaac agg 23

<210> SEQ ID NO 230
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 230

ggcagagaua uggcaaacan n 21

<210> SEQ ID NO 231
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 231

uguuugccau aucucugccn n 21

<210> SEQ ID NO 232
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 232

aggcagagau auggcaaaca gga 23

<210> SEQ ID NO 233
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 233

gcagagauau ggcaaacagn n 21

<210> SEQ ID NO 234
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 234

cuguuugcca uaucucugcn n 21

<210> SEQ ID NO 235
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 235

ggcagagaua uggcaaacag gau 23

<210> SEQ ID NO 236
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 236
cagagauaug gcaaacaggn n 21

<210> SEQ ID NO 237
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 237
ccuguuugcc auaucucugn n 21

<210> SEQ ID NO 238
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 238
gcagagauau ggcaaacagg auu 23

<210> SEQ ID NO 239
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 239
agagauaugg caaacaggn n 21

<210> SEQ ID NO 240
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 240
uccuguuugc cauauucun n 21

<210> SEQ ID NO 241
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 241

cagagauaug gcaaacagga uug 23

<210> SEQ ID NO 242

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 242

gagauauggc aaacaggaun n 21

<210> SEQ ID NO 243

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 243

auccuguuug ccuaucucn n 21

<210> SEQ ID NO 244

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 244

agagauaugg caaacaggau ugg 23

<210> SEQ ID NO 245

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 245

agauauggca aacaggauun n 21

<210> SEQ ID NO 246

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 246

aauccuguuu gccauaucun n

21

<210> SEQ ID NO 247

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 247

gagauauggc aaacaggauu ggc

23

<210> SEQ ID NO 248

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 248

gauauggcaa acaggauugn n

21

<210> SEQ ID NO 249

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 249

caauccuguu ugccauaucn n

21

<210> SEQ ID NO 250

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 250

agauauggca aacaggauug gcg

23

<210> SEQ ID NO 251

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 251

auauggcaaa caggauuggn n

21

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<210> SEQ ID NO 252
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 252

ccaauccugu uugccauaun n 21

<210> SEQ ID NO 253
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 253

gauauggcaa acaggauugg cgc 23

<210> SEQ ID NO 254
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 254

uauaggcaaac aggauuggcn n 21

<210> SEQ ID NO 255
<211> LENGTH: 21
<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 255

gccaauccug uuugccauan n 21

<210> SEQ ID NO 256
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 256

aauauggcaaa caggauuggc gcu 23

<210> SEQ ID NO 257
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 257

auggcaaaca ggauuggcgn n 21

<210> SEQ ID NO 258
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 258

cgccaauccu guuugccaun n 21

<210> SEQ ID NO 259
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 259

uauggcaaac aggauuggcg cuu 23

<210> SEQ ID NO 260
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 260

uggcaaacag gauuggcgc n 21

<210> SEQ ID NO 261
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 261

gcgccaaucc uguuugccan n 21

<210> SEQ ID NO 262
<211> LENGTH: 23
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 262

auggcaaaca ggauuggcgc uuu 23

<210> SEQ ID NO 263
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 263

ggcaaacagg auuggcgcun n 21

<210> SEQ ID NO 264
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 264

agcgccaauc cuguugccn n 21

<210> SEQ ID NO 265
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 265

uggcaaacag gauuggcgc uuu 23

<210> SEQ ID NO 266
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<212> TYPE: DNA
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
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<400> SEQUENCE: 266

gcaaacagga uuggcgcun n 21

<210> SEQ ID NO 267
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<212> TYPE: DNA
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 267

aagcgccaaU ccuguuugcn n 21

<210> SEQ ID NO 268
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 268

ggcaaacagg auuggcgcuu uug 23

<210> SEQ ID NO 269
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 269

caaacaggau uggcgcuuun n 21

<210> SEQ ID NO 270
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 270

aaagcgccaa uccuguuugn n 21

<210> SEQ ID NO 271
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 271

gcaaacagga uuggcgcuu ugg 23

<210> SEQ ID NO 272
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<400> SEQUENCE: 272

aaacaggauu ggcgcuuun n

21

<210> SEQ ID NO 273

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 273

aaaagcgcca auccuguuun n

21

<210> SEQ ID NO 274

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 275

aacaggauug gcgcuuuugn n

21

<210> SEQ ID NO 276

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 276

caaaagcgcc aauccuguun n

21

<210> SEQ ID NO 277

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 277

aaacaggauu ggcgcuuuug ggu

23

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<210> SEQ ID NO 278
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 278

acaggauugg cgcuuuuggn n 21

<210> SEQ ID NO 279
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 279

ccaaaagcgc caauccugun n 21

<210> SEQ ID NO 280
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 280

aacaggauug gcgcuuuugg gua 23

<210> SEQ ID NO 281
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 281

caggauuggc gcuuuugggn n 21

<210> SEQ ID NO 282
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 282

ccaaaagcgc ccaauccugn n 21

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<400> SEQUENCE: 283

acaggauugg cgcuuuuggg uac 23

<210> SEQ ID NO 284
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 284

aggauuggcg cuuuugggun n 21

<210> SEQ ID NO 285
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 285

acccaaaagc gccaauccun n 21

<210> SEQ ID NO 286
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 286

caggauuggc gcuuuugggu aca 23

<210> SEQ ID NO 287
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<212> TYPE: DNA
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 287

ggauuggcgc uuuuuggguan n 21

<210> SEQ ID NO 288
<211> LENGTH: 21
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 288

uacccaaaag cgccaaucn n

21

<210> SEQ ID NO 289
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 289

aggauuggcg cuuuugggua cau

23

<210> SEQ ID NO 290
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 290

gauuggcgcu uuuggguacn n

21

<210> SEQ ID NO 291
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 291

guacccaaaa gcgccaaucn n

21

<210> SEQ ID NO 292
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 292

ggauuggcgcu uuuggguac aug

23

<210> SEQ ID NO 293
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 293

auuggcgcuu uuggguacan n 21

<210> SEQ ID NO 294
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 294

uguacccaaa agcgccaaun n 21

<210> SEQ ID NO 295
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 295

gauuggcgcu uuuggguaca ugg 23

<210> SEQ ID NO 296
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 296

uuggcgcuu uggguacaun n 21

<210> SEQ ID NO 297
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
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<400> SEQUENCE: 297

auguacccaa aagcgccaan n 21

<210> SEQ ID NO 298
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 298

auuggcgcuu uuggguacau gga 23

<210> SEQ ID NO 299

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 299

uggcgcuuuu gguuacau n 21

<210> SEQ ID NO 300

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 300

cauguaccca aaagcgccan n 21

<210> SEQ ID NO 301

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 301

uuggcgcuu uugguacau gag 23

<210> SEQ ID NO 302

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 302

ggcgcuuuug gguuacau n 21

<210> SEQ ID NO 303

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 303

ccauguaccc aaaagcgccn n

21

<210> SEQ ID NO 304

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 304

uggcgcuuuu gguacaugg agu

23

<210> SEQ ID NO 305

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 305

gcgcuuuugg guacauggan n

21

<210> SEQ ID NO 306

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 306

uccauguacc caaaagcgcn n

21

<210> SEQ ID NO 307

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 307

ggcgcuuuug gguacaugga gug

23

<210> SEQ ID NO 308

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 308

cgcuuuuggg uacauggagn n

21

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<210> SEQ ID NO 309
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 309

cuccauguac ccaaaagcgn n 21

<210> SEQ ID NO 310
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 310

gcgcuuuugg guacauggag ugu 23

<210> SEQ ID NO 311
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 311

gcuuuugggu acauggagun n 21

<210> SEQ ID NO 312
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 312

acuccaugua cccaaaagcn n 21

<210> SEQ ID NO 313
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 313

cgcuuuuggg uacauggagu guu 23

<210> SEQ ID NO 314
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 314

cuuuugggua cauggagugn n                                     21

<210> SEQ ID NO 315
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 315

cacuccaugu acccaaaagn n                                     21

<210> SEQ ID NO 316
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 316

gcuuuugggu acauggagug uuc                                   23

<210> SEQ ID NO 317
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 317

uuuuggguac auggagugun n                                     21

<210> SEQ ID NO 318
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 318

acacuccaug uacccaaaan n                                     21

<210> SEQ ID NO 319
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 319

cuuuugggua cauggagugu uca                                     23

<210> SEQ ID NO 320
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 320

uuuggguaca uggaguguun n                                       21

<210> SEQ ID NO 321
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 321

aacacuccau guacccaaan n                                       21

<210> SEQ ID NO 322
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 322

uuuuggguac auggaguguu cag                                     23

<210> SEQ ID NO 323
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 323

uuggguacau ggaguguucn n                                       21

<210> SEQ ID NO 324
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<212> TYPE: DNA
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<220> FEATURE:
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 324

gaacacucca uguacccaan n 21

<210> SEQ ID NO 325
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 325

uuuggguaca uggaguguuc agc 23

<210> SEQ ID NO 326
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 326

uggguacaug gaguguucan n 21

<210> SEQ ID NO 327
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 327

ugaacacucc auguacccan n 21

<210> SEQ ID NO 328
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 328

uuggguacau ggaguguuca gca 23

<210> SEQ ID NO 329
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 329

ggguacaugg aguguucagn n

21

<210> SEQ ID NO 330

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 330

cugaacacuc cauguaccn n

21

<210> SEQ ID NO 331

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 331

ugguacaug gaguguucag caa

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<210> SEQ ID NO 332

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 332

gguacaugga guguucagn n

21

<210> SEQ ID NO 333

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 333

gcugaacacu ccauguaccn n

21

<210> SEQ ID NO 334

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 334

ggguacaugg aguguucagc aaa

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 335

guacauggag uguucagcan n 21

<210> SEQ ID NO 336
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 336

ugcugaacac uccauguacn n 21

<210> SEQ ID NO 337
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 337

gguacaugga guguucagca aag 23

<210> SEQ ID NO 338
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 338

uacauggagu guucagcaan n 21

<210> SEQ ID NO 339
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 339

uugcugaaca cuccauguan n 21

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 340

guacauggag uguucagcaa aga 23

<210> SEQ ID NO 341
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 341

acauggagug uucagcaaan n 21

<210> SEQ ID NO 342
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 342

uuugcugaac acuccaugun n 21

<210> SEQ ID NO 343
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 343

uacauggagu guucagcaaa gac 23

<210> SEQ ID NO 344
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 344

cauggagugu ucagcaaa n 21

<210> SEQ ID NO 345
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 345

cuuugcugaa cacuccaagn n 21

<210> SEQ ID NO 346
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 346

acauggagug uucagcaaag acc 23

<210> SEQ ID NO 347
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
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<400> SEQUENCE: 347

