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(71) Applicant(s)
Ionis Pharmaceuticals, Inc.

(72) Inventor(s)
BUI, Huynh-Hoa;FREIER, Susan M.

(74) Agent / Attorney
RnB IP Pty Ltd, PO Box 9530, DEAKIN, ACT, 2600, AU

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(71) Applicant: **IONIS PHARMACEUTICALS, INC.** [US/US]; 2855 Gazelle Court, Carlsbad, CA 92010 (US).

(72) Inventors: **BUI, Huynh-Hoa**; 2855 Gazelle Ct., Carlsbad, CA 92010 (US). **FREIER, Susan, M.**; 2855 Gazelle Ct., Carlsbad, CA 92010 (US).

(74) Agent: **SCARR, Rebecca, B.** et al.; McNeill Baur PLLC, 125 Cambridge Park Dr, Suite 301, Cambridge, MA 02140 (US).

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(54) Title: COMPOUNDS AND METHODS FOR REDUCING KCNT1 EXPRESSION

(57) Abstract: Provided are compounds, methods, and pharmaceutical compositions for reducing the amount or activity of KCNT1 RNA in a cell or subject, and in certain instances reducing the amount of KCNT1 protein in a cell or subject. These compounds, methods, and pharmaceutical compositions are useful to ameliorate at least one symptom or hallmark of a neurological condition. Such symptoms and hallmarks include seizures, encephalopathy, and behavioral abnormalities. Non-limiting examples of neurological conditions that benefit from these compounds, methods, and pharmaceutical compositions are epilepsy of infancy with migrating focal seizures (EIMFS), autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE), West syndrome, and Ohtahara syndrome.

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COMPOUNDS AND METHODS FOR REDUCING KCNT1 EXPRESSION

Sequence Listing

The present application is being filed along with a Sequence Listing in electronic format. The Sequence Listing is provided as a file entitled BIOL0358WOSEQ_ST25.txt, created on March 9, 2020, which is 716 kb in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

Field

Provided are compounds, methods, and pharmaceutical compositions for reducing the amount of potassium sodium-activated channel subfamily T member 1 (KCNT1) RNA in a cell or subject, and in certain instances reducing the amount of KCNT1 protein in a cell or subject. Such compounds, methods, and pharmaceutical compositions are useful to ameliorate at least one symptom or hallmark of a neurological condition. Such symptoms and hallmarks include, but are not limited to, encephalopathy, cerebral cortical atrophy, clonus, seizures (epilepsy), and behavioral abnormalities such as aggression, catatonia, psychosis, and other intellectual disabilities. Non-limiting examples of neurological conditions that may be treated with the compounds, methods, and pharmaceutical compositions disclosed herein are epilepsy of infancy with migrating focal seizures (EIMFS), autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE), and early onset epileptic encephalopathies including West syndrome and Ohtahara syndrome.

Background

Epilepsy is a neurological disorder characterized by periodic abnormalities in brain activity. By way of non-limiting example, an individual having epilepsy often displays abnormal behavior such as seizures (uncontrollable jerking or twitching of the limbs), loss of consciousness, catatonia, confusion, and psychosis. Epileptic individuals may experience focal seizures or generalized seizures. Focal seizures affect a particular area in the brain. In contrast, generalized seizures affect all areas of the brain. Tragically, onset of epilepsy can occur within the first few months of life, as seen in patients with EIMFS and early infantile epileptic encephalopathy (EIEE). EIMFS is a severely pharmaco-resistant epilepsy with a high rate of sudden unexpected death in epilepsy. Onset of seizures in subjects with EIMFS often occurs in the first month of life.

KCNT1, also known as Sequence Like a Calcium Activated K+ channel (SLACK), $K_{Ca}4.1$ and Slo2.2, is a sodium gated potassium channel subunit that forms a tetrameric channel with KCNT2 to mediate a sodium-sensitive potassium current in a range of neuronal cells. Two splice isoforms of KCNT1 mRNA are expressed in humans. These isoforms may produce different proteins with different electrophysical properties, similar to SLACK isoform variants found in rodents.

Gain of function mutations in KCNT1 can cause several types of epilepsy, including ADNFLE and EIMFS. To date, all KCNT1 mutations found in epileptic subjects are missense mutations that result in

KCNT1 protein gain of function. These missense mutations result in increased potassium channel activity and an increased peak potassium current. Approximately, 42-50% of EIMFS cases are due to KCNT1 gain of function mutations.

Summary of the Invention

Currently, there is a lack of acceptable options for treating infantile encephalopathies and epilepsies. Thus, these conditions present a high unmet need. In addition, there are many cases of epilepsy that are pharmaco-resistant, leaving patients with little or no therapeutic options. It is therefore an object herein to provide compounds, methods, and pharmaceutical compositions for the treatment of such diseases.

Provided herein are compounds, methods and pharmaceutical compositions for reducing the amount or activity of KCNT1 RNA, and in certain embodiments reducing the amount or activity of KCNT1 protein in a cell or a subject. In certain embodiments the subject is a human infant. In certain embodiments, the subject has a neurological condition. In certain embodiments, the neurological condition comprises encephalopathy. In certain embodiments, the neurological condition comprises epilepsy. In certain embodiments, the neurological condition is EIMFS. In certain embodiments, the neurological condition is ADNFLE. In certain embodiments, compounds useful for reducing the amount or activity of KCNT1 RNA are oligomeric compounds. In certain embodiments, compounds useful for reducing expression of KCNT1 RNA are modified oligonucleotides.

Also provided herein are methods useful for ameliorating at least one symptom or hallmark of a neurological condition. In certain embodiments, the neurological condition is EIMFS. In certain embodiments, the neurological condition is ADNFLE. In certain embodiments, the at least one symptom or hallmark is selected from seizure, brain damage, demyelination, hypotonia, microcephaly, depression, anxiety, cognitive function. In certain embodiments, methods disclosed herein are useful for reducing seizure occurrence. In certain embodiments, methods disclosed herein are useful for reducing seizure severity.

Detailed Description of the Invention

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

The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. All documents, or portions of documents, cited in this application,

including, but not limited to, patents, patent applications, articles, books, and treatises, are hereby expressly incorporated-by-reference for the portions of the document discussed herein, as well as in their entirety.

Definitions

Unless specific definitions are provided, the nomenclature used in connection with, and the procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well-known and commonly used in the art. Where permitted, all patents, applications, published applications and other publications and other data referred to throughout in the disclosure are incorporated by reference herein in their entirety.

Unless otherwise indicated, the following terms have the following meanings:

DEFINITIONS

As used herein, "2'-deoxynucleoside" means a nucleoside comprising a 2'-H(H) deoxyribosyl sugar moiety. In certain embodiments, a 2'-deoxynucleoside is a 2'-β-D-deoxynucleoside and comprises a 2'-β-D-deoxyribosyl sugar moiety, which has the β-D configuration as found in naturally occurring deoxyribonucleic acids (DNA). In certain embodiments, a 2'-deoxynucleoside or nucleoside comprising an unmodified 2'-deoxyribosyl sugar moiety may comprise a modified nucleobase or may comprise an RNA nucleobase (uracil).

As used herein, "2'-MOE" or "2'-MOE sugar moiety" means a 2'-$OCH_2CH_2OCH_3$ group in place of the 2'-OH group of a ribosyl sugar moiety. "MOE" means methoxyethyl.

As used herein, "2'-MOE nucleoside" means a nucleoside comprising a 2'-MOE sugar moiety.

As used herein, "2'-OMe" or "2'-O-methyl sugar moiety" means a 2'-OCH_3 group in place of the 2'-OH group of a ribosyl sugar moiety.

As used herein, "2'-OMe nucleoside" means a nucleoside comprising a 2'-OMe sugar moiety.

As used herein, "2'-substituted nucleoside" means a nucleoside comprising a 2'-substituted sugar moiety. As used herein, "2'-substituted" in reference to a sugar moiety means a sugar moiety comprising at least one 2'-substituent group other than H or OH.

As used herein, "5-methyl cytosine" means a cytosine modified with a methyl group attached to the 5 position. A 5-methyl cytosine is a modified nucleobase.

As used herein, "administering" means providing a pharmaceutical agent to a subject.

As used herein, "antisense activity" means any detectable and/or measurable change attributable to the hybridization of an antisense compound to its target nucleic acid. In certain embodiments, antisense activity is a decrease in the amount or expression of a target nucleic acid or protein encoded by such target nucleic acid compared to target nucleic acid levels or target protein levels in the absence of the antisense compound.

As used herein, "antisense compound" means an oligomeric compound capable of achieving at least one antisense activity.

As used herein, "ameliorate" in reference to a treatment means improvement in at least one symptom relative to the same symptom in the absence of the treatment. In certain embodiments, amelioration is the reduction in the severity or frequency of a symptom or the delayed onset or slowing of progression in the severity or frequency of a symptom.

As used herein, "bicyclic nucleoside" or "BNA" means a nucleoside comprising a bicyclic sugar moiety.

As used herein, "bicyclic sugar" or "bicyclic sugar moiety" means a modified sugar moiety comprising two rings, wherein the second ring is formed via a bridge connecting two of the atoms in the first ring thereby forming a bicyclic structure. In certain embodiments, the first ring of the bicyclic sugar moiety is a furanosyl moiety. In certain embodiments, the bicyclic sugar moiety does not comprise a furanosyl moiety.

As used herein, "cleavable moiety" means a bond or group of atoms that is cleaved under physiological conditions, for example, inside a cell or a subject.

As used herein, "complementary" in reference to an oligonucleotide means that at least 70% of the nucleobases of the oligonucleotide or one or more regions thereof and the nucleobases of another nucleic acid or one or more regions thereof are capable of hydrogen bonding with one another when the nucleobase sequence of the oligonucleotide and the other nucleic acid are aligned in opposing directions. As used herein, "complementary nucleobases" means nucleobases that are capable of forming hydrogen bonds with one another. Complementary nucleobase pairs include adenine (A) with thymine (T), adenine (A) with uracil (U), cytosine (C) with guanine (G), and 5-methyl cytosine (mC) with guanine (G). Complementary oligonucleotides and/or nucleic acids need not have nucleobase complementarity at each nucleoside. Rather, some mismatches are tolerated. As used herein, "fully complementary" or "100% complementary" in reference to an oligonucleotide, or portion thereof, means that oligonucleotide, or portion thereof, is complementary to another oligonucleotide or nucleic acid at each nucleobase of the oligonucleotide.

As used herein, "conjugate group" means a group of atoms that is directly or indirectly attached to an oligonucleotide. Conjugate groups include a conjugate moiety and a conjugate linker that attaches the conjugate moiety to the oligonucleotide.

As used herein, "conjugate linker" means a single bond or a group of atoms comprising at least one bond that connects a conjugate moiety to an oligonucleotide.

As used herein, "conjugate moiety" means a group of atoms that is attached to an oligonucleotide via a conjugate linker.

As used herein, "contiguous" in the context of an oligonucleotide refers to nucleosides, nucleobases, sugar moieties, or internucleoside linkages that are immediately adjacent to each other. For example, "contiguous nucleobases" means nucleobases that are immediately adjacent to each other in a sequence.

As used herein, “constrained ethyl” or “cEt” or “cEt modified sugar” means a β-D ribosyl bicyclic sugar moiety wherein the second ring of the bicyclic sugar is formed via a bridge connecting the 4’-carbon and the 2’-carbon of the β-D ribosyl sugar moiety, wherein the bridge has the formula 4'-CH(CH_3)-O-2', and wherein the methyl group of the bridge is in the *S* configuration.

As used herein, “cEt nucleoside” means a nucleoside comprising cEt modified sugar moiety.