auggaguguu cagcaaagan n 21

<210> SEQ ID NO 348
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 348

ucuuugcuga acacuccaun n 21

<210> SEQ ID NO 349
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 349

cauggagugu ucagcaaaga cca 23

<210> SEQ ID NO 350
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<212> TYPE: DNA
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<221> NAME/KEY: misc_feature
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<400> SEQUENCE: 350

uggaguguuc agcaaagacn n 21

<210> SEQ ID NO 351
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 351

gucuuugcug aacacuccan n 21

<210> SEQ ID NO 352
<211> LENGTH: 23
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 352

auggaguguu cagcaaagac caa 23

<210> SEQ ID NO 353
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<400> SEQUENCE: 353

ggaguguuca gcaaagaccn n 21

<210> SEQ ID NO 354
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 354

ggucuuugcu gaacacuccn n 21

<210> SEQ ID NO 355
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 355

uggaguguuc agcaaagacc aaa 23

<210> SEQ ID NO 356

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 356

gaguguucag caaagaccan n 21

<210> SEQ ID NO 357

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 357

uggucuuugc ugaacacucn n 21

<210> SEQ ID NO 358

<211> LENGTH: 23

<212> TYPE: RNA

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 358

ggaguguuca gcaaagacca aag 23

<210> SEQ ID NO 359

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 359

aguguucagc aaagaccaan n 21

<210> SEQ ID NO 360

<211> LENGTH: 21

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 360

uuggucuuug cugaacacun n 21

<210> SEQ ID NO 361

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 361

gaguguucag caaagaccaa aga 23

<210> SEQ ID NO 362

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 362

guguucagca aagaccaa n 21

<210> SEQ ID NO 363

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 363

uuuggucuuu gcugaacacn n 21

<210> SEQ ID NO 364

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 364

aguguucagc aaagacaaa gau 23

<210> SEQ ID NO 365

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 365

uguucagcaa agaccaaagn n 21

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<210> SEQ ID NO 366
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 366

cuuuggucuu ugcugaacan n 21

<210> SEQ ID NO 367
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 367

guguucagca aagaccaaag aug 23

<210> SEQ ID NO 368
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 368

guucagcaaa gaccaaagan n 21

<210> SEQ ID NO 369
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 369

uccuuggucu uugcugaacn n 21

<210> SEQ ID NO 370
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 370

auggagugag agagguuuuu gaa 23

<210> SEQ ID NO 371
<211> LENGTH: 21
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 371

ggagugagag agguuuuugn n 21

<210> SEQ ID NO 372
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 372

caaaaaccuc ucucacucn n 21

<210> SEQ ID NO 373
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 373

uggagugaga gagguuuuug aaa 23

<210> SEQ ID NO 374
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 374

gagugagaga gguuuuugan n 21

<210> SEQ ID NO 375
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 375

ucaaaaaccu cucucacucn n 21

<210> SEQ ID NO 376
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 376

cuacgagagc ugcucugcaa gcu 23

<210> SEQ ID NO 377
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 377

acgagagcug cucugcaagn n 21

<210> SEQ ID NO 378
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 378

cuugcagagc agcucucgun n 21

<210> SEQ ID NO 379
<211> LENGTH: 23
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 379

uacgagagcu gcucugcaag cua 23

<210> SEQ ID NO 380
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 380

cgagagcugc ucugcaagn n 21

<210> SEQ ID NO 381
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 381
gcuugcagag cagcucucgn n 21

<210> SEQ ID NO 382
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 382
acgagagcug cucugcaagc uag 23

<210> SEQ ID NO 383
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 383
gagagcugcu cugcaagcun n 21

<210> SEQ ID NO 384
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 384
agcuugcaga gcagcucun n 21

<210> SEQ ID NO 385
<211> LENGTH: 23
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 385
cgagagcugc ucugcaagcu aga 23

<210> SEQ ID NO 386
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 386

agagcugcuc ugcaagcuan n

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<210> SEQ ID NO 387

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 387

uagcuugcag agcagcucun n

21

<210> SEQ ID NO 388

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 388

gagagcugcu cugcaagcua gac

23

<210> SEQ ID NO 389

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 389

gagcugcucu gcaagcuagn n

21

<210> SEQ ID NO 390

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 390

cuagcuugca gagcagcucn n

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<210> SEQ ID NO 391

<211> LENGTH: 23

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 391

agagcugcuc ugcaagcuag acg

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<210> SEQ ID NO 392
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 392

agcugcucug caagcuagan n 21

<210> SEQ ID NO 393
<211> LENGTH: 21
<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 393

ucuagcuugc agagcagcun n 21

<210> SEQ ID NO 394
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 394

gagcugcucu gcaagcuaga cgu 23

<210> SEQ ID NO 395
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 395

gcugcucugc aagcuagacn n 21

<210> SEQ ID NO 396
<211> LENGTH: 21
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 396

gucuagcuug cagagcagcn n 21

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<210> SEQ ID NO 397
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 397

agcugcucug caagcuagac gug 23

<210> SEQ ID NO 398
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 398

cugcucugca agcuagacgn n 21

<210> SEQ ID NO 399
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<212> TYPE: DNA
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 399

cgucuagcuu gcagagcagn n 21

<210> SEQ ID NO 400
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 400

uugaagugcu guuuauuaau cuu 23

<210> SEQ ID NO 401
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 401

gaagugcugu uuauuaaun n 21

<210> SEQ ID NO 402
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 402

gauuaauaaa cagcacuucn n 21

<210> SEQ ID NO 403
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 403

ugaagugcug uuuaauaauc uua 23

<210> SEQ ID NO 404
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 404

aagugcuguu uauuaaunc n 21

<210> SEQ ID NO 405
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 405

agauuaauaa acagcacuun n 21

<210> SEQ ID NO 406
<211> LENGTH: 23
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 406

gaagugcugu uuauuaaucu uag 23

<210> SEQ ID NO 407
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 407

agugcuguuu auuaaucuun n 21

<210> SEQ ID NO 408
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 408

aagauuaaua aacagcacun n 21

<210> SEQ ID NO 409
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 409

aagugcuguu uauuaaucuu agu 23

<210> SEQ ID NO 410
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<212> TYPE: DNA
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 410

gugcuguuua uuaaucuuan n 21

<210> SEQ ID NO 411
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 411

uaagauuaau aaacagcacn n 21

<210> SEQ ID NO 412
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 412

agugcuguuu auuaaucuua gug 23

<210> SEQ ID NO 413

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 413

ugcuguuuau uaaucuuagn n 21

<210> SEQ ID NO 414

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 414

cuaagauuaa uaaacagcan n 21

<210> SEQ ID NO 415

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 415

gugcuguuua uaaucuuag ugu 23

<210> SEQ ID NO 416

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 416

gcuguuuauu aaucuuagun n 21

<210> SEQ ID NO 417

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 417

acuaagauua auaaacagcn n 21

<210> SEQ ID NO 418

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 418

ugcuguuuau uaaucuugu gua 23

<210> SEQ ID NO 419

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 419

cuguuuauua aucuuagugn n 21

<210> SEQ ID NO 420

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 420

cacuaagauu auaaaacagn n 21

<210> SEQ ID NO 421

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 421

gcuguuuauu aaucuugug uau 23

<210> SEQ ID NO 422

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 422

uguuuauuaa ucuuagugun n 21

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<210> SEQ ID NO 423
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 423

acacuaagau uauuaaacn n 21

<210> SEQ ID NO 424
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 424

cuguuuauua aucuagugu aug 23

<210> SEQ ID NO 425
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 425

guuuuuauu cuuaguguan n 21

<210> SEQ ID NO 426
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 426

uacacuaaga uuaauaacn n 21

<210> SEQ ID NO 427
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 427

uguuuauua ucuagugua uga 23

<210> SEQ ID NO 428
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 428

uuuauuaaauc uuaguguaun n 21

<210> SEQ ID NO 429
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 429

auacacuaag auuaauaaan n 21

<210> SEQ ID NO 430
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 430

guuuauuaau cuuaguguau gau 23

<210> SEQ ID NO 431
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 431

uuauuaaau cuuaguguaun n 21

<210> SEQ ID NO 432
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 432

cauacacuaa gauuaaaan n 21

<210> SEQ ID NO 433
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 433

uuuuuuuauuc uuaguguaug auu 23

<210> SEQ ID NO 434
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 434

uaauuaucuu aguguaugan n 21

<210> SEQ ID NO 435
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 435

ucauacacua agauuaauan n 21

<210> SEQ ID NO 436
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 436

uuauuaaauu uaguguauga uua 23

<210> SEQ ID NO 437
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 437

auuaaauuua guguaugaun n 21

<210> SEQ ID NO 438
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 438

aucauacacu aagauuaaun n 21

<210> SEQ ID NO 439
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 439

uaauaaucuu aguguaugau uac 23

<210> SEQ ID NO 440
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 440

uaaaucuuag uguaugauun n 21

<210> SEQ ID NO 441
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 441

aaucauacac uaagauuaan n 21

<210> SEQ ID NO 442
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 442

auuaaucuua guguaugauu acu 23

<210> SEQ ID NO 443
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 443

uaaucuuagu guaugauuan n

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<210> SEQ ID NO 444

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 444

uaaucauaca cuaagauuan n

21

<210> SEQ ID NO 445

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 445

uuaaucuuag uguaugauua cug

23

<210> SEQ ID NO 446

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 446

aaucuuagug uaugauuacn n

21

<210> SEQ ID NO 447

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 447

guaaucauac acuaagauun n

21

<210> SEQ ID NO 448

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 448

uaaucuuagu guaugauuac ugg

23

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<210> SEQ ID NO 449
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 449

aucuuagugu augauuacun n 21

<210> SEQ ID NO 450
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 450

aguaaucaua cacuaagaun n 21

<210> SEQ ID NO 451
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 451

aaucuuagug uaugauuacu ggc 23

<210> SEQ ID NO 452
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 452

ucuuagugua ugauuacugn n 21

<210> SEQ ID NO 453
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 453

caguaaucau acacuaagan n 21

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<210> SEQ ID NO 454
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 454

aucuuagugu augauuacug gcc 23

<210> SEQ ID NO 455
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 455

cuuaguguau gauuacuggn n 21

<210> SEQ ID NO 456
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 456

ccaguaauca uacacuaagn n 21

<210> SEQ ID NO 457
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 457

ucuuagugua ugauuacugg ccu 23

<210> SEQ ID NO 458
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 458

uuaguguauug auuacuggcn n 21

<210> SEQ ID NO 459
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 459

gccaguaauc auacacuaan n 21

<210> SEQ ID NO 460
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 460

cuuaguguau gauuacuggc cuu 23

<210> SEQ ID NO 461
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 461

uaguguauga uuacuggccn n 21

<210> SEQ ID NO 462
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 462

ggccaguaau cauacacuan n 21

<210> SEQ ID NO 463
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<212> TYPE: RNA
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 463

uuaguguau auuacuggcc uuu 23

<210> SEQ ID NO 464
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<212> TYPE: DNA
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<221> NAME/KEY: misc_feature
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<400> SEQUENCE: 464

aguguaugau uacuggccun n 21

<210> SEQ ID NO 465
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 465

aggccaguua ucauacacun n 21

<210> SEQ ID NO 466
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 466

uaguguauga uuacuggccu uuu 23

<210> SEQ ID NO 467
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<400> SEQUENCE: 467

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<210> SEQ ID NO 468
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aaggccagua aucauacacn n 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 470

uguaugauua cuggccuuun n 21

<210> SEQ ID NO 471

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<212> TYPE: DNA

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 471

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<210> SEQ ID NO 472

<211> LENGTH: 23

<212> TYPE: RNA

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 472

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 473

guaugauuac uggccuuuun n 21

<210> SEQ ID NO 474

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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aaaaggccag uaaucuaacn n 21

<210> SEQ ID NO 475

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uucauuuauac uauaauuuac cua 23

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 476

cauuuaua uaaauuacn n 21

<210> SEQ ID NO 477

<211> LENGTH: 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 477

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<210> SEQ ID NO 478

<211> LENGTH: 23

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 478

ucauuuaua uaaauuacc uaa 23

<210> SEQ ID NO 479

<211> LENGTH: 21

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 479

auuuaua uaaauuaccun n 21

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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 480

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<210> SEQ ID NO 481
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 481

cauuuaua uaaauuaccu aag 23

<210> SEQ ID NO 482
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 482

uuuaua uaaauuaccu n 21

<210> SEQ ID NO 483
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 483

uagguaaaau auagauaaan n 21

<210> SEQ ID NO 484
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 484

auuuaua uaaauuaccu aga 23

<210> SEQ ID NO 485
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 485

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21

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 486

uuagguaaa uauaguaan n

21

<210> SEQ ID NO 487
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 487

uuuaucauaa auuuaccuaa gau

23

<210> SEQ ID NO 488
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 488

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21

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 489

cuuagguaaa uuauagauan n

21

<210> SEQ ID NO 490
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 490
uuaucuaaua uuuaccuaag auu 23

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 491
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 492
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<210> SEQ ID NO 493
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 493
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<210> SEQ ID NO 494
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 494
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<210> SEQ ID NO 495
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 495

aucuuaggua aaauauagan n 21

<210> SEQ ID NO 496
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 496

aucuauuuu uaccuaagau uac 23

<210> SEQ ID NO 497
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 497

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<210> SEQ ID NO 498
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 498

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<210> SEQ ID NO 499
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 499

ucuauuuu accuaagauu aca 23

<210> SEQ ID NO 500
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 500

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<210> SEQ ID NO 501

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 501

uaaauuuagg uaaauuauan n 21

<210> SEQ ID NO 502

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 502

cuauuuuuu ccuaagauua caa 23

<210> SEQ ID NO 503

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 503

auuuuuuacc uaagauuacn n 21

<210> SEQ ID NO 504

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 504

guuuuuuag guuuuuuau n 21

<210> SEQ ID NO 505

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 505

uaauuuuac cuaagauuac aaa 23

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<210> SEQ ID NO 506
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 506

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<210> SEQ ID NO 507
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 507

uguaaucuua gguaaaauan n 21

<210> SEQ ID NO 508
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 508

auaauuuacc uaagauuaca aa 23

<210> SEQ ID NO 509
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 509

aaauuaccua agauuacaan n 21

<210> SEQ ID NO 510
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 510

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<210> SEQ ID NO 511
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 511

uaauuuaccu aagauuacaa auc 23

<210> SEQ ID NO 512
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 512

auuuaccuaa gauuacaaan n 21

<210> SEQ ID NO 513
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 513

uuuguaaucu uagguaaaun n 21

<210> SEQ ID NO 514
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 514

aaauuaccua agauuacaaa uca 23

<210> SEQ ID NO 515
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 515

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<210> SEQ ID NO 516
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 516

auuuguaauc uuagguaaan n 21

<210> SEQ ID NO 517
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 517

auuuaccuaa gauuacaaau cag 23

<210> SEQ ID NO 518
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 518

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<210> SEQ ID NO 519
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 519

gauuuguaau cuuagguaan n 21

<210> SEQ ID NO 520
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 520

uuuaccuaag auuacaaauc aga 23

<210> SEQ ID NO 521
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 521

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<210> SEQ ID NO 522
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 522

ugauuuguaa ucuuagguan n 21

<210> SEQ ID NO 523
<211> LENGTH: 23
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 523

agaagucauc uugcuaccag uau 23

<210> SEQ ID NO 524
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 524

aagucaucuu gcuaccagun n 21

<210> SEQ ID NO 525
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 525

acugguagca agaagacuun n 21

<210> SEQ ID NO 526
<211> LENGTH: 23
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 526

gaagucaucu ugcuaaccagu auu

23

<210> SEQ ID NO 527

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 527

agucaucuug cuaccaguan n

21

<210> SEQ ID NO 528

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 528

uacugguagc aagaugacun n

21

<210> SEQ ID NO 529

<211> LENGTH: 23

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<220> FEATURE:

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

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<220> FEATURE:

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 534

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<220> FEATURE:

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<222> LOCATION: 20, 21

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aaauacuggu agcaagaugn n 21

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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 541

caucuugcua ccagauuuua gaa 23

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<223> OTHER INFORMATION: Exemplary iRNA agents
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<210> SEQ ID NO 543
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 543

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<210> SEQ ID NO 544
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 544

aucuugcuac caguauuuag aag 23

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<400> SEQUENCE: 548

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<210> SEQ ID NO 549
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<400> SEQUENCE: 549

uucuaaaauac ugguagcaan n 21

<210> SEQ ID NO 550
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 550

cuugcuacca guauuuagaa gcc 23

<210> SEQ ID NO 551
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<400> SEQUENCE: 551

ugcuaccagu auuuagaagn n 21

<210> SEQ ID NO 552
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cuucuaaaaua cugguagcan n 21

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<400> SEQUENCE: 553

uugcuaccag uauuuagaag cca 23

<210> SEQ ID NO 554
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 554

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<210> SEQ ID NO 555
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 555

gcuucuaaaau acugguagcn n 21

<210> SEQ ID NO 556
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 556

ugcuaccagu auuuagaagc caa 23

<210> SEQ ID NO 557
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 557

cuaccaguau uuagaagccn n

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<210> SEQ ID NO 558

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 558

ggcuucuaaa uacugguagn n

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<210> SEQ ID NO 559

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 559

gcuaccagua uuuagaagcc aac

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<210> SEQ ID NO 560

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 560

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<210> SEQ ID NO 561

<211> LENGTH: 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 561

uggcuucuaa auacugguan n

21

<210> SEQ ID NO 562

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 562

cuaccaguau uuagaagcca acu

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<210> SEQ ID NO 563
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<212> TYPE: DNA
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 563

accaguaauu agaagccaan n 21

<210> SEQ ID NO 564
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 564

uuggcuucua aaucuggun n 21

<210> SEQ ID NO 565
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 565

uaccaguaau uagaagccaa cua 23

<210> SEQ ID NO 566
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 566

ccaguaauua gaagccaacn n 21

<210> SEQ ID NO 567
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 567

guuggcuucu aaauacuggn n 21

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<210> SEQ ID NO 568
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 568

cuugcuucuu ucuagaaaga gaa 23

<210> SEQ ID NO 569
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 569

ugcuucuuuc uagaaagagn n 21

<210> SEQ ID NO 570
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 570

cucuucucag aaagaagcan n 21

<210> SEQ ID NO 571
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 571

uugcuucuuu cuagaaagag aaa 23

<210> SEQ ID NO 572
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 572

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<210> SEQ ID NO 573
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 573

ucucuuucua gaaagaagcn n 21

<210> SEQ ID NO 574
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 574

ugcuucuuuc uagaaagaga aac 23

<210> SEQ ID NO 575
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 575

cuucuuucua gaaagagaan n 21

<210> SEQ ID NO 576
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 576

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<210> SEQ ID NO 577
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 577

gcuucuuucu agaaagagaa aca 23

<210> SEQ ID NO 578
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 578

uucuuucua g aaagagaaan n 21

<210> SEQ ID NO 579
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 579

uuucucuuc u agaaagaan n 21

<210> SEQ ID NO 580
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 580

cuucuuucua gaaagagaaa cag 23

<210> SEQ ID NO 581
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 581

ucuuucua g aagagaaan n 21

<210> SEQ ID NO 582
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 582

guuucucu u cuagaaagan n 21

<210> SEQ ID NO 583
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 583

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<210> SEQ ID NO 584

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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cuuucua gaa agagaaacan n 21

<210> SEQ ID NO 585

<211> LENGTH: 21

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 585

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<210> SEQ ID NO 586

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 586

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<210> SEQ ID NO 587

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<212> TYPE: DNA

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<220> FEATURE:

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 587

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<210> SEQ ID NO 588

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 588

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<210> SEQ ID NO 589

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<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 589

cuuucuagaa agagaaacag uug

23

<210> SEQ ID NO 590

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 590

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<210> SEQ ID NO 591

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 591

acuguuucuc uuucuagaan n

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<210> SEQ ID NO 592

<211> LENGTH: 23

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<220> FEATURE:

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<400> SEQUENCE: 592

uuucuagaaa gagaaacagu ugg

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<210> SEQ ID NO 593

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<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 593

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<210> SEQ ID NO 594
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 594

aacuguuucu cuuucuagan n 21

<210> SEQ ID NO 595
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 595

uucuagaaaag agaaacaguu ggu 23

<210> SEQ ID NO 596
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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cuagaaaagag aaacaguugn n 21

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 597

caacuguuuc uuuuucuagn n 21

<210> SEQ ID NO 598
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<220> FEATURE:
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<400> SEQUENCE: 598

ucuagaaaga gaaacaguug gua 23

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<223> OTHER INFORMATION: Exemplary iRNA agents
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uagaaagaga aacaguuggn n 21

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ccaacuguuu cucuuucuan n 21

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cuagaaagag aaacaguugg uaa 23

<210> SEQ ID NO 602
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agaaagagaa acaguuggun n 21

<210> SEQ ID NO 603
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accaacuguu ucucuucun n 21

<210> SEQ ID NO 604
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uagaaagaga aacaguuggu aac 23

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gaaagagaaa caguugguan n 21

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agaaagagaa acaguuggua acu 23

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aaagagaaac aguugguaan n 21

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uuaccaacug uuucucuun n 21

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<400> SEQUENCE: 610

gaaagagaaa caguugguaa cuu 23

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aaagagaaaca guugguaacn n 21

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<400> SEQUENCE: 612

guuaccaacu guuucucuun n 21

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<400> SEQUENCE: 613

aaagagaaac aguugguaac uuu 23

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<221> NAME/KEY: misc_feature
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agagaaacag uugguaacun n

21

<210> SEQ ID NO 615

<211> LENGTH: 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 615

aguuaccaac uguuucucun n

21

<210> SEQ ID NO 616

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 616

aagagaaaca guugguaacu uuu

23

<210> SEQ ID NO 617

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 617

gagaaacagu ugguacuun n

21

<210> SEQ ID NO 618

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 618

aaguuaacaa cuguuucun n

21

<210> SEQ ID NO 619

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 619

agagaaacag uugguaacuu uug

23

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<222> LOCATION: 20, 21
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<400> SEQUENCE: 620

agaaacaguu gguaacuuun n 21

<210> SEQ ID NO 621
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 621

aaaguuacca acuguuucun n 21

<210> SEQ ID NO 622
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 622

gagaaacagu ugguaacuuu ugu 23

<210> SEQ ID NO 623
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 623

gaaacaguug guaacuuun n 21

<210> SEQ ID NO 624
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 624

aaaaguuacc aacuguuucn n 21

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<210> SEQ ID NO 625
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 625

agaaacaguu gguaacuuuu gug 23

<210> SEQ ID NO 626
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 626

aaacaguugg uaacuuuugn n 21

<210> SEQ ID NO 627
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 627

caaaaguuac caacuguuun n 21

<210> SEQ ID NO 628
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 628

gaaacaguug guaacuuuug uga 23

<210> SEQ ID NO 629
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 629

aacaguuggu aacuuuugun n 21

<210> SEQ ID NO 630
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<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
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<400> SEQUENCE: 630

acaaaaguua ccaacuguun n 21

<210> SEQ ID NO 631
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 631

aaacaguugg uaacuuuugu gaa 23

<210> SEQ ID NO 632
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 632

acaguuggua acuuuugugn n 21

<210> SEQ ID NO 633
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 633

cacaaaaguu accaacugun n 21

<210> SEQ ID NO 634
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 634

aacaguuggu aacuuuugug aau 23

<210> SEQ ID NO 635
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 635

caguugguaa cuuuugugan n 21

<210> SEQ ID NO 636
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 636

ucacaaaagu uaccaacugn n 21

<210> SEQ ID NO 637
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 637

acaguuggua acuuuuguga auu 23

<210> SEQ ID NO 638
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 638

aguugguaac uuuugugaan n 21

<210> SEQ ID NO 639
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 639

uucacaaaag uuaccaacun n 21

<210> SEQ ID NO 640
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 640

caguugguaa cuuuugugaa uua 23

<210> SEQ ID NO 641

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 641

guugguaacu uuugugaaun n 21

<210> SEQ ID NO 642

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 642

auucacaaaa guuaccaacn n 21

<210> SEQ ID NO 643

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 643

aguugguaac uuugugaaau uag 23

<210> SEQ ID NO 644

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 644

uugguaacuu uugugaaun n 21

<210> SEQ ID NO 645

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 645

aaauucacaaa aguuaccaan n

21

<210> SEQ ID NO 646

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 646

guugguaacu uuugugaaau agg

23

<210> SEQ ID NO 647

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 647

ugguaacuuu ugugaauuan n

21

<210> SEQ ID NO 648

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 648

uaauucacaa aaguuaccan n

21

<210> SEQ ID NO 649

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 649

uugguaacuu uuugaaaaua ggc

23

<210> SEQ ID NO 650

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 650

gguaacuuuu gugaauuagn n

21

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<210> SEQ ID NO 651
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 651

cuaauucaca aaaguuacn n 21

<210> SEQ ID NO 652
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 652

ugguaacuuu ugugaauuag gcu 23

<210> SEQ ID NO 653
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 653

guaacuuuug ugaauuaggn n 21

<210> SEQ ID NO 654
<211> LENGTH: 21
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 654

ccuaauucac aaaaguacn n 21

<210> SEQ ID NO 655
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 655

gguaacuuu gugaauuagg cug 23

<210> SEQ ID NO 656
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 656

uaacuuuugu gaauuaggcn n 21

<210> SEQ ID NO 657
<211> LENGTH: 21
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 657

gccuaauuca caaaaguuan n 21

<210> SEQ ID NO 658
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 658

guaacuuuug ugaauuaggc ugu 23

<210> SEQ ID NO 659
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 659

aacuuuugug aaauaggcun n 21

<210> SEQ ID NO 660
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 660

agccuaauuc acaaaaguun n 21

<210> SEQ ID NO 661
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 661
uaacuuuugu gaauuaggcu gua 23

<210> SEQ ID NO 662
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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uuuugugaau uaggcuguaa cua

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<400> SEQUENCE: 674

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<211> LENGTH: 23

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 676

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<400> SEQUENCE: 679

uugugaauua ggcuguaacu acu 23

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<400> SEQUENCE: 681

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ugugaaauag gcuguaacua cuu 23

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<400> SEQUENCE: 685

gugaauuagg cuguaacuac uuu 23

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<400> SEQUENCE: 686

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<210> SEQ ID NO 687
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<400> SEQUENCE: 687

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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 688

ugaauuaggc uguaacuacu uua 23

<210> SEQ ID NO 689
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<400> SEQUENCE: 689

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<400> SEQUENCE: 691

gaauuaggcu guaacuacuu uau 23

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<222> LOCATION: 20, 21
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auuaggcugu aacuacuuun n 21

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<400> SEQUENCE: 693

aaaguaguua cagccuaun n 21

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<220> FEATURE:
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<400> SEQUENCE: 694

aaauaggcug uaacuacuuu aua 23

<210> SEQ ID NO 695
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<400> SEQUENCE: 695

uuaggcugua acuacuuuan n 21

<210> SEQ ID NO 696
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<210> SEQ ID NO 697
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<212> TYPE: RNA
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<220> FEATURE:
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<400> SEQUENCE: 697

auuaggcugu aacuacuuua uaa 23

<210> SEQ ID NO 698

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<211> LENGTH: 23

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<220> FEATURE:

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<210> SEQ ID NO 706

<211> LENGTH: 23

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aggcuguuac uacuuuauaa cua 23

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<220> FEATURE:

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gcuguuacua cuuuuuaacn n 21

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<400> SEQUENCE: 708

guuauaaagu aguacagcn n 21

<210> SEQ ID NO 709
<211> LENGTH: 23
<212> TYPE: RNA
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<220> FEATURE:
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<400> SEQUENCE: 709

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<210> SEQ ID NO 710
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cuguaacuac uuuuuaacun n 21

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<400> SEQUENCE: 711

aguauaaaag uaguacagn n 21

<210> SEQ ID NO 712
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gcuguaacua cuuuuaaacu aac 23

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<223> OTHER INFORMATION: Exemplary iRNA agents
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uguaacuacu uuauaacuan n 21

<210> SEQ ID NO 714
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uaguauaaaa guaguuaan n 21

<210> SEQ ID NO 715
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents

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cuguaacuac uuuaaacua aca 23

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guaacuacuu uauaacuaan n 21

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<400> SEQUENCE: 717

uuaguauaaa aguaguuaan n 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 718

uguaacuacu uuauaacuaa cau 23

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uaacuacuuu auaacuaacn n 21

<210> SEQ ID NO 720
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<400> SEQUENCE: 720

guuaguuaa aaguaguuan n 21

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guaacuacuu uauaacuaac aug 23

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aacuacuuua uaacuaacan n 21

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<221> NAME/KEY: misc_feature
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<400> SEQUENCE: 723

uguuaguau aaaguaguun n 21

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uaacuacuuu auaacuaaca ugu 23

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acuacuuuau aacuaacaun n 21

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<400> SEQUENCE: 726

auguaguua uaaaguagun n 21

<210> SEQ ID NO 727
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<400> SEQUENCE: 727

aacuacuuua uaacuaacau guc 23

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cuacuuuaua acuaacaugn n

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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cauguuaguu auaaaguagn n

21

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<212> TYPE: RNA

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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acuacuuuau aacuaacaug ucc

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<222> LOCATION: 20, 21

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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acauguuagu uauaaaguan n

21

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cuacuuuaua acuaacaugu ccu

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acuuuuaaac uaacaugucn n 21

<210> SEQ ID NO 735
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gacauguuag uuauaaagun n 21

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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cuuuuaaacu aacauguccn n 21

<210> SEQ ID NO 738
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ggacauguua guuauaaagn n 21

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acuuuauaac uaacaugucc ugc 23