As used herein, “chirally enriched population” means a plurality of molecules of identical molecular formula, wherein the number or percentage of molecules within the population that contain a particular stereochemical configuration at a particular chiral center is greater than the number or percentage of molecules expected to contain the same particular stereochemical configuration at the same particular chiral center within the population if the particular chiral center were stereorandom. Chirally enriched populations of molecules having multiple chiral centers within each molecule may contain one or more stereorandom chiral centers. In certain embodiments, the molecules are modified oligonucleotides. In certain embodiments, the molecules are compounds comprising modified oligonucleotides.

As used herein, “gapmer” means a modified oligonucleotide comprising an internal region having a plurality of nucleosides that support RNase H cleavage positioned between external regions having one or more nucleosides, wherein the nucleosides comprising the internal region are chemically distinct from the nucleoside or nucleosides comprising the external regions. The internal region may be referred to as the “gap” and the external regions may be referred to as the “wings.” Unless otherwise indicated, “gapmer” refers to a sugar motif. Unless otherwise indicated, the sugar moiety of each nucleoside of the gap is a 2’-β-D-deoxyribosyl sugar moiety. Thus, the term “MOE gapmer” indicates a gapmer having a gap comprising 2’-β-D-deoxynucleosides and wings comprising 2’-MOE nucleosides. Unless otherwise indicated, a MOE gapmer may comprise one or more modified internucleoside linkages and/or modified nucleobases and such modifications do not necessarily follow the gapmer pattern of the sugar modifications.

As used herein, “hotspot region” is a range of nucleobases on a target nucleic acid that is amenable to oligomeric compound-mediated reduction of the amount or activity of the target nucleic acid.

As used herein, "hybridization" means the pairing or annealing of complementary oligonucleotides and/or nucleic acids. While not limited to a particular mechanism, the most common mechanism of hybridization involves hydrogen bonding, which may be Watson-Crick, Hoogsteen or reversed Hoogsteen hydrogen bonding, between complementary nucleobases.

As used herein, “internucleoside linkage” means the covalent linkage between contiguous nucleosides in an oligonucleotide. As used herein “modified internucleoside linkage” means any internucleoside linkage other than a phosphodiester internucleoside linkage. “Phosphorothioate internucleoside linkage” is a modified internucleoside linkage in which one of the non-bridging oxygen atoms of a phosphodiester internucleoside linkage is replaced with a sulfur atom.

As used herein, “linker-nucleoside” means a nucleoside that links, either directly or indirectly, an oligonucleotide to a conjugate moiety. Linker-nucleosides are located within the conjugate linker of an oligomeric compound. Linker-nucleosides are not considered part of the oligonucleotide portion of an oligomeric compound even if they are contiguous with the oligonucleotide.

As used herein, “non-bicyclic modified sugar moiety” means a modified sugar moiety that comprises a modification, such as a substituent, that does not form a bridge between two atoms of the sugar to form a second ring.

As used herein, “mismatch” or “non-complementary” means a nucleobase of a first oligonucleotide that is not complementary with the corresponding nucleobase of a second oligonucleotide or target nucleic acid when the first and second oligonucleotide are aligned.

As used herein, “motif” means the pattern of unmodified and/or modified sugar moieties, nucleobases, and/or internucleoside linkages, in an oligonucleotide.

As used herein, “neurological condition” means a condition of the brain, central nervous system, peripheral nervous system, or combination thereof. A neurological condition may be marked by at least one of neuronal malfunction, neuronal damage, and neuronal death. A neurological condition may comprise decreased motor function. A neurological condition may comprise decreased motor control.

As used herein, "nucleobase" means an unmodified nucleobase or a modified nucleobase. As used herein an “unmodified nucleobase” is adenine (A), thymine (T), cytosine (C), uracil (U), or guanine (G). As used herein, a “modified nucleobase” is a group of atoms other than unmodified A, T, C, U, or G capable of pairing with at least one unmodified nucleobase. A “5-methyl cytosine” is a modified nucleobase. A universal base is a modified nucleobase that can pair with any one of the five unmodified nucleobases. As used herein, “nucleobase sequence” means the order of contiguous nucleobases in a nucleic acid or oligonucleotide independent of any sugar or internucleoside linkage modification.

As used herein, “nucleoside” means a compound comprising a nucleobase and a sugar moiety. The nucleobase and sugar moiety are each, independently, unmodified or modified. As used herein, “modified nucleoside” means a nucleoside comprising a modified nucleobase and/or a modified sugar moiety. Modified nucleosides include abasic nucleosides, which lack a nucleobase. “Linked nucleosides” are nucleosides that are connected in a contiguous sequence (i.e., no additional nucleosides are presented between those that are linked).

As used herein, "oligomeric compound" means an oligonucleotide and optionally one or more additional features, such as a conjugate group or terminal group. An oligomeric compound may be paired with a second oligomeric compound that is complementary to the first oligomeric compound or may be unpaired. A “singled-stranded oligomeric compound” is an unpaired oligomeric compound. The term “oligomeric duplex” means a duplex formed by two oligomeric compounds having complementary

nucleobase sequences. Each oligomeric compound of an oligomeric duplex may be referred to as a "duplexed oligomeric compound."

As used herein, "oligonucleotide" means a strand of linked nucleosides connected via internucleoside linkages, wherein each nucleoside and internucleoside linkage may be modified or unmodified. Unless otherwise indicated, oligonucleotides consist of 8-50 linked nucleosides. As used herein, "modified oligonucleotide" means an oligonucleotide, wherein at least one nucleoside or internucleoside linkage is modified. As used herein, "unmodified oligonucleotide" means an oligonucleotide that does not comprise any nucleoside modifications or internucleoside modifications.

As used herein, "pharmaceutically acceptable carrier or diluent" means any substance suitable for use in administering to a subject. Certain such carriers enable pharmaceutical compositions to be formulated as, for example, tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspension and lozenges for the oral ingestion by a subject. In certain embodiments, a pharmaceutically acceptable carrier or diluent is sterile water, sterile saline, sterile buffer solution or sterile artificial cerebrospinal fluid.

As used herein "pharmaceutically acceptable salts" means physiologically and pharmaceutically acceptable salts of compounds. Pharmaceutically acceptable salts retain the desired biological activity of the parent compound and do not impart undesired toxicological effects thereto.

As used herein "pharmaceutical composition" means a mixture of substances suitable for administering to a subject. For example, a pharmaceutical composition may comprise an oligomeric compound and a sterile aqueous solution. In certain embodiments, a pharmaceutical composition shows activity in a free uptake assay in certain cell lines.

As used herein "prodrug" means a therapeutic agent in a form outside the body that is converted to a different form within a subject or cells thereof. Typically, conversion of a prodrug within the subject is facilitated by the action of an enzymes (*e.g.*, endogenous or viral enzyme) or chemicals present in cells or tissues and/or by physiologic conditions.

As used herein, "reducing or inhibiting the amount or activity" refers to a reduction or blockade of the transcriptional expression or activity relative to the transcriptional expression or activity in an untreated or control sample and does not necessarily indicate a total elimination of transcriptional expression or activity.

As used herein, "RNA" means an RNA transcript and includes pre-mRNA and mature mRNA unless otherwise specified.

As used herein, "RNAi compound" means an antisense compound that acts, at least in part, through RISC or Ago2 to modulate a target nucleic acid and/or protein encoded by a target nucleic acid. RNAi compounds include, but are not limited to double-stranded siRNA, single-stranded RNA (ssRNA), and microRNA, including microRNA mimics. In certain embodiments, an RNAi compound modulates the amount, activity, and/or splicing of a target nucleic acid. The term RNAi compound excludes antisense compounds that act through RNase H.

As used herein, “self-complementary” in reference to an oligonucleotide means an oligonucleotide that at least partially hybridizes to itself.

As used herein, “standard cell assay” means the assay described in Example 1 and reasonable variations thereof.

As used herein, “stereorandom” in the context of a population of molecules of identical molecular formula means a chiral center having a random stereochemical configuration. For example, in a population of molecules comprising a stereorandom chiral center, the number of molecules having the (*S*) configuration of the stereorandom chiral center may be but is not necessarily the same as the number of molecules having the (*R*) configuration of the stereorandom chiral center. The stereochemical configuration of a chiral center is considered random when it is the result of a synthetic method that is not designed to control the stereochemical configuration. In certain embodiments, a stereorandom chiral center is a stereorandom phosphorothioate internucleoside linkage.

As used herein, “subject” means a human or non-human animal. In certain embodiments, the subject is a human.

As used herein, “sugar moiety” means an unmodified sugar moiety or a modified sugar moiety. As used herein, “unmodified sugar moiety” means a 2’-OH(H) ribosyl moiety, as found in RNA (an “unmodified RNA sugar moiety”), or a 2’-H(H) deoxyribosyl moiety, as found in DNA (an “unmodified DNA sugar moiety”). Unmodified sugar moieties have one hydrogen at each of the 1’, 3’, and 4’ positions, an oxygen at the 3’ position, and two hydrogens at the 5’ position. As used herein, “modified sugar moiety” or “modified sugar” means a modified furanosyl sugar moiety or a sugar surrogate.

As used herein, "sugar surrogate" means a modified sugar moiety having other than a furanosyl moiety that can link a nucleobase to another group, such as an internucleoside linkage, conjugate group, or terminal group in an oligonucleotide. Modified nucleosides comprising sugar surrogates can be incorporated into one or more positions within an oligonucleotide and such oligonucleotides are capable of hybridizing to complementary oligomeric compounds or nucleic acids.

As used herein, “symptom or hallmark” means any physical feature or test result that indicates the existence or extent of a disease or disorder. In certain embodiments, a symptom is apparent to a subject or to a medical professional examining or testing said subject. In certain embodiments, a hallmark is apparent upon invasive diagnostic testing, including, but not limited to, post-mortem tests.

As used herein, “target nucleic acid” and “target RNA” mean a nucleic acid that an antisense compound is designed to affect.

As used herein, “target region” means a portion of a target nucleic acid to which an oligomeric compound is designed to hybridize.

As used herein, "terminal group" means a chemical group or group of atoms that is covalently linked to a terminus of an oligonucleotide.

As used herein, "therapeutically effective amount" means an amount of a pharmaceutical agent that provides a therapeutic benefit to a subject. For example, a therapeutically effective amount improves a symptom or hallmark of a disease.

CERTAIN EMBODIMENTS

The present disclosure provides the following non-limiting numbered embodiments:

Embodiment 1. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides wherein the nucleobase sequence of the modified oligonucleotide is at least 90% complementary to an equal length portion of a KCNT1 nucleic acid, and wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

Embodiment 2. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 contiguous nucleobases of any of SEQ ID NOS: 21-2939.

Embodiment 3. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or at least 20 contiguous nucleobases complementary to:

an equal length portion of nucleobases 24523-24561 of SEQ ID NO: 2,
an equal length portion of nucleobases 27568-27603 of SEQ ID NO: 2,
an equal length portion of nucleobases 30772-30811 of SEQ ID NO: 2,
an equal length portion of nucleobases 54372-54428of SEQ ID NO: 2,
an equal length portion of nucleobases 55785-55818 of SEQ ID NO: 2,
an equal length portion of nucleobases 56048-56073 of SEQ ID NO: 2,
an equal length portion of nucleobases 56319-56349 of SEQ ID NO: 2,
an equal length portion of nucleobases 57683-57710 of SEQ ID NO: 2,
an equal length portion of nucleobases 61117-61153 of SEQ ID NO: 2,
an equal length portion of nucleobases 71033-71060 of SEQ ID NO: 2,
an equal length portion of nucleobases 87135-87174 of SEQ ID NO: 2,
an equal length portion of nucleobases 92109-92149 of SEQ ID NO: 2,
an equal length portion of nucleobases 94221-94280 of SEQ ID NO: 2,
an equal length portion of nucleobases 94352-94380 of SEQ ID NO: 2,
an equal length portion of nucleobases 94993-95036 of SEQ ID NO: 2, or
an equal length portion of nucleobases 95074-95144 of SEQ ID NO: 2.