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uuuauaacua acauguccun n 21

<210> SEQ ID NO 741
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aggacauguu aguauaaan n 21

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cuuuauaacu aacauguccu gcc 23

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<222> LOCATION: 20, 21
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uuauaacuaa cauguccugn n 21

<210> SEQ ID NO 744
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caggacaugu uaguuuaan n 21

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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 745

uuuuaaacua acauguccug ccu 23

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uaauaacuaac auguccugcn n 21

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 747

gcaggacaug uuaguuauan n 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 748

uuauaacuaa cauguccugc cua 23

<210> SEQ ID NO 749
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<212> TYPE: DNA
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<210> SEQ ID NO 750
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 750

ggcaggacau guuaguuaun n 21

<210> SEQ ID NO 751
<211> LENGTH: 23
<212> TYPE: RNA
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 751

uauaacuaac auguccugcc uau 23

<210> SEQ ID NO 752
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 752

uaacuaacau guccugccun n 21

<210> SEQ ID NO 753
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<400> SEQUENCE: 753

aggcaggaca uguaguuan n 21

<210> SEQ ID NO 754
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<212> TYPE: RNA
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<220> FEATURE:
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auaacuaaca uguccugccu auu 23

<210> SEQ ID NO 755

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 755

aacuaacaug uccugccuan n 21

<210> SEQ ID NO 756

<211> LENGTH: 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 756

uaggcaggac auguuaguun n 21

<210> SEQ ID NO 757

<211> LENGTH: 23

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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 757

uggcagaguu acaguucugu ggu 23

<210> SEQ ID NO 758

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<212> TYPE: DNA

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 758

gcagaguac aguucugun n 21

<210> SEQ ID NO 759

<211> LENGTH: 21

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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cacagaacug uaacucugcn n 21

<210> SEQ ID NO 760

<211> LENGTH: 23

<212> TYPE: RNA

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 760

ggcagaguua caguucugug guu 23

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<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 761

cagaguuaca guucuguggn n 21

<210> SEQ ID NO 762

<211> LENGTH: 21

<212> TYPE: DNA

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 762

ccacagaacu guaacucugn n 21

<210> SEQ ID NO 763

<211> LENGTH: 23

<212> TYPE: RNA

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 763

gcagaguuac aguucugugg uuu 23

<210> SEQ ID NO 764

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 764

agaguuacag uucuguggun n 21

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 765

accacagaac uguaacucun n 21

<210> SEQ ID NO 766
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 766

uuucauguua guuaccuuau agu 23

<210> SEQ ID NO 767
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 767

ucauguuagu uaccuuauan n 21

<210> SEQ ID NO 768
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 768

uauaagguaa cuaacaugan n 21

<210> SEQ ID NO 769
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 769

uucauguuag uuaccuuaua guu 23

<210> SEQ ID NO 770
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 770

cauguuaguu accuuauagn n 21

<210> SEQ ID NO 771
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<400> SEQUENCE: 771

cuauaaggua acuaacaugn n 21

<210> SEQ ID NO 772
<211> LENGTH: 23
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 772

ucauguuagu uaccuuauag uua 23

<210> SEQ ID NO 773
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<212> TYPE: DNA
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<400> SEQUENCE: 773

auguuaguua ccuuauagun n 21

<210> SEQ ID NO 774
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 774

acuauaaggu aacuaacaun n 21

<210> SEQ ID NO 775
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 775
cauguuaguu accuuauagu uac 23

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<223> OTHER INFORMATION: Exemplary iRNA agents
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uguuaguauac cuuauaguun n 21

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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 777
aacuauaagg uaacuaacan n 21

<210> SEQ ID NO 778
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 778
auguaguua ccuauaguu acu 23

<210> SEQ ID NO 779
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<400> SEQUENCE: 779
guuaguauacc uuauaguuan n 21

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<221> NAME/KEY: misc_feature
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<400> SEQUENCE: 780

uaacuaaag gaaacuaacn n 21

<210> SEQ ID NO 781
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 781

uguuaguac cuuauaguua cug 23

<210> SEQ ID NO 782
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 782

uuaguauaccu uauaguuaacn n 21

<210> SEQ ID NO 783
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 783

gaaacuaaa ggaaacuaan n 21

<210> SEQ ID NO 784
<211> LENGTH: 23
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 784

guuaguauacc uuauaguuaac ugu 23

<210> SEQ ID NO 785
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<223> OTHER INFORMATION: Exemplary iRNA agents
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uaguuaccuu auaguuaacun n

21

<210> SEQ ID NO 786

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 786

aguaacuaua agguaacuan n

21

<210> SEQ ID NO 787

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 787

uuaguuaccu uauaguuaacu gug

23

<210> SEQ ID NO 788

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<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 788

aguuaccuua uaguuacugn n

21

<210> SEQ ID NO 789

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 789

caguaacuau aagguaacun n

21

<210> SEQ ID NO 790

<211> LENGTH: 23

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 791

guuaccuuau aguacugun n 21

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 792

acaguaacua uaagguaacn n 21

<210> SEQ ID NO 793
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 793

aguuaccuua uaguacugu gua 23

<210> SEQ ID NO 794
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<222> LOCATION: 20, 21
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uuaccuuaua guuacugun n 21

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cacaguaacu auaagguaan n 21

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guuaccuuau aguacugug uaa

23

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uaccuuauag uuacugugun n

21

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acacaguaac uauaagguan n

21

<210> SEQ ID NO 799
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uuaccuuaua guuacugugu aa

23

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accuuauagu uacuguguan n

21

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<400> SEQUENCE: 801

uacacaguaa cuauaaggun n 21

<210> SEQ ID NO 802
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<212> TYPE: RNA
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uaccuuauag uuacugugua auu 23

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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
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ccuuauaguu acuguguaan n 21

<210> SEQ ID NO 804
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uuacacagua acuauaaggn n 21

<210> SEQ ID NO 805
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<212> TYPE: RNA
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accuuauagu uacuguguaa uua 23

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cuuauaguua cuguguaaun n 21

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auuacacagu aacuuaaagn n 21

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ccuuauaguu acuguguaau uag 23

<210> SEQ ID NO 809
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<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 809

uuauaguuaac uguguaauun n 21

<210> SEQ ID NO 810
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 810

aauuacacag uaacuuaan n 21

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<220> FEATURE:
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cuuauaguua cuguguaauu agu 23

<210> SEQ ID NO 812

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<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 812

uauaguuaacu guguaauuan n 21

<210> SEQ ID NO 813

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 813

uaauuacaca guaacuauan n 21

<210> SEQ ID NO 814

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 814

uuauaguuaac uguguaauua gug 23

<210> SEQ ID NO 815

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 815

auaguuaacug uguauuagn n 21

<210> SEQ ID NO 816

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 816

cuaauuacac aguaacuaun n

21

<210> SEQ ID NO 817

<211> LENGTH: 23

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 817

uauaguuacu guguaauuag ugc

23

<210> SEQ ID NO 818

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 818

uaguauacugu guaaauagun n

21

<210> SEQ ID NO 819

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 819

acuaauuaca caguaacuan n

21

<210> SEQ ID NO 820

<211> LENGTH: 23

<212> TYPE: RNA

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 820

auaguauacug uguaaauagu gcc

23

<210> SEQ ID NO 821

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<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 821

aguauacugug uaaauagugn n

21

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<210> SEQ ID NO 822
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 822

cacuaauuac acaguaacun n 21

<210> SEQ ID NO 823
<211> LENGTH: 23
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 823

uaguuacugu guaaauagug cca 23

<210> SEQ ID NO 824
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 824

guuacugugu aaauagugcn n 21

<210> SEQ ID NO 825
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 825

gcacuaauua cacaguaacn n 21

<210> SEQ ID NO 826
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 826

aguuacugug uaaauagugc cac 23

<210> SEQ ID NO 827
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 827

uuacugugua auuagugccn n 21

<210> SEQ ID NO 828
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 828

ggcacuaauu acacaguaan n 21

<210> SEQ ID NO 829
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 829

guuacugugu aaauagugcc acu 23

<210> SEQ ID NO 830
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 830

uacuguguaa uuagugccan n 21

<210> SEQ ID NO 831
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 831

uggcacuaau uacacaguan n 21

<210> SEQ ID NO 832
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 832

uuacugugua auuagugcca cuu 23

<210> SEQ ID NO 833
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<212> TYPE: DNA
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 833

acuguguaau uagugccacn n 21

<210> SEQ ID NO 834
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 834

guggcacuaa uuacacagun n 21

<210> SEQ ID NO 835
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 835

uacuguguaa uuagugccac uua 23

<210> SEQ ID NO 836
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<212> TYPE: DNA
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<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 836

cuguguaauu agugccacun n 21

<210> SEQ ID NO 837
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 837

aguggcacua auuacacagn n 21

<210> SEQ ID NO 838
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 838

acuguguaau uagugccacu uaa 23

<210> SEQ ID NO 839
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 839

uguguaauua gugccacuun n 21

<210> SEQ ID NO 840
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 840

aaguggcacu aauuacacan n 21

<210> SEQ ID NO 841
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 841

cuguguaauu agugccacuu aau 23

<210> SEQ ID NO 842
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 842

guguaauuag ugccacuuan n

21

<210> SEQ ID NO 843

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 843

uaaguggcac uaaauacacn n

21

<210> SEQ ID NO 844

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 844

uguguaauua gugccacuua aug

23

<210> SEQ ID NO 845

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 845

uguaauuagu gccacuuaan n

21

<210> SEQ ID NO 846

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 846

uuaaguggca cuaauacan n

21

<210> SEQ ID NO 847

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 847

guguaauuag ugccacuuaa ugu

23

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<210> SEQ ID NO 848
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 848

guaaauagug ccacuaaun n 21

<210> SEQ ID NO 849
<211> LENGTH: 21
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 849

auuaaguggc acuaauacn n 21

<210> SEQ ID NO 850
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 850

uguaauuagu gccacuaau gua 23

<210> SEQ ID NO 851
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 851

uaauuagugc cacuaaun n 21

<210> SEQ ID NO 852
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 852

cauaaagugg cacuaauan n 21

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<210> SEQ ID NO 853
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 853

guaauuagug ccacuaaauug uau 23

<210> SEQ ID NO 854
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 854

aaauuagugcc acuaaauun n 21

<210> SEQ ID NO 855
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<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 855

acauuaagug gcacuaauun n 21

<210> SEQ ID NO 856
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 856

uaauuagugc cacuaaauug aug 23

<210> SEQ ID NO 857
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 857

auuagugcca cuuaaauun n 21

<210> SEQ ID NO 858
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 858

uacauuaagu ggcacuaun n 21

<210> SEQ ID NO 859
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 859

aaauagugcc acuaaagua ugu 23

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uuagugccac uuaaaguaun n 21

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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auacauuaag uggcacuaan n 21