Embodiment 4. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least

11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or at least 20 contiguous nucleobases complementary to:

an equal length portion of nucleobases 16586-16649 of SEQ ID NO: 2,
an equal length portion of nucleobases 16586-17823 of SEQ ID NO: 2,
an equal length portion of nucleobases 16586-18663 of SEQ ID NO: 2,
an equal length portion of nucleobases 19220-20568 of SEQ ID NO: 2,
an equal length portion of nucleobases 23003-25391 of SEQ ID NO: 2,
an equal length portion of nucleobases 27095-29908 of SEQ ID NO: 2,
an equal length portion of nucleobases 30452-30891 of SEQ ID NO: 2,
an equal length portion of nucleobases 31773-34427 of SEQ ID NO: 2,
an equal length portion of nucleobases 38458-47003 of SEQ ID NO: 2,
an equal length portion of nucleobases 40432-42873 of SEQ ID NO: 2,
an equal length portion of nucleobases 44414-45718 of SEQ ID NO: 2,
an equal length portion of nucleobases 52096-52153 of SEQ ID NO: 2,
an equal length portion of nucleobases 52096-58525 of SEQ ID NO: 2,
an equal length portion of nucleobases 59308-61697 of SEQ ID NO: 2,
an equal length portion of nucleobases 60111-61697 of SEQ ID NO: 2,
an equal length portion of nucleobases 65270-67169 of SEQ ID NO: 2,
an equal length portion of nucleobases 65270-67150 of SEQ ID NO: 2,
an equal length portion of nucleobases 67026-67065 of SEQ ID NO: 2,
an equal length portion of nucleobases 67026-67087 of SEQ ID NO: 2,
an equal length portion of nucleobases 67648-68527 of SEQ ID NO: 2,
an equal length portion of nucleobases 67955-67998 of SEQ ID NO: 2,
an equal length portion of nucleobases 68515-68583 of SEQ ID NO: 2,
an equal length portion of nucleobases 68538-68592 of SEQ ID NO: 2,
an equal length portion of nucleobases 68571-70874 of SEQ ID NO: 2,
an equal length portion of nucleobases 71037-71313 of SEQ ID NO: 2,
an equal length portion of nucleobases 71037-71184 of SEQ ID NO: 2,
an equal length portion of nucleobases 72851-72887 of SEQ ID NO: 2,
an equal length portion of nucleobases 79368-79483 of SEQ ID NO: 2,
an equal length portion of nucleobases 86554-90150 of SEQ ID NO: 2,
an equal length portion of nucleobases 88332-88448 of SEQ ID NO: 2,
an equal length portion of nucleobases 91686-95485 of SEQ ID NO: 2,
an equal length portion of nucleobases 91686-94431 of SEQ ID NO: 2, or
an equal length portion of nucleobases 94219-94275 of SEQ ID NO: 2.

Embodiment 5. The oligomeric compound of any one of embodiments 1-4, wherein the modified oligonucleotide has a nucleobase sequence that is at least 80%, 85%, 90%, 95%, or 100% complementary to an equal length portion of a nucleobase sequence selected from SEQ ID NOS: 1-3 when measured across the entire nucleobase sequence of the modified oligonucleotide.

Embodiment 6. The oligomeric compound of any one of embodiments 1-5, wherein at least one modified nucleoside comprises a modified sugar moiety.

Embodiment 7. The oligomeric compound of embodiment 6, wherein the modified sugar moiety comprises a bicyclic sugar moiety.

Embodiment 8. The oligomeric compound of embodiment 7, wherein the bicyclic sugar moiety comprises a 2'-4' bridge selected from –O-CH_2-; and –O-CH(CH_3)-.

Embodiment 9. The oligomeric compound of embodiment 6, wherein the modified sugar moiety comprises a non-bicyclic modified sugar moiety.

Embodiment 10. The oligomeric compound of embodiment 9, wherein the non-bicyclic modified sugar moiety comprises a 2'-MOE sugar moiety or 2'-OMe sugar moiety.

Embodiment 11. The oligomeric compound of any one of embodiments 1-5, wherein at least one modified nucleoside comprises a sugar surrogate.

Embodiment 12. The oligomeric compound of embodiment 11, wherein the sugar surrogate is selected from morpholino and PNA.

Embodiment 13. The oligomeric compound of any of embodiments 1-12, wherein the modified oligonucleotide has a sugar motif comprising:

a 5'-region consisting of 1-5 linked 5'-region nucleosides;

a central region consisting of 6-10 linked central region nucleosides; and

a 3'-region consisting of 1-5 linked 3'-region nucleosides; wherein

each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety and each of the central region nucleosides comprises an unmodified 2'-deoxyribosyl sugar moiety.

Embodiment 14. The oligomeric compound of any one of embodiments 1-13, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage.

Embodiment 15. The oligomeric compound of embodiment 14, wherein each internucleoside linkage of the modified oligonucleotide is a modified internucleoside linkage.

Embodiment 16. The oligomeric compound of embodiment 14 or 15 wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage.

Embodiment 17. The oligomeric compound of embodiment 14 or 16 wherein the modified oligonucleotide comprises at least one phosphodiester internucleoside linkage.

Embodiment 18. The oligomeric compound of any of embodiments 14, 16, or 17, wherein each internucleoside linkage is independently selected from a phosphodiester internucleoside linkage or a phosphorothioate internucleoside linkage.

Embodiment 19. The oligomeric compound of any of embodiments 1-18, wherein the modified oligonucleotide comprises at least one modified nucleobase.

Embodiment 20. The oligomeric compound of embodiment 19, wherein the modified nucleobase is a 5-methyl cytosine.

Embodiment 21. The oligomeric compound of any of embodiments 1-20, wherein the modified oligonucleotide consists of 12-30, 12-22, 12-20, 14-20, 15-25, 16-20, 18-22 or 18-20 linked nucleosides.

Embodiment 22. The oligomeric compound of any of embodiments 1-21, wherein the modified oligonucleotide consists of 20 linked nucleosides.

Embodiment 23. The oligomeric compound of embodiment 22, wherein the modified oligonucleotide has the internucleoside linkage motif soooossssssssssooss, wherein "s" represents a phosphorothioate internucleoside linkage and "o" represents a phosphodiester internucleoside linkage.

Embodiment 24. The oligomeric compound of any of embodiments 1-23, consisting of the modified oligonucleotide.

Embodiment 25. The oligomeric compound of any of embodiments 1-23, comprising a conjugate group comprising a conjugate moiety and a conjugate linker.

Embodiment 26. The oligomeric compound of embodiment 25, wherein the conjugate group comprises a GalNAc cluster comprising 1-3 GalNAc ligands.

Embodiment 27. The oligomeric compound of embodiments 25 or 26, wherein the conjugate linker consists of a single bond.

Embodiment 28. The oligomeric compound of embodiment 25, wherein the conjugate linker is cleavable.

Embodiment 29. The oligomeric compound of embodiment 28, wherein the conjugate linker comprises 1-3 linker-nucleosides.

Embodiment 30. The oligomeric compound of any of embodiments 25-29, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.

Embodiment 31. The oligomeric compound of any of embodiments 25-29, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.

Embodiment 32. The oligomeric compound of any of embodiments 1-31 comprising a terminal group.

Embodiment 33. The oligomeric compound of any of embodiments 1-32 wherein the oligomeric compound is a singled-stranded oligomeric compound.

Embodiment 34. The oligomeric compound of any of embodiments 1-28 or 30-31, wherein the oligomeric compound does not comprise linker-nucleosides.

Embodiment 35. The oligomeric compound of any one of embodiments 1-34, wherein the modified oligonucleotide of the oligomeric compound is a salt, and wherein the salt is a sodium salt or a potassium salt.

Embodiment 36. An oligomeric duplex comprising an oligomeric compound of any of embodiments 1-32, 34, or 35.

Embodiment 37. An antisense compound comprising or consisting of an oligomeric compound of any of embodiments 1-35 or an oligomeric duplex of embodiment 36.

Embodiment 38. A pharmaceutical composition comprising an oligomeric compound of any of embodiments 1-35 or an oligomeric duplex of embodiment 36, and a pharmaceutically acceptable carrier or diluent.

Embodiment 39. The pharmaceutical composition of embodiment 38, wherein the pharmaceutically acceptable diluent is artificial cerebrospinal fluid or PBS.

Embodiment 40. The pharmaceutical composition of embodiment 39, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and artificial cerebrospinal fluid.

Embodiment 41. A method comprising administering to a subject a pharmaceutical composition of any of embodiments 38-40.

Embodiment 42. A method of treating a neurological condition comprising administering to an individual having or at risk for developing the neurological condition a therapeutically effective amount of a pharmaceutical composition according to any of embodiments 38-40; and thereby treating the neurological condition.

Embodiment 43. A method of reducing KCNT1 RNA or KCNT1 protein in the central nervous system of an individual having or at risk for developing a neurological condition comprising administering a therapeutically effective amount of a pharmaceutical composition according to any of embodiments 38-40; and thereby reducing KCNT1 RNA or KCNT1 protein in the central nervous system.

Embodiment 44. The method of embodiment 42 or 43, wherein the neurological condition comprises encephalopathy.

Embodiment 45. The method of embodiment 42 or 43, wherein the neurological condition comprises epilepsy.

Embodiment 46. The method of embodiment 42 or 43, wherein the neurological condition comprises infantile epilepsy.

Embodiment 47. The method of embodiment 46, wherein the infantile epilepsy is epilepsy of infancy with migrating focal seizures (EIMFS).

Embodiment 48. The method of embodiment 42 or 43, wherein the neurological condition is autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE).

Embodiment 49. The method of any of embodiments 42-48, wherein the administering is by intrathecal administration.

Embodiment 50. The method of any of embodiments 42-49, wherein at least one symptom or hallmark of the neurological condition is ameliorated.

Embodiment 51. The method of embodiment 50, wherein the symptom or hallmark is selected from seizure, brain damage, demyelination, hypotonia, microcephaly, depression, anxiety, cognitive function.

Embodiment 52. The method of any of embodiments 42-51, wherein the method prevents or slows disease regression.

Embodiment 53. A method of reducing KCNT1 RNA in a cell comprising contacting the cell with an oligomeric compound according to any of embodiments 1-35, an oligomeric duplex according to embodiment 36, or an antisense compound according to embodiment 37; and thereby reducing KCNT1 RNA in the cell.

Embodiment 4. A method of reducing KCNT1 protein in a cell comprising contacting the cell with an oligomeric compound according to any of embodiments 1-35, an oligomeric duplex according to embodiment 36, or an antisense compound according to embodiment 37; and thereby reducing KCNT1 protein in the cell.

I. Certain Oligonucleotides

In certain embodiments, provided herein are oligomeric compounds comprising oligonucleotides, which consist of linked nucleosides. Oligonucleotides may be unmodified oligonucleotides (RNA or DNA) or may be modified oligonucleotides. Modified oligonucleotides comprise at least one modification relative to unmodified RNA or DNA. That is, modified oligonucleotides comprise at least one modified nucleoside (comprising a modified sugar moiety and/or a modified nucleobase) and/or at least one modified internucleoside linkage.

A. Certain Modified Nucleosides

Modified nucleosides comprise a modified sugar moiety or a modified nucleobase or both a modifed sugar moiety and a modified nucleobase.

1. Certain Sugar Moieties

In certain embodiments, modified sugar moieties are non-bicyclic modified sugar moieties. In certain embodiments, modified sugar moieties are bicyclic or tricyclic sugar moieties. In certain embodiments, modified sugar moieties are sugar surrogates. Such sugar surrogates may comprise one or more substitutions corresponding to those of other types of modified sugar moieties.

In certain embodiments, modified sugar moieties are non-bicyclic modified sugar moieties comprising a furanosyl ring with one or more substituent groups none of which bridges two atoms of the furanosyl ring to form a bicyclic structure. Such non-bridging substituents may be at any position of the furanosyl, including but not limited to substituents at the 2', 4', and/or 5' positions. In certain embodiments one or more non-bridging substituent of non-bicyclic modified sugar moieties is branched. Examples of 2'-substituent groups suitable for non-bicyclic modified sugar moieties include but are not limited to: 2'-F, 2'-

OCH_3 ("OMe" or "O-methyl"), and 2'-$O(CH_2)_2OCH_3$ ("MOE"). In certain embodiments, 2'-substituent groups are selected from among: halo, allyl, amino, azido, SH, CN, OCN, CF_3, OCF_3, O-C_1-C_{10} alkoxy, O-C_1-C_{10} substituted alkoxy, O-C_1-C_{10} alkyl, O-C_1-C_{10} substituted alkyl, S-alkyl, N(R_m)-alkyl, O-alkenyl, S-alkenyl, N(R_m)-alkenyl, O-alkynyl, S-alkynyl, N(R_m)-alkynyl, O-alkylenyl-O-alkyl, alkynyl, alkaryl, aralkyl, O-alkaryl, O-aralkyl, $O(CH_2)_2SCH_3$, $O(CH_2)_2ON(R_m)(R_n)$ or $OCH_2C(=O)$-$N(R_m)(R_n)$, where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C_1-C_{10} alkyl, and the 2'-substituent groups described in Cook et al., U.S. 6,531,584; Cook et al., U.S. 5,859,221; and Cook et al., U.S. 6,005,087. Certain embodiments of these 2'-substituent groups can be further substituted with one or more substituent groups independently selected from among: hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro (NO_2), thiol, thioalkoxy, thioalkyl, halogen, alkyl, aryl, alkenyl and alkynyl. Examples of 4'-substituent groups suitable for non-bicyclic modified sugar moieties include but are not limited to alkoxy (*e.g.*, methoxy), alkyl, and those described in Manoharan et al., WO 2015/106128. Examples of 5'-substituent groups suitable for non-bicyclic modified sugar moieties include but are not limited to: 5-methyl (R or S), 5'-vinyl, and 5'-methoxy. In certain embodiments, non-bicyclic modified sugar moieties comprise more than one non-bridging sugar substituent, for example, 2'-F-5'-methyl sugar moieties and the modified sugar moieties and modified nucleosides described in Migawa et al., WO 2008/101157 and Rajeev et al., US2013/0203836.).

In certain embodiments, a 2'-substituted non-bicyclic modified nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, NH_2, N_3, OCF_3, OCH_3, $O(CH_2)_3NH_2$, $CH_2CH{=}CH_2$, $OCH_2CH{=}CH_2$, $OCH_2CH_2OCH_3$, $O(CH_2)_2SCH_3$, $O(CH_2)_2ON(R_m)(R_n)$, $O(CH_2)_2O(CH_2)_2N(CH_3)_2$, and N-substituted acetamide ($OCH_2C(=O)$-$N(R_m)(R_n)$), where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C_1-C_{10} alkyl.

In certain embodiments, a 2'-substituted nucleoside non-bicyclic modified nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, OCF_3, OCH_3, $OCH_2CH_2OCH_3$, $O(CH_2)_2SCH_3$, $O(CH_2)_2ON(CH_3)_2$, $O(CH_2)_2O(CH_2)_2N(CH_3)_2$, and $OCH_2C(=O)$-$N(H)CH_3$ ("NMA").

In certain embodiments, a 2'-substituted non-bicyclic modified nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, OCH_3, and $OCH_2CH_2OCH_3$.

Certain modifed sugar moieties comprise a substituent that bridges two atoms of the furanosyl ring to form a second ring, resulting in a bicyclic sugar moiety. In certain such embodiments, the bicyclic sugar moiety comprises a bridge between the 4' and the 2' furanose ring atoms. Examples of such 4' to 2' bridging sugar substituents include but are not limited to: 4'-CH_2-2', 4'-$(CH_2)_2$-2', 4'-$(CH_2)_3$-2', 4'-CH_2-O-2' ("LNA"), 4'-CH_2-S-2', 4'-$(CH_2)_2$-O-2' ("ENA"), 4'-$CH(CH_3)$-O-2' (referred to as "constrained ethyl" or "cEt"), 4'-CH_2-O-CH_2-2', 4'-CH_2-N(R)-2', 4'-$CH(CH_2OCH_3)$-O-2' ("constrained MOE" or "cMOE") and analogs thereof (*see, e.g.,* Seth et al., U.S. 7,399,845, Bhat et al., U.S. 7,569,686, Swayze et al., U.S. 7,741,457, and Swayze

et al., U.S. 8,022,193), 4'-C(CH_3)(CH_3)-O-2' and analogs thereof (*see, e.g.*,Seth et al., U.S. 8,278,283), 4'-CH_2-N(OCH_3)-2' and analogs thereof (*see, e.g.,* Prakash et al., U.S. 8,278,425), 4'-CH_2-O-N(CH_3)-2' (*see, e.g.,* Allerson et al., U.S. 7,696,345 and Allerson et al., U.S. 8,124,745), 4'-CH_2-C(H)(CH_3)-2' (*see, e.g.,* Zhou, *et al., J. Org. Chem.*,2009, *74*, 118-134), 4'-CH_2-C(=CH_2)-2' and analogs thereof (*see e.g.*, Seth et al., U.S. 8,278,426), 4'-C(R_aR_b)-N(R)-O-2', 4'-C(R_aR_b)-O-N(R)-2', 4'-CH_2-O-N(R)-2', and 4'-CH_2-N(R)-O-2', wherein each R, R_a, and R_b is, independently, H, a protecting group, or C_1-C_{12} alkyl (*see, e.g.* Imanishi et al., U.S. 7,427,672).

In certain embodiments, such 4' to 2' bridges independently comprise from 1 to 4 linked groups independently selected from: -[C(R_a)(R_b)]$_n$-, -[C(R_a)(R_b)]$_n$-O-, -C(R_a)=C(R_b)-, -C(R_a)=N-, -C(=NR_a)-, -C(=O)-, -C(=S)-, -O-, -Si(R_a)$_2$-, -S(=O)$_x$-, and -N(R_a)-;

wherein:

x is 0, 1, or 2;

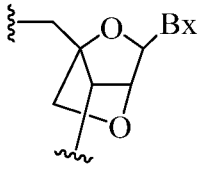
n is 1, 2, 3, or 4;

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

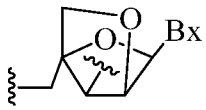
each J_1 and J_2 is, independently, H, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, acyl (C(=O)-H), substituted acyl, a heterocycle radical, a substituted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

Additional bicyclic sugar moieties are known in the art, see, for example: Freier *et al., Nucleic Acids Research*, 1997, *25*(*22*), 4429-4443, Albaek *et al., J. Org. Chem.*, 2006, *71*, 7731-7740, Singh et al., *Chem. Commun.*, 1998, *4*, 455-456; Koshkin et al., *Tetrahedron*, 1998, *54*, 3607-3630; Kumar et al., *Bioorg. Med. Chem. Lett.*, 1998, *8*, 2219-2222; Singh et al., *J. Org. Chem.*, 1998, *63*, 10035-10039; Srivastava et al., *J. Am. Chem. Soc.*, 2007, *129,* 8362-8379;Wengel et a., U.S. 7,053,207; Imanishi et al., U.S. 6,268,490; Imanishi et al. U.S. 6,770,748; Imanishi et al., U.S. RE44,779; Wengel et al., U.S. 6,794,499; Wengel et al., U.S. 6,670,461; Wengel et al., U.S. 7,034,133; Wengel et al., U.S. 8,080,644; Wengel et al., U.S. 8,034,909; Wengel et al., U.S. 8,153,365; Wengel et al., U.S. 7,572,582; and Ramasamy et al., U.S. 6,525,191; Torsten et al., WO 2004/106356;Wengel et al., WO 1999/014226; Seth et al., WO 2007/134181; Seth et al., U.S. 7,547,684; Seth et al., U.S. 7,666,854; Seth et al., U.S. 8,088,746; Seth et al., U.S. 7,750,131; Seth et al., U.S. 8,030,467; Seth et al., U.S. 8,268,980; Seth et al., U.S. 8,546,556; Seth et al., U.S. 8,530,640; Migawa et al., U.S. 9,012,421; Seth et al., U.S. 8,501,805; and U.S. Patent Publication Nos. Allerson et al., US2008/0039618 and Migawa et al., US2015/0191727.

In certain embodiments, bicyclic sugar moieties and nucleosides incorporating such bicyclic sugar moieties are further defined by isomeric configuration. For example, an LNA nucleoside (described herein) may be in the α-L configuration or in the β-D configuration.



LNA (β-D-configuration)
bridge = 4'-CH_2-O-2'



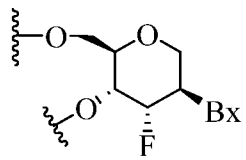
α-*L*-LNA (α-*L*-configuration)
bridge = 4'-CH_2-O-2'

α-L-methyleneoxy (4'-CH_2-O-2') or α-L-LNA bicyclic nucleosides have been incorporated into oligonucleotides that showed antisense activity (Frieden et al., *Nucleic Acids Research,* 2003, *21*, 6365-6372). Herein, general descriptions of bicyclic nucleosides include both isomeric configurations. When the positions of specific bicyclic nucleosides (*e.g.*, LNA or cEt) are identified in exemplified embodiments herein, they are in the β-D configuration, unless otherwise specified.

In certain embodiments, modified sugar moieties comprise one or more non-bridging sugar substituent and one or more bridging sugar substituent (*e.g.*, 5'-substituted and 4'-2' bridged sugars).

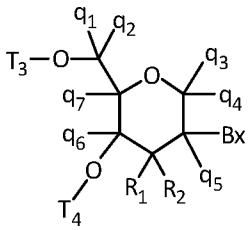
In certain embodiments, modified sugar moieties are sugar surrogates. In certain such embodiments, the oxygen atom of the sugar moiety is replaced, *e.g.,* with a sulfur, carbon or nitrogen atom. In certain such embodiments, such modified sugar moieties also comprise bridging and/or non-bridging substituents as described herein. For example, certain sugar surrogates comprise a 4'-sulfur atom and a substitution at the 2'-position (*see*, *e.g.,* Bhat et al., U.S. 7,875,733 and Bhat et al., U.S. 7,939,677) and/or the 5' position.