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auuagugcca cuuaaaguau guu 23

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uuagugccac uuaauguaug uua 23

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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uagugccacu uaauguaugu uac 23

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gugccacuua auguauguun n 21

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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agugccacuu aauguauguu acc 23

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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ugccacuuaa uguauguan n 21

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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uaacauacau uaaguggcan n 21

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gugccacuua auguanguua cca 23

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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gccacuuaau guauguuacn n 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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guaacauaca uuaaguggcn n 21

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<211> LENGTH: 23

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 877

ugccacuuaa uguauguac caa 23

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 878

ccacuuaaug uauguuacn n 21

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gccacuuaau guauguuacc aaa 23

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cacuuaaugu auguuaccan n 21

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<400> SEQUENCE: 882

ugguaacaua cauuaagugn n 21

<210> SEQ ID NO 883
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<400> SEQUENCE: 883

ccacuuaaug uauguuacca aaa 23

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<400> SEQUENCE: 884

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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 886

cacuuuaugu auguuaccaa aaa 23

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cuuaauguau guuaccaa n 21

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<400> SEQUENCE: 888

uuugguaaca uacauuaagn n 21

<210> SEQ ID NO 889
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 889

acuuaaugua uguuacacaaa aau 23

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<222> LOCATION: 20, 21
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uuaaaguaug uuacacaaan n 21

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<222> LOCATION: 20, 21
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<400> SEQUENCE: 891

uuuugguaac auacauuaan n 21

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cuuaauguau guuacacaaa aua 23

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uaaaguaugu uacacaaan n 21

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<400> SEQUENCE: 894

uuuuugguuaa cauacauuan n 21

<210> SEQ ID NO 895
<211> LENGTH: 23
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 895

aauaaaaua ucuacccag acu 23

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ucuggguag auauuuuan n 21

<210> SEQ ID NO 898
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<223> OTHER INFORMATION: Exemplary iRNA agents

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auaaaauau cuacccaga cua 23

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<220> FEATURE:

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 900

gucuggggua gauauuuun n

21

<210> SEQ ID NO 901

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 901

uaaaauauc uacccagac uag

23

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<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 902

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<220> FEATURE:

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 903

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<210> SEQ ID NO 904

<211> LENGTH: 23

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<210> SEQ ID NO 906
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 906

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<210> SEQ ID NO 907
<211> LENGTH: 23
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<400> SEQUENCE: 907

aaauauaucua ccccagacua gau 23

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uauaucuacc ccagacuagn n 21

<210> SEQ ID NO 909
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 909

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auauaucuac cccagacuag aug 23

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<223> OTHER INFORMATION: Exemplary iRNA agents
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<400> SEQUENCE: 911

auaucuaccc cagacuagan n 21

<210> SEQ ID NO 912
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<223> OTHER INFORMATION: Exemplary iRNA agents

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uauaucuacc ccagacuaga ugu 23

<210> SEQ ID NO 914
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<400> SEQUENCE: 914

uauaucuaccc agacuagaun n 21

<210> SEQ ID NO 915
<211> LENGTH: 21
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 915

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<210> SEQ ID NO 916
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 916

auauacuacc cagacuagau gua 23

<210> SEQ ID NO 917
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 917

aucuacccca gacuagaun n 21

<210> SEQ ID NO 918
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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caucuagucu gggua gaun n 21

<210> SEQ ID NO 919
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uaucuacccc agacuagaug uag 23

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 920
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<400> SEQUENCE: 921
acaucuaguc uggguagan n 21

<210> SEQ ID NO 922
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<223> OTHER INFORMATION: Exemplary iRNA agents
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cuaccccaga cuagauguan n 21

<210> SEQ ID NO 924
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 924
uacaucuagu cuggguagn n 21

<210> SEQ ID NO 925
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<223> OTHER INFORMATION: Exemplary iRNA agents

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 934

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 943

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<222> LOCATION: 20, 21
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<400> SEQUENCE: 946

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<400> SEQUENCE: 947

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 948

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<210> SEQ ID NO 949
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<212> TYPE: RNA
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<400> SEQUENCE: 949

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<400> SEQUENCE: 950

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<210> SEQ ID NO 951
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<221> NAME/KEY: misc_feature
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<400> SEQUENCE: 951

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<400> SEQUENCE: 952

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<400> SEQUENCE: 953

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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 954

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<210> SEQ ID NO 955
<211> LENGTH: 23
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<220> FEATURE:
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<400> SEQUENCE: 955

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<400> SEQUENCE: 956

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<210> SEQ ID NO 957

<211> LENGTH: 21

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 957

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<210> SEQ ID NO 958

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 958

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<210> SEQ ID NO 959

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 959

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<210> SEQ ID NO 960

<211> LENGTH: 21

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 960

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<210> SEQ ID NO 961

<211> LENGTH: 23

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 961

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<210> SEQ ID NO 962
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<400> SEQUENCE: 962

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<210> SEQ ID NO 963
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 963

auacaaaaaa uacuacaun n 21

<210> SEQ ID NO 964
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 964

agauguagua uuuuuuguau aaU 23

<210> SEQ ID NO 965
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 965

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<210> SEQ ID NO 966
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 966

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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 967

gauguaguau uuuuuguaua auu 23

<210> SEQ ID NO 968
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 968

uguaguauuu uuuguauaan n 21

<210> SEQ ID NO 969
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 969

uuauacaaaa aaacuacan n 21

<210> SEQ ID NO 970
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 970

auguaguauu uuuuguauaa uug 23

<210> SEQ ID NO 971
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 971

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<210> SEQ ID NO 972
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 972

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<210> SEQ ID NO 973
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 973

uguaguauuu uuuguauauu ugg

23

<210> SEQ ID NO 974
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 974

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<210> SEQ ID NO 975
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 975

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21

<210> SEQ ID NO 976
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 976

guaguauuuu uuuguauauu gga

23

<210> SEQ ID NO 977
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<212> TYPE: DNA
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<221> NAME/KEY: misc_feature
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<400> SEQUENCE: 977

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<210> SEQ ID NO 978
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<400> SEQUENCE: 978

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<210> SEQ ID NO 979
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 979

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<210> SEQ ID NO 980
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<210> SEQ ID NO 981
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 981

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<210> SEQ ID NO 982
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<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 982

aguauuuuuu guauaaugg auu 23

<210> SEQ ID NO 983

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 983

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<210> SEQ ID NO 984

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 984

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<210> SEQ ID NO 985

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 985

guauuuuuug uauaaugga uuu 23

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<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 986

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<210> SEQ ID NO 987

<211> LENGTH: 21

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 987

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<210> SEQ ID NO 988

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 988

uaauuuuuugu auaauuggau uuc 23

<210> SEQ ID NO 989

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 989

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<210> SEQ ID NO 990

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 990

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<210> SEQ ID NO 991

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<223> OTHER INFORMATION: Exemplary iRNA agents

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<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 992

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uuuuuuguau aaugggauuu ccu 23

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gaaauccaau uauacaaaaan n 21

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uuuuuguaua auugggauuuc cua 23

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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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ggaaauccaa uuauacaaan n 21

<210> SEQ ID NO 1000
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1000

uuuuguauaa uuggauuucc uaa 23

<210> SEQ ID NO 1001
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<210> SEQ ID NO 1002
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<223> OTHER INFORMATION: Exemplary iRNA agents
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<210> SEQ ID NO 1005
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<220> FEATURE:
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<400> SEQUENCE: 1006
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<221> NAME/KEY: misc_feature
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<220> FEATURE:
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<400> SEQUENCE: 1009
uguauaaauug gauuuccuaa uac 23

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1011
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<400> SEQUENCE: 1012
guauuuggaa auaaagucag aug 23

<210> SEQ ID NO 1013
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<400> SEQUENCE: 1013

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1014

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21

<210> SEQ ID NO 1015

<211> LENGTH: 23

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1015

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23

<210> SEQ ID NO 1016

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1016

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21

<210> SEQ ID NO 1017

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1017

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21

<210> SEQ ID NO 1018

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1018

auuuggaaa aaagucagau gga

23

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<210> SEQ ID NO 1019
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1019

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<210> SEQ ID NO 1020
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1020

caucugacuu uauuuccaan n 21

<210> SEQ ID NO 1021
<211> LENGTH: 23
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1021

uuuggaaaaua aagucagaug gaa 23

<210> SEQ ID NO 1022
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<212> TYPE: DNA
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<210> SEQ ID NO 1023
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
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<400> SEQUENCE: 1023

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<210> SEQ ID NO 1024
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 1024

uuggaaaauaa agucagaugg aaa 23

<210> SEQ ID NO 1025
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1025

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<210> SEQ ID NO 1026
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1026

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<210> SEQ ID NO 1027
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1027

uggaaaauaaa gucagaugga aaa 23

<210> SEQ ID NO 1028
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1028

gaaaauaagu cagauggaan n 21

<210> SEQ ID NO 1029
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1029

uuccaucuga cuuuauuucn n 21

<210> SEQ ID NO 1030
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1030

ucccucccag aggagccacc agu 23

<210> SEQ ID NO 1031
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1031

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<210> SEQ ID NO 1032
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1032

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<210> SEQ ID NO 1033
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1033

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<210> SEQ ID NO 1034
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
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<400> SEQUENCE: 1034
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<210> SEQ ID NO 1035
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<222> LOCATION: 20, 21
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<400> SEQUENCE: 1035
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<210> SEQ ID NO 1036
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1036
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<210> SEQ ID NO 1037
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<212> TYPE: DNA
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1037
ucccagagga gccaccagun n 21

<210> SEQ ID NO 1038
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1038
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<210> SEQ ID NO 1039
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