In certain embodiments, sugar surrogates comprise rings having other than 5 atoms. For example, in certain embodiments, a sugar surrogate comprises a six-membered tetrahydropyran ("THP"). Such tetrahydropyrans may be further modified or substituted. Nucleosides comprising such modified tetrahydropyrans include but are not limited to hexitol nucleic acid ("HNA"), anitol nucleic acid ("ANA"), manitol nucleic acid ("MNA") (*see, e.g.,* Leumann, CJ. *Bioorg. & Med. Chem.* 2002, *10*, 841-854), fluoro HNA:



F-HNA

("F-HNA", *see e.g.* Swayze et al., U.S. 8,088,904; Swayze et al., U.S. 8,440,803; Swayze et al., U.S. 8,796,437; and Swayze et al., U.S. 9,005,906; F-HNA can also be referred to as a F-THP or 3'-fluoro tetrahydropyran), and nucleosides comprising additional modified THP compounds having the formula:



wherein, independently, for each of said modified THP nucleoside:

Bx is a nucleobase moiety;

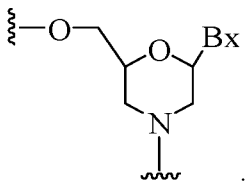
T_3 and T_4 are each, independently, an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide or one of T_3 and T_4 is an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide and the other of T_3 and T_4 is H, a hydroxyl protecting group, a linked conjugate group, or a 5' or 3'-terminal group;

q_1, q_2, q_3, q_4, q_5, q_6 and q_7 are each, independently, H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl, or substituted C_2-C_6 alkynyl; and

each of R_1 and R_2 is independently selected from among: hydrogen, halogen, substituted or unsubstituted alkoxy, NJ_1J_2, SJ_1, N_3, $OC(=X)J_1$, $OC(=X)NJ_1J_2$, $NJ_3C(=X)NJ_1J_2$, and CN, wherein X is O, S or NJ_1, and each J_1, J_2, and J_3 is, independently, H or C_1-C_6 alkyl.

In certain embodiments, modified THP nucleosides are provided wherein q_1, q_2, q_3, q_4, q_5, q_6 and q_7 are each H. In certain embodiments, at least one of q_1, q_2, q_3, q_4, q_5, q_6 and q_7 is other than H. In certain embodiments, at least one of q_1, q_2, q_3, q_4, q_5, q_6 and q_7 is methyl. In certain embodiments, modified THP nucleosides are provided wherein one of R_1 and R_2 is F. In certain embodiments, R_1 is F and R_2 is H, in certain embodiments, R_1 is methoxy and R_2 is H, and in certain embodiments, R_1 is methoxyethoxy and R_2 is H.

In certain embodiments, sugar surrogates comprise rings having more than 5 atoms and more than one heteroatom. For example, nucleosides comprising morpholino sugar moieties and their use in oligonucleotides have been reported (*see, e.g.,* Braasch et al., Biochemistry, 2002, *41*, 4503-4510 and Summerton et al., U.S. 5,698,685; Summerton et al., U.S. 5,166,315; Summerton et al., U.S. 5,185,444; and Summerton et al., U.S. 5,034,506). As used here, the term "morpholino" means a sugar surrogate having the following structure:



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

In certain embodiments, sugar surrogates comprise acyclic moieites. Examples of nucleosides and oligonucleotides comprising such acyclic sugar surrogates include but are not limited to: peptide nucleic acid ("PNA"), acyclic butyl nucleic acid (*see, e.g.,* Kumar et al., *Org. Biomol. Chem.*, 2013, *11*, 5853-5865), and nucleosides and oligonucleotides described in Manoharan et al., WO2011/133876.

Many other bicyclic and tricyclic sugar and sugar surrogate ring systems are known in the art that can be used in modified nucleosides.

2. Certain Modified Nucleobases

In certain embodiments, modified oligonucleotides comprise one or more nucleoside comprising an unmodified nucleobase. In certain embodiments, modified oligonucleotides comprise one or more nucleoside comprising a modified nucleobase. In certain embodiments, modified oligonucleotides comprise one or more nucleoside that does not comprise a nucleobase, referred to as an abasic nucleoside.

In certain embodiments, modified nucleobases are selected from: 5-substituted pyrimidines, 6-azapyrimidines, alkyl or alkynyl substituted pyrimidines, alkyl substituted purines, and N-2, N-6 and O-6 substituted purines. In certain embodiments, modified nucleobases are selected from: 2-aminopropyladenine, 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-N-methylguanine, 6-N-methyladenine, 2-propyladenine , 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-propynyl (-C≡C-CH_3) uracil, 5-propynylcytosine, 6-azouracil, 6-azocytosine, 6-azothymine, 5-ribosyluracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl, 8-aza and other 8-substituted purines, 5-halo, particularly 5-bromo, 5-trifluoromethyl, 5-halouracil, and 5-halocytosine, 7-methylguanine, 7-methyladenine, 2-F-adenine, 2-aminoadenine, 7-deazaguanine, 7-deazaadenine, 3-deazaguanine, 3-deazaadenine, 6-N-benzoyladenine, 2-N-isobutyrylguanine, 4-N-benzoylcytosine, 4-N-benzoyluracil, 5-methyl 4-N-benzoylcytosine, 5-methyl 4-N-benzoyluracil, universal bases, hydrophobic bases, promiscuous bases, size-expanded bases, and fluorinated bases. Further modified nucleobases include tricyclic pyrimidines, such as 1,3-diazaphenoxazine-2-one, 1,3-diazaphenothiazine-2-one and 9-(2-aminoethoxy)-1,3-diazaphenoxazine-2-one (G-clamp). Modified nucleobases may also include those in which the purine or pyrimidine base is replaced with other heterocycles, for example 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine and 2-pyridone. Further nucleobases include those disclosed in Merigan et al., U.S. 3,687,808, those disclosed in *The Concise Encyclopedia Of Polymer Science And Engineering*, Kroschwitz, J.I., Ed., John Wiley & Sons, 1990, 858-859; Englisch *et al.*, *Angewandte Chemie*, International Edition, 1991, *30*, 613; Sanghvi, Y.S., Chapter 15, *Antisense Research and Applications*, Crooke, S.T. and Lebleu, B., Eds., CRC Press, 1993, 273-288; and those disclosed in Chapters 6 and 15, *Antisense Drug Technology*, Crooke S.T., Ed., CRC Press, 2008, 163-166 and 442-443.

Publications that teach the preparation of certain of the above noted modified nucleobases as well as other modified nucleobases include without limitation, Manoharan et al., US2003/0158403; Manoharan et al., US2003/0175906; Dinh et al., U.S. 4,845,205; Spielvogel et al., U.S. 5,130,302; Rogers et al., U.S.

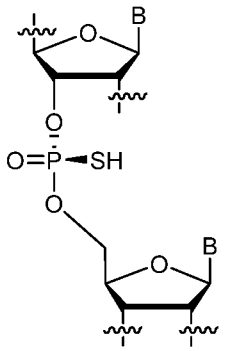
5,134,066; Bischofberger et al., U.S. 5,175,273; Urdea et al., U.S. 5,367,066; Benner et al., U.S. 5,432,272; Matteucci et al., U.S. 5,434,257; Gmeiner et al., U.S. 5,457,187; Cook et al., U.S. 5,459,255; Froehler et al., U.S. 5,484,908; Matteucci et al., U.S. 5,502,177; Hawkins et al., U.S. 5,525,711; Haralambidis et al., U.S. 5,552,540; Cook et al., U.S. 5,587,469; Froehler et al., U.S. 5,594,121; Switzer et al., U.S. 5,596,091; Cook et al., U.S. 5,614,617; Froehler et al., U.S. 5,645,985; Cook et al., U.S. 5,681,941; Cook et al., U.S. 5,811,534; Cook et al., U.S. 5,750,692; Cook et al., U.S. 5,948,903; Cook et al., U.S. 5,587,470; Cook et al., U.S. 5,457,191; Matteucci et al., U.S. 5,763,588; Froehler et al., U.S. 5,830,653; Cook et al., U.S. 5,808,027; Cook et al., 6,166,199; and Matteucci et al., U.S. 6,005,096.

3. Certain Modified Internucleoside Linkages

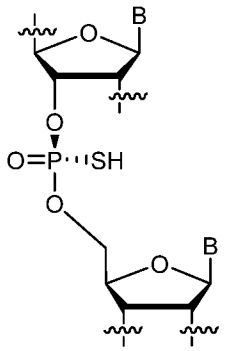
In certain embodiments, nucleosides of modified oligonucleotides may be linked together using any internucleoside linkage. The two main classes of internucleoside linking groups are defined by the presence or absence of a phosphorus atom. Representative phosphorus-containing internucleoside linkages include but are not limited to phosphates, which contain a phosphodiester bond ("P=O") (also referred to as unmodified or naturally occurring linkages), phosphotriesters, methylphosphonates, phosphoramidates, and phosphorothioates ("P=S"), and phosphorodithioates ("HS-P=S"). Representative non-phosphorus containing internucleoside linking groups include but are not limited to methylenemethylimino ($-CH_2-N(CH_3)-O-CH_2-$), thiodiester, thionocarbamate (-O-C(=O)(NH)-S-); siloxane ($-O-SiH_2-O-$); and N,N'-dimethylhydrazine ($-CH_2-N(CH_3)-N(CH_3)-$). Modified internucleoside linkages, compared to naturally occurring phosphate linkages, can be used to alter, typically increase, nuclease resistance of the oligonucleotide. In certain embodiments, internucleoside linkages having a chiral atom can be prepared as a racemic mixture, or as separate enantiomers. Methods of preparation of phosphorous-containing and non-phosphorous-containing internucleoside linkages are well known to those skilled in the art.

Representative internucleoside linkages having a chiral center include but are not limited to alkylphosphonates and phosphorothioates. Modified oligonucleotides comprising internucleoside linkages having a chiral center can be prepared as populations of modified oligonucleotides comprising stereorandom internucleoside linkages, or as populations of modified oligonucleotides comprising phosphorothioate linkages in particular stereochemical configurations. In certain embodiments, populations of modified oligonucleotides comprise phosphorothioate internucleoside linkages wherein all of the phosphorothioate internucleoside linkages are stereorandom. Such modified oligonucleotides can be generated using synthetic methods that result in random selection of the stereochemical configuration of each phosphorothioate linkage. Nonetheless, as is well understood by those of skill in the art, each individual phosphorothioate of each individual oligonucleotide molecule has a defined stereoconfiguration. In certain embodiments, populations of modified oligonucleotides are enriched for modified oligonucleotides comprising one or more particular phosphorothioate internucleoside linkages in a particular, independently selected stereochemical configuration. In certain embodiments, the particular configuration of the particular phosphorothioate linkage

is present in at least 65% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 70% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 80% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 90% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 99% of the molecules in the population. Such chirally enriched populations of modified oligonucleotides can be generated using synthetic methods known in the art, *e.g.*, methods described in Oka et al., *JACS* 125, 8307 (2003), Wan et al. *Nuc. Acid. Res.* 42, 13456 (2014), and WO 2017/015555. In certain embodiments, a population of modified oligonucleotides is enriched for modified oligonucleotides having at least one indicated phosphorothioate in the (*S*p) configuration. In certain embodiments, a population of modified oligonucleotides is enriched for modified oligonucleotides having at least one phosphorothioate in the (*R*p) configuration. In certain embodiments, modified oligonucleotides comprising (*R*p) and/or (*S*p) phosphorothioates comprise one or more of the following formulas, respectively, wherein "B" indicates a nucleobase:



(R_p)



(S_p)

Unless otherwise indicated, chiral internucleoside linkages of modified oligonucleotides described herein can be stereorandom or in a particular stereochemical configuration.

Neutral internucleoside linkages include, without limitation, phosphotriesters, methylphosphonates, MMI (3'-CH_2-N(CH_3)-O-5'), amide-3 (3'-CH_2-C(=O)-N(H)-5'), amide-4 (3'-CH_2-N(H)-C(=O)-5'), formacetal (3'-O-CH_2-O-5'), methoxypropyl, and thioformacetal (3'-S-CH_2-O-5'). Further neutral internucleoside linkages include nonionic linkages comprising siloxane (dialkylsiloxane), carboxylate ester, carboxamide, sulfide, sulfonate ester and amides (See for example: *Carbohydrate Modifications in Antisense Research*; Y.S. Sanghvi and P.D. Cook, Eds., ACS Symposium Series 580; Chapters 3 and 4, 40-65). Further neutral internucleoside linkages include nonionic linkages comprising mixed N, O, S and CH_2 component parts.

B. Certain Motifs

In certain embodiments, modified oligonucleotides comprise one or more modified nucleosides comprising a modified sugar moiety. In certain embodiments, modified oligonucleotides comprise one or

more modified nucleosides comprising a modified nucleobase. In certain embodiments, modified oligonucleotides comprise one or more modified internucleoside linkage. In such embodiments, the modified, unmodified, and differently modified sugar moieties, nucleobases, and/or internucleoside linkages of a modified oligonucleotide define a pattern or motif. In certain embodiments, the patterns of sugar moieties, nucleobases, and internucleoside linkages are each independent of one another. Thus, a modified oligonucleotide may be described by its sugar motif, nucleobase motif and/or internucleoside linkage motif (as used herein, nucleobase motif describes the modifications to the nucleobases independent of the sequence of nucleobases).

1. **Certain Sugar Motifs**

In certain embodiments, oligonucleotides comprise one or more type of modified sugar and/or unmodified sugar moiety arranged along the oligonucleotide or region thereof in a defined pattern or sugar motif. In certain instances, such sugar motifs include but are not limited to any of the sugar modifications discussed herein.

In certain embodiments, modified oligonucleotides comprise or consist of a region having a gapmer motif, which is defined by two external regions or "wings" and a central or internal region or "gap." The three regions of a gapmer motif (the 5'-wing, the gap, and the 3'-wing) form a contiguous sequence of nucleosides wherein at least some of the sugar moieties of the nucleosides of each of the wings differ from at least some of the sugar moieties of the nucleosides of the gap. Specifically, at least the sugar moieties of the nucleosides of each wing that are closest to the gap (the 3'-most nucleoside of the 5'-wing and the 5'-most nucleoside of the 3'-wing) differ from the sugar moiety of the neighboring gap nucleosides, thus defining the boundary between the wings and the gap (i.e., the wing/gap junction). In certain embodiments, the sugar moieties within the gap are the same as one another. In certain embodiments, the gap includes one or more nucleoside having a sugar moiety that differs from the sugar moiety of one or more other nucleosides of the gap. In certain embodiments, the sugar motifs of the two wings are the same as one another (symmetric gapmer). In certain embodiments, the sugar motif of the 5'-wing differs from the sugar motif of the 3'-wing (asymmetric gapmer).

In certain embodiments, the wings of a gapmer comprise 1-5 nucleosides. In certain embodiments, each nucleoside of each wing of a gapmer is a modified nucleoside. In certain embodiments, at least one nucleoside of each wing of a gapmer is a modified nucleoside. In certain embodiments, at least two nucleosides of each wing of a gapmer are modified nucleosides. In certain embodiments, at least three nucleosides of each wing of a gapmer are modified nucleosides. In certain embodiments, at least four nucleosides of each wing of a gapmer are modified nucleosides.

In certain embodiments, the gap of a gapmer comprises 7-12 nucleosides. In certain embodiments, each nucleoside of the gap of a gapmer is an unmodified 2'-deoxynucleoside. In certain embodiments, at least one nucleoside of the gap of a gapmer is a modified nucleoside.

In certain embodiments, the gapmer is a deoxy gapmer. In certain embodiments, the nucleosides on the gap side of each wing/gap junction are unmodified 2'-deoxynucleosides and the nucleosides on the wing sides of each wing/gap junction are modified nucleosides. In certain embodiments, each nucleoside of the gap is an unmodified 2'-deoxynucleoside. In certain embodiments, each nucleoside of each wing of a gapmer is a modified nucleoside.

In certain embodiments, modified oligonucleotides comprise or consist of a region having a fully modified sugar motif. In such embodiments, each nucleoside of the fully modified region of the modified oligonucleotide comprises a modified sugar moiety. In certain embodiments, each nucleoside of the entire modified oligonucleotide comprises a modified sugar moiety. In certain embodiments, modified oligonucleotides comprise or consist of a region having a fully modified sugar motif, wherein each nucleoside within the fully modified region comprises the same modified sugar moiety, referred to herein as a uniformly modified sugar motif. In certain embodiments, a fully modified oligonucleotide is a uniformly modified oligonucleotide. In certain embodiments, each nucleoside of a uniformly modified comprises the same 2'-modification.

Herein, the lengths (number of nucleosides) of the three regions of a gapmer may be provided using the notation [# of nucleosides in the 5'-wing] – [# of nucleosides in the gap] – [# of nucleosides in the 3'-wing]. Thus, a 5-10-5 gapmer consists of 5 linked nucleosides in each wing and 10 linked nucleosides in the gap. Where such nomenclature is followed by a specific modification, that modification is the modification in each sugar moiety of each wing and the gap nucleosides comprise unmodified deoxynucleosides sugars. Thus, a 5-10-5 MOE gapmer consists of 5 linked MOE modified nucleosides in the 5'-wing, 10 linked deoxynucleosides in the gap, and 5 linked MOE nucleosides in the 3'-wing.

In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, modified oligonucleotides are 3-10-3 BNA gapmers. In certain embodiments, modified oligonucleotides are 3-10-3 cEt gapmers. In certain embodiments, modified oligonucleotides are 3-10-3 LNA gapmers.

2. Certain Nucleobase Motifs

In certain embodiments, oligonucleotides comprise modified and/or unmodified nucleobases arranged along the oligonucleotide or region thereof in a defined pattern or motif. In certain embodiments, each nucleobase is modified. In certain embodiments, none of the nucleobases are modified. In certain embodiments, each purine or each pyrimidine is modified. In certain embodiments, each adenine is modified. In certain embodiments, each guanine is modified. In certain embodiments, each thymine is modified. In certain embodiments, each uracil is modified. In certain embodiments, each cytosine is modified. In certain embodiments, some or all of the cytosine nucleobases in a modified oligonucleotide are 5-methyl cytosines. In certain embodiments, all of the cytosine nucleobases are 5-methyl cytosines and all of the other nucleobases of the modified oligonucleotide are unmodified nucleobases.

In certain embodiments, modified oligonucleotides comprise a block of modified nucleobases. In certain such embodiments, the block is at the 3'-end of the oligonucleotide. In certain embodiments the block is within 3 nucleosides of the 3'-end of the oligonucleotide. In certain embodiments, the block is at the 5'-end of the oligonucleotide. In certain embodiments the block is within 3 nucleosides of the 5'-end of the oligonucleotide.

In certain embodiments, oligonucleotides having a gapmer motif comprise a nucleoside comprising a modified nucleobase. In certain such embodiments, one nucleoside comprising a modified nucleobase is in the central gap of an oligonucleotide having a gapmer motif. In certain such embodiments, the sugar moiety of said nucleoside is a 2'-deoxyribosyl moiety. In certain embodiments, the modified nucleobase is selected from: a 2-thiopyrimidine and a 5-propynepyrimidine.

3. Certain Internucleoside Linkage Motifs

In certain embodiments, oligonucleotides comprise modified and/or unmodified internucleoside linkages arranged along the oligonucleotide or region thereof in a defined pattern or motif. In certain embodiments, each internucleoside linking group is a phosphodiester internucleoside linkage (P=O). In certain embodiments, each internucleoside linking group of a modified oligonucleotide is a phosphorothioate internucleoside linkage (P=S). In certain embodiments, each internucleoside linkage of a modified oligonucleotide is independently selected from a phosphorothioate internucleoside linkage and phosphodiester internucleoside linkage. In certain embodiments, each phosphorothioate internucleoside linkage is independently selected from a stereorandom phosphorothioate a (*S*p) phosphorothioate, and a (*R*p) phosphorothioate. In certain embodiments, the sugar motif of a modified oligonucleotide is a gapmer and the internucleoside linkages within the gap are all modified. In certain such embodiments, some or all of the internucleoside linkages in the wings are unmodified phosphodiester internucleoside linkages. In certain embodiments, the terminal internucleoside linkages are modified. In certain embodiments, the sugar motif of a modified oligonucleotide is a gapmer, and the internucleoside linkage motif comprises at least one phosphodiester internucleoside linkage in at least one wing, wherein the at least one phosphodiester linkage is not a terminal internucleoside linkage, and the remaining internucleoside linkages are phosphorothioate internucleoside linkages. In certain such embodiments, all of the phosphorothioate linkages are stereorandom. In certain embodiments, all of the phosphorothioate linkages in the wings are (*S*p) phosphorothioates, and the gap comprises at least one *S*p, *S*p, *R*p motif. In certain embodiments, populations of modified oligonucleotides are enriched for modified oligonucleotides comprising such internucleoside linkage motifs.

C. Certain Lengths

It is possible to increase or decrease the length of an oligonucleotide without eliminating activity. For example, in Woolf et al. (Proc. Natl. Acad. Sci. USA 89:7305-7309, 1992), a series of oligonucleotides 13-25 nucleobases in length were tested for their ability to induce cleavage of a target RNA in an oocyte injection model. Oligonucleotides 25 nucleobases in length with 8 or 11 mismatch bases near

the ends of the oligonucleotides were able to direct specific cleavage of the target RNA, albeit to a lesser extent than the oligonucleotides that contained no mismatches. Similarly, target specific cleavage was achieved using 13 nucleobase oligonucleotides, including those with 1 or 3 mismatches.

In certain embodiments, oligonucleotides (including modified oligonucleotides) can have any of a variety of ranges of lengths. In certain embodiments, oligonucleotides consist of X to Y linked nucleosides, where X represents the fewest number of nucleosides in the range and Y represents the largest number nucleosides in the range. In certain such embodiments, X and Y are each independently selected from 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and 50; provided that $X \leq Y$. For example, in certain embodiments, oligonucleotides consist of 12 to 13, 12 to 14, 12 to 15, 12 to 16, 12 to 17, 12 to 18, 12 to 19, 12 to 20, 12 to 21, 12 to 22, 12 to 23, 12 to 24, 12 to 25, 12 to 26, 12 to 27, 12 to 28, 12 to 29, 12 to 30, 13 to 14, 13 to 15, 13 to 16, 13 to 17, 13 to 18, 13 to 19, 13 to 20, 13 to 21, 13 to 22, 13 to 23, 13 to 24, 13 to 25, 13 to 26, 13 to 27, 13 to 28, 13 to 29, 13 to 30, 14 to 15, 14 to 16, 14 to 17, 14 to 18, 14 to 19, 14 to 20, 14 to 21, 14 to 22, 14 to 23, 14 to 24, 14 to 25, 14 to 26, 14 to 27, 14 to 28, 14 to 29, 14 to 30, 15 to 16, 15 to 17, 15 to 18, 15 to 19, 15 to 20, 15 to 21, 15 to 22, 15 to 23, 15 to 24, 15 to 25, 15 to 26, 15 to 27, 15 to 28, 15 to 29, 15 to 30, 16 to 17, 16 to 18, 16 to 19, 16 to 20, 16 to 21, 16 to 22, 16 to 23, 16 to 24, 16 to 25, 16 to 26, 16 to 27, 16 to 28, 16 to 29, 16 to 30, 17 to 18, 17 to 19, 17 to 20, 17 to 21, 17 to 22, 17 to 23, 17 to 24, 17 to 25, 17 to 26, 17 to 27, 17 to 28, 17 to 29, 17 to 30, 18 to 19, 18 to 20, 18 to 21, 18 to 22, 18 to 23, 18 to 24, 18 to 25, 18 to 26, 18 to 27, 18 to 28, 18 to 29, 18 to 30, 19 to 20, 19 to 21, 19 to 22, 19 to 23, 19 to 24, 19 to 25, 19 to 26, 19 to 29, 19 to 28, 19 to 29, 19 to 30, 20 to 21, 20 to 22, 20 to 23, 20 to 24, 20 to 25, 20 to 26, 20 to 27, 20 to 28, 20 to 29, 20 to 30, 21 to 22, 21 to 23, 21 to 24, 21 to 25, 21 to 26, 21 to 27, 21 to 28, 21 to 29, 21 to 30, 22 to 23, 22 to 24, 22 to 25, 22 to 26, 22 to 27, 22 to 28, 22 to 29, 22 to 30, 23 to 24, 23 to 25, 23 to 26, 23 to 27, 23 to 28, 23 to 29, 23 to 30, 24 to 25, 24 to 26, 24 to 27, 24 to 28, 24 to 29, 24 to 30, 25 to 26, 25 to 27, 25 to 28, 25 to 29, 25 to 30, 26 to 27, 26 to 28, 26 to 29, 26 to 30, 27 to 28, 27 to 29, 27 to 30, 28 to 29, 28 to 30, or 29 to 30 linked nucleosides.