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<400> SEQUENCE: 1039

cucccagagg agccaccagu ucu 23

<210> SEQ ID NO 1040

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1040

cccagaggag ccaccaguun n 21

<210> SEQ ID NO 1041

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1041

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<210> SEQ ID NO 1042

<211> LENGTH: 23

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<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1042

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1043

ccagaggagc caccaguucn n 21

<210> SEQ ID NO 1044

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 1044

gaacuggugg cuccucuggn n

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<210> SEQ ID NO 1045

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1046

cagaggagcc accaguucun n

21

<210> SEQ ID NO 1047

<211> LENGTH: 21

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1047

agaacuggug gcuccucugn n

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<210> SEQ ID NO 1048

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1048

cuucucucca gcugacuaaa cuu

23

<210> SEQ ID NO 1049

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1049

ucucuccagc ugacuaaach n

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1050

guuuagucag cuggagagan n 21

<210> SEQ ID NO 1051
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1051

uucuguacca guuaauuuuu cca 23

<210> SEQ ID NO 1052
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<212> TYPE: DNA
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1052

cuguaccagu uaaauuuuucn n 21

<210> SEQ ID NO 1053
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1053

gaaaaauuaa cugguacagn n 21

<210> SEQ ID NO 1054
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1054

ucuguaccag uuaauuuuuc caa 23

<210> SEQ ID NO 1055
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1055

uguaccaguu aaauuuuccn n 21

<210> SEQ ID NO 1056
<211> LENGTH: 21
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents
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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1056

ggaaaaauua acugguacan n 21

<210> SEQ ID NO 1057
<211> LENGTH: 23
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1057

cuguaccagu uaaauuuucc aac 23

<210> SEQ ID NO 1058
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1058

guaccaguaa auuuuuccan n 21

<210> SEQ ID NO 1059
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1059

uggaaaaauu aacugguacn n 21

<210> SEQ ID NO 1060
<211> LENGTH: 23
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1060
uguaccaguu aaauuuucca acu 23

<210> SEQ ID NO 1061
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1061
uaccaguuaa uuuuuccaan n 21

<210> SEQ ID NO 1062
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1062
uuggaaaaau uaacugguan n 21

<210> SEQ ID NO 1063
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1063
guaccaguua auuuuuucca cua 23

<210> SEQ ID NO 1064
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1064
accaguuaau uuuuccaen n 21

<210> SEQ ID NO 1065
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1065

guuggaaaaa uuaacuggun n 21

<210> SEQ ID NO 1066
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1066

uaccaguuaa uuuuuccaac uac 23

<210> SEQ ID NO 1067
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1067

ccaguuaauu uuuccaacun n 21

<210> SEQ ID NO 1068
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1068

aguuggaaaa auuaacuggn n 21

<210> SEQ ID NO 1069
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1069

accaguuaau uuuuccaacu acu 23

<210> SEQ ID NO 1070
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<400> SEQUENCE: 1070

caguuaauuu uuccaacuan n

21

<210> SEQ ID NO 1071

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1071

uaguuggaaa aaauaacugn n

21

<210> SEQ ID NO 1072

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1072

uaauagaaua aaggcaguuu ucu

23

<210> SEQ ID NO 1073

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1073

auagaauaaa ggcaguuuun n

21

<210> SEQ ID NO 1074

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20, 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1074

aaaacugccu uuauucuaun n

21

<210> SEQ ID NO 1075

<211> LENGTH: 23

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1075

aaauagaaua aaggcaguuuu cua

23

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<210> SEQ ID NO 1076
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1076

uagaauaaag gcaguuuucn n 21

<210> SEQ ID NO 1077
<211> LENGTH: 21
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<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1077

gaaaacugcc uuuauucuan n 21

<210> SEQ ID NO 1078
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents

<400> SEQUENCE: 1078

auagaauaaa ggcaguuuuc uaa 23

<210> SEQ ID NO 1079
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1079

agaauaaagg caguuuucun n 21

<210> SEQ ID NO 1080
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Exemplary iRNA agents
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1080

agaaaacugc cuuuauucun n 21

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<210> SEQ ID NO 1081
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1081

gauuauagacc gucugaggcn n 21

<210> SEQ ID NO 1082
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1082

gccucagucg gucauaaunc n 21

<210> SEQ ID NO 1083
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1083

ggaucuucgg aaugaugagn n 21

<210> SEQ ID NO 1084
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1084

cucaucauuc cgaagaucn n 21

<210> SEQ ID NO 1085

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<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1085

agaccaaaga cggagugagn n

21

<210> SEQ ID NO 1086
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1086

cucacuccgu cuuuggucun n

21

<210> SEQ ID NO 1087
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20, 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1087

ugaagcagga gccgguaaan n

21

<210> SEQ ID NO 1088
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1088

uuuaccggu ccugcuucan n

21

<210> SEQ ID NO 1089
<211> LENGTH: 21
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 2, 3, 5, 6, 9, 11, 12, 13,19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20,
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1089

gcuaccagua uuuagaagcn n 21

<210> SEQ ID NO 1090
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 6, 10, 16
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1090

gcuucuaaaau acugguagcn n 21

<210> SEQ ID NO 1091
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 4, 5, 8, 10, 11, 12, 18, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1091

cuaccaguau uuagaagccn n 21

<210> SEQ ID NO 1092
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 7, 11, 17
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1092

ggcuucuaaaa uacugguagn n

21

<210> SEQ ID NO 1093
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 2, 3, 5, 8, 9, 11, 12, 13, 14, 16, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1093

gcuguaacua cuuuauaacn n

21

<210> SEQ ID NO 1094
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 3, 5, 10, 14, 16
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1094

guuauaaagu aguacagcn n

21

<210> SEQ ID NO 1095
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 2, 3, 5, 6, 8, 10, 13, 14, 17, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1095

guuacugugu aaauagugcn n

21

<210> SEQ ID NO 1096
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 5, 9, 11, 13, 16
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1096

gcacuaauua cacaguaacn n

21

<210> SEQ ID NO 1097
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 4, 5, 6, 9, 11, 13, 15, 16, 18, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1097

ccacuuaaug uauguuacn n

21

<210> SEQ ID NO 1098
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 3, 6, 8, 10, 13
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1098

gguaacauac auuaaguggn n

21

<210> SEQ ID NO 1099
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 4, 5, 6, 7, 10, 13, 14, 15
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1099

cagcccugau aguuuagaan n

21

<210> SEQ ID NO 1100
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 4, 9, 12
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1100

uucuaaacua ucagggcugn n

21

<210> SEQ ID NO 1101
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:

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<221> NAME/KEY: modified_base
<222> LOCATION: 2, 3, 4, 5, 8, 11, 12, 13
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1101

gcccgauag uuuagaaaan n 21

<210> SEQ ID NO 1102
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 6, 11, 14
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1102

uuuucuaaac uaucaggcn n 21

<210> SEQ ID NO 1103
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 3, 4, 7, 10, 11, 12, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1103

cccguagu uuaaaaaacn n 21

<210> SEQ ID NO 1104
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base

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<222> LOCATION: 7, 12, 15
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
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<222> LOCATION: 20
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<400> SEQUENCE: 1104

guuuucuaaa cuaucagggn n

21

<210> SEQ ID NO 1105
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<212> TYPE: DNA
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<220> FEATURE:
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<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
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<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1105

gauaguuuag aaaacauccn n

21

<210> SEQ ID NO 1106
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<222> LOCATION: 11, 16
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
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<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1106

ggauguuuuc uaaacuaucn n

21

<210> SEQ ID NO 1107
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
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<221> NAME/KEY: modified_base
<222> LOCATION: 1, 4, 5, 6, 13, 15, 16, 17, 18
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

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<220> FEATURE:
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<222> LOCATION: 20
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1107

uaguuuagaa aacaucccan n 21

<210> SEQ ID NO 1108
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetically generated oligonucleotide
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<222> LOCATION: 13, 18
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
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<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1108

ugggauguuu ucuaaacuan n 21

<210> SEQ ID NO 1109
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<221> NAME/KEY: modified_base
<222> LOCATION: 1, 5, 6, 10, 12, 15, 17, 18, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1109

cagacuagau guaguauuun n 21

<210> SEQ ID NO 1110
<211> LENGTH: 21
<212> TYPE: DNA
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 4, 7, 9, 13
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
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<221> NAME/KEY: misc_feature
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1110

aaauacuaca ucuagucugn n 21

<210> SEQ ID NO 1111
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<213> ORGANISM: Artificial Sequence
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<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 3, 4, 8, 9, 13, 15, 18
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1111

ccccagacua gauguaguan n 21

<210> SEQ ID NO 1112
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<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 4, 6, 10
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1112

uacuacaucau agucuggggn n 21

<210> SEQ ID NO 1113
<211> LENGTH: 21
<212> TYPE: DNA
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<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 6, 7, 11, 13, 16, 18, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature

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<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate
linkages

<400> SEQUENCE: 1113

ccagacuaga uguaguauun n

21

<210> SEQ ID NO 1114
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 3, 6, 8, 12
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate
linkages

<400> SEQUENCE: 1114

aauacuacau cuagucuggn n

21

<210> SEQ ID NO 1115
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 3, 7, 8, 12, 14, 17, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate
linkages

<400> SEQUENCE: 1115

cccagacuag auguagauun n

21

<210> SEQ ID NO 1116
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 2, 5, 7, 11
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate
linkages

<400> SEQUENCE: 1116

auacuacau uagucugggn n

21

<210> SEQ ID NO 1117
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 3, 4, 6, 7, 8, 11, 13, 15, 17, 18
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate
linkages

<400> SEQUENCE: 1117

ugccacuuaa uguauguan n

21

<210> SEQ ID NO 1118
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
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<221> NAME/KEY: modified_base
<222> LOCATION: 1, 4, 6, 8, 11, 18
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate
linkages

<400> SEQUENCE: 1118

uaacauacau uaaguggcan n

21

<210> SEQ ID NO 1119
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 3, 4, 6, 7, 8, 10, 11, 14, 15, 16, 17
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1119

ugcuguuuau uaaucuuagn n 21

<210> SEQ ID NO 1120
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 2, 8, 11, 15, 18
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
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<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1120

cuaagauuaa uaaacagcan n 21

<210> SEQ ID NO 1121
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 4, 6, 7, 10, 11, 13, 14, 15, 16, 18
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1121

ucauguuagu uaccuuauan n 21

<210> SEQ ID NO 1122
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
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<221> NAME/KEY: modified_base
<222> LOCATION: 1, 3, 8, 12, 15
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1122

uauaagguaa cuaacaugan n

21

<210> SEQ ID NO 1123
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 5, 6, 9, 10, 11, 12, 13,, 14, 15, 18, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
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<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1123

ccaguuaauu uuuccaacun n

21

<210> SEQ ID NO 1124
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
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<222> LOCATION: 13
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
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<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1124

aguuggaaaa auuaacuggn n

21

<210> SEQ ID NO 1125
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 3, 4, 5, 10, 11, 13, 17, 18
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature

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<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1125

uaccuaagau uacaaauca n

21

<210> SEQ ID NO 1126
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 8, 14, 18
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1126

ugauuuguaa ucuuaggua n

21

<210> SEQ ID NO 1127
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetically generated oligonucleotide
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<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 3, 4, 6, 7, 9, 10, 13, 15, 16, 17
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1127

ucuugcuacc aguauuuagn n

21

<210> SEQ ID NO 1128
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
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<222> LOCATION: 2, 6, 12, 15
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21

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<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1128

cuaaauacug guagcaagan n

21

<210> SEQ ID NO 1129

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetically generated oligonucleotide

<220> FEATURE:

<221> NAME/KEY: modified_base

<222> LOCATION: 1, 3, 5, 8, 9, 12, 14, 15, 17, 18, 19

<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1129

uguguaauua gugccacuun n

21

<210> SEQ ID NO 1130

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetically generated oligonucleotide

<220> FEATURE:

<221> NAME/KEY: modified_base

<222> LOCATION: 7, 10, 14, 16, 18

<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1130

aaguggcacu aaauacacan n

21

<210> SEQ ID NO 1131

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetically generated oligonucleotide

<220> FEATURE:

<221> NAME/KEY: modified_base

<222> LOCATION: 2, 3, 4, 5, 7, 8, 10, 11, 14, 16, 17, 18

<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate

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linkages

<400> SEQUENCE: 1131

aucuugcuac caguauuuan n 21

<210> SEQ ID NO 1132
<211> LENGTH: 21
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 5, 11, 14
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1132

uaaaauacugg uagcaagaun n 21

<210> SEQ ID NO 1133
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 4, 7, 8, 10, 11, 12, 13, 15, 18, 19
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1133

cuguaacuac uuuaaacun n 21

<210> SEQ ID NO 1134
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
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<221> NAME/KEY: modified_base
<222> LOCATION: 4, 6, 11, 15, 17
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

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<400> SEQUENCE: 1134

aguuaauaaag uaguuacagn n

21

<210> SEQ ID NO 1135

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetically generated oligonucleotide

<220> FEATURE:

<221> NAME/KEY: modified_base

<222> LOCATION: 2, 6, 7, 11, 12, 14, 17, 18

<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1135

gugaauuagg cuguaacuan n

21

<210> SEQ ID NO 1136

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetically generated oligonucleotide

<220> FEATURE:

<221> NAME/KEY: modified_base

<222> LOCATION: 1, 5, 7, 12, 17,

<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

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<221> NAME/KEY: misc_feature

<222> LOCATION: 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1136

uaguacagc cuaauacacn n

21

<210> SEQ ID NO 1137

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetically generated oligonucleotide

<220> FEATURE:

<221> NAME/KEY: modified_base

<222> LOCATION: 1, 2, 4, 5, 8, 10, 11, 12, 18, 19

<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages, conjugated 1-{6-[cholester-3-yloxy-carbonylamino]-hexanoyl}-4-hydroxy-pyrrolidin-3-phosphorothioate diester

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<400> SEQUENCE: 1137

cuaccaguau uuagaagccn n

21

<210> SEQ ID NO 1138

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetically generated oligonucleotide

<220> FEATURE:

<221> NAME/KEY: modified_base

<222> LOCATION: 7, 11, 17

<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

<400> SEQUENCE: 1138

ggcuucuaaa uacugguagn n

21

<210> SEQ ID NO 1139

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetically generated oligonucleotide

<220> FEATURE:

<221> NAME/KEY: modified_base

<222> LOCATION: 1, 3, 4, 6, 7, 8, 10, 11, 14, 15, 16, 17

<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages, conjugated 1-{6-[cholester-3-yloxy-carbonylamino]-hexanoyl}-4-hydroxy-pyrrolidin-3-phosphorothioate diester

<400> SEQUENCE: 1139

ugcuguuuau uaaucuuagn n

21

<210> SEQ ID NO 1140

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetically generated oligonucleotide

<220> FEATURE:

<221> NAME/KEY: modified_base

<222> LOCATION: 2, 8, 11, 15, 18

<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 20

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine

<220> FEATURE:

<221> NAME/KEY: misc_feature

<222> LOCATION: 21

<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate linkages

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<400> SEQUENCE: 1140

cuaagauuaa uaaacagcan n

21

<210> SEQ ID NO 1141

<211> LENGTH: 46

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1141

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46

<210> SEQ ID NO 1142

<211> LENGTH: 45

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1142

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45

<210> SEQ ID NO 1143

<211> LENGTH: 41

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1143

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41

<210> SEQ ID NO 1144

<211> LENGTH: 43

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1144

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43

<210> SEQ ID NO 1145

<211> LENGTH: 43

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1145

ttggtctttg ctgaacactc catttttctc ttggaaagaa agt

43

<210> SEQ ID NO 1146

<211> LENGTH: 40

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1146

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40

<210> SEQ ID NO 1147

<211> LENGTH: 44

<212> TYPE: DNA

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1147

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44

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<210> SEQ ID NO 1148
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1148

gccttggtg ctcacattc ctttttaggc ataggaccg tgtct 45

<210> SEQ ID NO 1149
<211> LENGTH: 46
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1149

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<210> SEQ ID NO 1150
<211> LENGTH: 44
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1150

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<210> SEQ ID NO 1151
<211> LENGTH: 43
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1151

gcagctctcg tggccatctt ttttaggcat aggaccgtg tct 43

<210> SEQ ID NO 1152
<211> LENGTH: 44
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1152

aggcaccg actttttctt ttttaggca taggaccgt gtct 44

<210> SEQ ID NO 1153
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1153

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<210> SEQ ID NO 1154
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1154

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<210> SEQ ID NO 1155
<211> LENGTH: 23
<212> TYPE: DNA
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<400> SEQUENCE: 1155

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caaaaacctc tctcactccg tct 23

<210> SEQ ID NO 1156
<211> LENGTH: 41
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1156

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<210> SEQ ID NO 1157
<211> LENGTH: 41
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1157

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<210> SEQ ID NO 1158
<211> LENGTH: 41
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1158

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<210> SEQ ID NO 1159
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<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1159

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<210> SEQ ID NO 1160
<211> LENGTH: 44
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1160

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<210> SEQ ID NO 1161
<211> LENGTH: 47
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1161

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<210> SEQ ID NO 1162
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<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1162

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<210> SEQ ID NO 1163
<211> LENGTH: 21

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<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1163
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<210> SEQ ID NO 1164
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<212> TYPE: DNA
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<400> SEQUENCE: 1164
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<210> SEQ ID NO 1165
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 1165
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<210> SEQ ID NO 1166
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<222> LOCATION: 21
<223> OTHER INFORMATION: conjugated 1-{6-[cholester-3-
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phosphorothioate diester

<400> SEQUENCE: 1166
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<210> SEQ ID NO 1167
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 21
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 22
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
phosphorothioate linkages
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 23
<223> OTHER INFORMATION: phosphorothioate linkages corresponding base

<400> SEQUENCE: 1167
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<210> SEQ ID NO 1168
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<220> FEATURE:
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<222> LOCATION: 20, 21,
<223> OTHER INFORMATION: phosphorothioate linkages corresponding base

<400> SEQUENCE: 1168

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<210> SEQ ID NO 1169
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<220> FEATURE:
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phosphorothioate linkages
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 23
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<400> SEQUENCE: 1169

aagucgugcu gcucaugug guc 23

<210> SEQ ID NO 1170
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 1, 2, 3, 5, 7, 8, 12, 14, 15, 16, 17
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate
linkages, conjugated 1-{6-[cholester-3-yloxy-carbonylamino]-
hexanoyl}-4-hydroxy-pyrrolidin-3-phosphorothioate diester

<400> SEQUENCE: 1170

cuuacgcuga guacuucgan n 21

<210> SEQ ID NO 1171
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetically generated oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: 7, 11, 16
<223> OTHER INFORMATION: 2'- O-methyl modification corresponding base
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: 20
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine
<220> FEATURE:

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<221> NAME/KEY: misc_feature
<222> LOCATION: 21
<223> OTHER INFORMATION: n = 2'-deoxy-thymidine phosphorothioate
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      hexanoyl}-4-hydroxy-pyrrolidin-3-phosphorothioate diester

<400> SEQUENCE: 1171
ucgaaguacu cagcguaagn n

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21

We claim:

1. A method of stimulating neuronal cell outgrowth in a neural cell culture comprising contacting the neural cell culture with an iRNA agent, wherein the iRNA agent comprises (i) a sense strand, wherein the sense strand comprises at least 15 contiguous nucleotides that differ by no more than 1, 2, or 3 nucleotides from the sense strand sequences of any one agent selected from the group consisting of agents number 5850 to 6177, and (ii) an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides that differ by no more than 1, 2, or 3 nucleotides from the antisense sequences of any one agent selected from the group consisting of agents number 5850 to 6177.

2. A method of performing an animal study comprising:

(a) providing an animal having a neural disfunction;

(b) administering an iRNA agent wherein the iRNA agent comprises (i) a sense strand, wherein the sense strand comprises at least 15 contiguous nucleotides that differ by no more than 1, 2, or 3 nucleotides from the sense strand sequences of any one agent selected from the group consisting of agents number 5850 to 6177, and (ii) an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides that differ by no more than 1, 2, or 3 nucleotides from the antisense sequences of any one agent selected from the group consisting of agents number 5850 to 6177; and

(c) monitoring the animal for an improvement in neural function.

* * * * *