D. Certain Modified Oligonucleotides

In certain embodiments, the above modifications (sugar, nucleobase, internucleoside linkage) are incorporated into a modified oligonucleotide. In certain embodiments, modified oligonucleotides are characterized by their modification motifs and overall lengths. In certain embodiments, such parameters are each independent of one another. Thus, unless otherwise indicated, each internucleoside linkage of an oligonucleotide having a gapmer sugar motif may be modified or unmodified and may or may not follow the gapmer modification pattern of the sugar modifications. For example, the internucleoside linkages within the wing regions of a sugar gapmer may be the same or different from one another and may be the same or different from the internucleoside linkages of the gap region of the sugar motif. Likewise, such sugar gapmer

oligonucleotides may comprise one or more modified nucleobase independent of the gapmer pattern of the sugar modifications. Unless otherwise indicated, all modifications are independent of nucleobase sequence.

E. Certain Populations of Modified Oligonucleotides

Populations of modified oligonucleotides in which all of the modified oligonucleotides of the population have the same molecular formula can be stereorandom populations or chirally enriched populations. All of the chiral centers of all of the modified oligonucleotides are stereorandom in a stereorandom population. In a chirally enriched population, at least one particular chiral center is not stereorandom in the modified oligonucleotides of the population. In certain embodiments, the modified oligonucleotides of a chirally enriched population are enriched for β-D ribosyl sugar moieties, and all of the phosphorothioate internucleoside linkages are stereorandom. In certain embodiments, the modified oligonucleotides of a chirally enriched population are enriched for both β-D ribosyl sugar moieties and at least one, particular phosphorothioate internucleoside linkage in a particular stereochemical configuration.

F. Nucleobase Sequence

In certain embodiments, oligonucleotides (unmodified or modified oligonucleotides) are further described by their nucleobase sequence. In certain embodiments oligonucleotides have a nucleobase sequence that is complementary to a second oligonucleotide or an identified reference nucleic acid, such as a target nucleic acid. In certain such embodiments, a region of an oligonucleotide has a nucleobase sequence that is complementary to a second oligonucleotide or an identified reference nucleic acid, such as a target nucleic acid. In certain embodiments, the nucleobase sequence of a region or entire length of an oligonucleotide is at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% complementary to the second oligonucleotide or nucleic acid, such as a target nucleic acid.

I. Certain Oligomeric Compounds

In certain embodiments, provided herein are oligomeric compounds, which consist of an oligonucleotide (modified or unmodified) and optionally one or more conjugate groups and/or terminal groups. Conjugate groups consist of one or more conjugate moiety and a conjugate linker which links the conjugate moiety to the oligonucleotide. Conjugate groups may be attached to either or both ends of an oligonucleotide and/or at any internal position. In certain embodiments, conjugate groups are attached to the 2'-position of a nucleoside of a modified oligonucleotide. In certain embodiments, conjugate groups that are attached to either or both ends of an oligonucleotide are terminal groups. In certain such embodiments, conjugate groups or terminal groups are attached at the 3' and/or 5'-end of oligonucleotides. In certain such embodiments, conjugate groups (or terminal groups) are attached at the 3'-end of oligonucleotides. In certain embodiments, conjugate groups are attached near the 3'-end of oligonucleotides. In certain embodiments, conjugate groups (or terminal groups) are attached at the 5'-end of oligonucleotides. In certain embodiments, conjugate groups are attached near the 5'-end of oligonucleotides.

Examples of terminal groups include but are not limited to conjugate groups, capping groups,

phosphate moieties, protecting groups, modified or unmodified nucleosides, and two or more nucleosides that are independently modified or unmodified.

A. Certain Conjugate Groups

In certain embodiments, oligonucleotides are covalently attached to one or more conjugate groups. In certain embodiments, conjugate groups modify one or more properties of the attached oligonucleotide, including but not limited to pharmacodynamics, pharmacokinetics, stability, binding, absorption, tissue distribution, cellular distribution, cellular uptake, charge and clearance. In certain embodiments, conjugate groups impart a new property on the attached oligonucleotide, *e.g.*, fluorophores or reporter groups that enable detection of the oligonucleotide. Certain conjugate groups and conjugate moieties have been described previously, for example: cholesterol moiety (Letsinger et al., Proc. Natl. Acad. Sci. USA, 1989, 86, 6553-6556), cholic acid (Manoharan et al., *Bioorg. Med. Chem. Lett.*, 1994, *4*, 1053-1060), a thioether, *e.g.*, hexyl-S-tritylthiol (Manoharan et al., *Ann. N.Y. Acad. Sci.*, 1992, *660*, 306-309; Manoharan et al., *Bioorg. Med. Chem. Lett.*, 1993, *3*, 2765-2770), a thiocholesterol (Oberhauser et al., *Nucl. Acids Res.*, 1992, *20*, 533-538), an aliphatic chain, *e.g.*, do-decan-diol or undecyl residues (Saison-Behmoaras et al., *EMBO J.*, 1991, *10*, 1111-1118; Kabanov et al., *FEBS Lett.*, 1990, *259*, 327-330; Svinarchuk et al., *Biochimie*, 1993, *75*, 49-54), a phospholipid, *e.g.*, di-hexadecyl-rac-glycerol or triethyl-ammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate (Manoharan et al., *Tetrahedron Lett.*, 1995, *36*, 3651-3654; Shea et al., *Nucl. Acids Res.*, 1990, *18*, 3777-3783), a polyamine or a polyethylene glycol chain (Manoharan et al., *Nucleosides & Nucleotides*, 1995, *14*, 969-973), or adamantane acetic acid a palmityl moiety (Mishra et al., *Biochim. Biophys. Acta*, 1995, *1264*, 229-237), an octadecylamine or hexylamino-carbonyl-oxycholesterol moiety (Crooke et al., *J. Pharmacol. Exp. Ther.*, 1996, *277*, 923-937), a tocopherol group (Nishina et al., *Molecular Therapy Nucleic Acids*, 2015, *4*, e220; and Nishina et al., *Molecular Therapy*, 2008, *16*, 734-740), or a GalNAc cluster (*e.g.*, WO2014/179620).

1. Conjugate Moieties

Conjugate moieties include, without limitation, intercalators, reporter molecules, polyamines, polyamides, peptides, carbohydrates, vitamin moieties, polyethylene glycols, thioethers, polyethers, cholesterols, thiocholesterols, cholic acid moieties, folate, lipids, phospholipids, biotin, phenazine, phenanthridine, anthraquinone, adamantane, acridine, fluoresceins, rhodamines, coumarins, fluorophores, and dyes.

In certain embodiments, a conjugate moiety comprises an active drug substance, for example, aspirin, warfarin, phenylbutazone, ibuprofen, suprofen, fen-bufen, ketoprofen, (*S*)-(+)-pranoprofen, carprofen, dansylsarcosine, 2,3,5-triiodobenzoic acid, fingolimod, flufenamic acid, folinic acid, a benzothiadiazide, chlorothiazide, a diazepine, indo-methicin, a barbiturate, a cephalosporin, a sulfa drug, an antidiabetic, an antibacterial or an antibiotic.

2. Conjugate Linkers

Conjugate moieties are attached to oligonucleotides through conjugate linkers. In certain oligomeric compounds, the conjugate linker is a single chemical bond (i.e., the conjugate moiety is attached directly to an oligonucleotide through a single bond). In certain embodiments, the conjugate linker comprises a chain structure, such as a hydrocarbyl chain, or an oligomer of repeating units such as ethylene glycol, nucleosides, or amino acid units.

In certain embodiments, a conjugate linker comprises one or more groups selected from alkyl, amino, oxo, amide, disulfide, polyethylene glycol, ether, thioether, and hydroxylamino. In certain such embodiments, the conjugate linker comprises groups selected from alkyl, amino, oxo, amide and ether groups. In certain embodiments, the conjugate linker comprises groups selected from alkyl and amide groups. In certain embodiments, the conjugate linker comprises groups selected from alkyl and ether groups. In certain embodiments, the conjugate linker comprises at least one phosphorus moiety. In certain embodiments, the conjugate linker comprises at least one phosphate group. In certain embodiments, the conjugate linker includes at least one neutral linking group.

In certain embodiments, conjugate linkers, including the conjugate linkers described above, are bifunctional linking moieties, *e.g.*, those known in the art to be useful for attaching conjugate groups to parent compounds, such as the oligonucleotides provided herein. In general, a bifunctional linking moiety comprises at least two functional groups. One of the functional groups is selected to bind to a particular site on a parent compound and the other is selected to bind to a conjugate group. Examples of functional groups used in a bifunctional linking moiety include but are not limited to electrophiles for reacting with nucleophilic groups and nucleophiles for reacting with electrophilic groups. In certain embodiments, bifunctional linking moieties comprise one or more groups selected from amino, hydroxyl, carboxylic acid, thiol, alkyl, alkenyl, and alkynyl.

Examples of conjugate linkers include but are not limited to pyrrolidine, 8-amino-3,6-dioxaoctanoic acid (ADO), succinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC) and 6-aminohexanoic acid (AHEX or AHA). Other conjugate linkers include but are not limited to substituted or unsubstituted C_1-C_{10} alkyl, substituted or unsubstituted C_2-C_{10} alkenyl or substituted or unsubstituted C_2-C_{10} alkynyl, wherein a nonlimiting list of preferred substituent groups includes hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl.

In certain embodiments, conjugate linkers comprise 1-10 linker-nucleosides. In certain embodiments, conjugate linkers comprise 2-5 linker-nucleosides. In certain embodiments, conjugate linkers comprise exactly 3 linker-nucleosides. In certain embodiments, conjugate linkers comprise the TCA motif. In certain embodiments, such linker-nucleosides are modified nucleosides. In certain embodiments such linker-nucleosides comprise a modified sugar moiety. In certain embodiments, linker-nucleosides are unmodified. In certain embodiments, linker-nucleosides comprise an optionally protected heterocyclic base selected from a purine, substituted purine, pyrimidine or substituted pyrimidine. In certain embodiments, a

cleavable moiety is a nucleoside selected from uracil, thymine, cytosine, 4-N-benzoylcytosine, 5-methyl cytosine, 4-N-benzoyl-5-methyl cytosine, adenine, 6-N-benzoyladenine, guanine and 2-N-isobutyrylguanine. It is typically desirable for linker-nucleosides to be cleaved from the oligomeric compound after it reaches a target tissue. Accordingly, linker-nucleosides are typically linked to one another and to the remainder of the oligomeric compound through cleavable bonds. In certain embodiments, such cleavable bonds are phosphodiester bonds.

Herein, linker-nucleosides are not considered to be part of the oligonucleotide. Accordingly, in embodiments in which an oligomeric compound comprises an oligonucleotide consisting of a specified number or range of linked nucleosides and/or a specified percent complementarity to a reference nucleic acid and the oligomeric compound also comprises a conjugate group comprising a conjugate linker comprising linker-nucleosides, those linker-nucleosides are not counted toward the length of the oligonucleotide and are not used in determining the percent complementarity of the oligonucleotide for the reference nucleic acid. For example, an oligomeric compound may comprise (1) a modified oligonucleotide consisting of 8-30 nucleosides and (2) a conjugate group comprising 1-10 linker-nucleosides that are contiguous with the nucleosides of the modified oligonucleotide. The total number of contiguous linked nucleosides in such an oligomeric compound is more than 30. Alternatively, an oligomeric compound may comprise a modified oligonucleotide consisting of 8-30 nucleosides and no conjugate group. The total number of contiguous linked nucleosides in such an oligomeric compound is no more than 30. Unless otherwise indicated conjugate linkers comprise no more than 10 linker-nucleosides. In certain embodiments, conjugate linkers comprise no more than 5 linker-nucleosides. In certain embodiments, conjugate linkers comprise no more than 3 linker-nucleosides. In certain embodiments, conjugate linkers comprise no more than 2 linker-nucleosides. In certain embodiments, conjugate linkers comprise no more than 1 linker-nucleoside.

In certain embodiments, it is desirable for a conjugate group to be cleaved from the oligonucleotide. For example, in certain circumstances oligomeric compounds comprising a particular conjugate moiety are better taken up by a particular cell type, but once the oligomeric compound has been taken up, it is desirable that the conjugate group be cleaved to release the unconjugated or parent oligonucleotide. Thus, certain conjugate linkers may comprise one or more cleavable moieties. In certain embodiments, a cleavable moiety is a cleavable bond. In certain embodiments, a cleavable moiety is a group of atoms comprising at least one cleavable bond. In certain embodiments, a cleavable moiety comprises a group of atoms having one, two, three, four, or more than four cleavable bonds. In certain embodiments, a cleavable moiety is selectively cleaved inside a cell or subcellular compartment, such as a lysosome. In certain embodiments, a cleavable moiety is selectively cleaved by endogenous enzymes, such as nucleases.

In certain embodiments, a cleavable bond is selected from among: an amide, an ester, an ether, one or both esters of a phosphodiester, a phosphate ester, a carbamate, or a disulfide. In certain embodiments, a cleavable bond is one or both of the esters of a phosphodiester. In certain embodiments, a cleavable moiety

comprises a phosphate or phosphodiester. In certain embodiments, the cleavable moiety is a phosphate linkage between an oligonucleotide and a conjugate moiety or conjugate group.

In certain embodiments, a cleavable moiety comprises or consists of one or more linker-nucleosides. In certain such embodiments, the one or more linker-nucleosides are linked to one another and/or to the remainder of the oligomeric compound through cleavable bonds. In certain embodiments, such cleavable bonds are unmodified phosphodiester bonds. In certain embodiments, a cleavable moiety is 2'-deoxynucleoside that is attached to either the 3' or 5'-terminal nucleoside of an oligonucleotide by a phosphate internucleoside linkage and covalently attached to the remainder of the conjugate linker or conjugate moiety by a phosphate or phosphorothioate linkage. In certain such embodiments, the cleavable moiety is 2'-deoxyadenosine.

B. Certain Terminal Groups

In certain embodiments, oligomeric compounds comprise one or more terminal groups. In certain such embodiments, oligomeric compounds comprise a stabilized 5'-phophate. Stabilized 5'-phosphates include, but are not limited to 5'-phosphanates, including, but not limited to 5'-vinylphosphonates. In certain embodiments, terminal groups comprise one or more abasic nucleosides and/or inverted nucleosides. In certain embodiments, terminal groups comprise one or more 2'-linked nucleosides. In certain such embodiments, the 2'-linked nucleoside is an abasic nucleoside.

III. Oligomeric Duplexes

In certain embodiments, oligomeric compounds described herein comprise an oligonucleotide, having a nucleobase sequence complementary to that of a target nucleic acid. In certain embodiments, an oligomeric compound is paired with a second oligomeric compound to form an oligomeric duplex. Such oligomeric duplexes comprise a first oligomeric compound having a region complementary to a target nucleic acid and a second oligomeric compound having a region complementary to the first oligomeric compound. In certain embodiments, the first oligomeric compound of an oligomeric duplex comprises or consists of (1) a modified or unmodified oligonucleotide and optionally a conjugate group and (2) a second modified or unmodified oligonucleotide and optionally a conjugate group. Either or both oligomeric compounds of an oligomeric duplex may comprise a conjugate group. The oligonucleotides of each oligomeric compound of an oligomeric duplex may include non-complementary overhanging nucleosides.

IV. Antisense Activity

In certain embodiments, oligomeric compounds and oligomeric duplexes are capable of hybridizing to a target nucleic acid, resulting in at least one antisense activity; such oligomeric compounds and oligomeric duplexes are antisense compounds. In certain embodiments, antisense compounds have antisense activity when they reduce or inhibit the amount or activity of a target nucleic acid by 25% or more in the standard cell assay. In certain embodiments, antisense compounds selectively affect one or more target nucleic acid. Such antisense compounds comprise a nucleobase sequence that hybridizes to one or more

target nucleic acid, resulting in one or more desired antisense activity and does not hybridize to one or more non-target nucleic acid or does not hybridize to one or more non-target nucleic acid in such a way that results in significant undesired antisense activity.

In certain antisense activities, hybridization of an antisense compound to a target nucleic acid results in recruitment of a protein that cleaves the target nucleic acid. For example, certain antisense compounds result in RNase H mediated cleavage of the target nucleic acid. RNase H is a cellular endonuclease that cleaves the RNA strand of an RNA:DNA duplex. The DNA in such an RNA:DNA duplex need not be unmodified DNA. In certain embodiments, described herein are antisense compounds that are sufficiently "DNA-like" to elicit RNase H activity. In certain embodiments, one or more non-DNA-like nucleoside in the gap of a gapmer is tolerated.

In certain antisense activities, an antisense compound or a portion of an antisense compound is loaded into an RNA-induced silencing complex (RISC), ultimately resulting in cleavage of the target nucleic acid. For example, certain antisense compounds result in cleavage of the target nucleic acid by Argonaute. Antisense compounds that are loaded into RISC are RNAi compounds. RNAi compounds may be double-stranded (siRNA) or single-stranded (ssRNA).

In certain embodiments, hybridization of an antisense compound to a target nucleic acid does not result in recruitment of a protein that cleaves that target nucleic acid. In certain embodiments, hybridization of the antisense compound to the target nucleic acid results in alteration of splicing of the target nucleic acid. In certain embodiments, hybridization of an antisense compound to a target nucleic acid results in inhibition of a binding interaction between the target nucleic acid and a protein or other nucleic acid. In certain embodiments, hybridization of an antisense compound to a target nucleic acid results in alteration of translation of the target nucleic acid.

Antisense activities may be observed directly or indirectly. In certain embodiments, observation or detection of an antisense activity involves observation or detection of a change in an amount of a target nucleic acid or protein encoded by such target nucleic acid, a change in the ratio of splice variants of a nucleic acid or protein and/or a phenotypic change in a cell or subject.

V. Certain Target Nucleic Acids

In certain embodiments, oligomeric compounds comprise or consist of an oligonucleotide comprising a region that is complementary to a target nucleic acid. In certain embodiments, the target nucleic acid is an endogenous RNA molecule. In certain embodiments, the target nucleic acid encodes a protein. In certain such embodiments, the target nucleic acid is selected from: a mature mRNA and a pre-mRNA, including intronic, exonic and untranslated regions. In certain embodiments, the target RNA is a mature mRNA. In certain embodiments, the target nucleic acid is a pre-mRNA. In certain such embodiments, the target region is entirely within an intron. In certain embodiments, the target region spans an intron/exon junction. In certain embodiments, the target region is at least 50% within an intron. In certain embodiments, the target

nucleic acid is the RNA transcriptional product of a retrogene. In certain embodiments, the target nucleic acid is a non-coding RNA. In certain such embodiments, the target non-coding RNA is selected from: a long non-coding RNA, a short non-coding RNA, an intronic RNA molecule.

A. Complementarity/Mismatches to the Target Nucleic Acid

It is possible to introduce mismatch bases without eliminating activity. For example, Gautschi et al (J. Natl. Cancer Inst. 93:463-471, March 2001) demonstrated the ability of an oligonucleotide having 100% complementarity to the bcl-2 mRNA and having 3 mismatches to the bcl-xL mRNA to reduce the expression of both bcl-2 and bcl-xL *in vitro* and in vivo. Furthermore, this oligonucleotide demonstrated potent anti-tumor activity in vivo. Maher and Dolnick (Nuc. Acid. Res. 16:3341-3358, 1988) tested a series of tandem 14 nucleobase oligonucleotides, and a 28 and 42 nucleobase oligonucleotides comprised of the sequence of two or three of the tandem oligonucleotides, respectively, for their ability to arrest translation of human DHFR in a rabbit reticulocyte assay. Each of the three 14 nucleobase oligonucleotides alone was able to inhibit translation, albeit at a more modest level than the 28 or 42 nucleobase oligonucleotides.

In certain embodiments, oligonucleotides are complementary to the target nucleic acid over the entire length of the oligonucleotide. In certain embodiments, oligonucleotides are 99%, 95%, 90%, 85%, or 80% complementary to the target nucleic acid. In certain embodiments, oligonucleotides are at least 80% complementary to the target nucleic acid over the entire length of the oligonucleotide and comprise a region that is 100% or fully complementary to a target nucleic acid. In certain embodiments, the region of full complementarity is from 6 to 20, 10 to 18, or 18 to 20 nucleobases in length.

In certain embodiments, oligonucleotides comprise one or more mismatched nucleobases relative to the target nucleic acid. In certain embodiments, antisense activity against the target is reduced by such mismatch, but activity against a non-target is reduced by a greater amount. Thus, in certain embodiments selectivity of the oligonucleotide is improved. In certain embodiments, the mismatch is specifically positioned within an oligonucleotide having a gapmer motif. In certain embodiments, the mismatch is at position 1, 2, 3, 4, 5, 6, 7, or 8 from the 5'-end of the gap region. In certain embodiments, the mismatch is at position 9, 8, 7, 6, 5, 4, 3, 2, 1 from the 3'-end of the gap region. In certain embodiments, the mismatch is at position 1, 2, 3, or 4 from the 5'-end of the wing region. In certain embodiments, the mismatch is at position 4, 3, 2, or 1 from the 3'-end of the wing region.

B. KCNT1

In certain embodiments, oligomeric compounds comprise or consist of an oligonucleotide comprising a region that is complementary to a KCNT1 nucleic acid. In certain embodiments, the KCNT1 nucleic acid has the sequence set forth in SEQ ID NO: 1 (GENBANK Accession No: NM_020822.2). In certain embodiments, the KCNT1 nucleic acid has the sequence set forth in SEQ ID NO: 2 (GENBANK Accession No: NC_000009.12 truncated from nucleotides 135698001 to 135796000). In certain embodiments, the KCNT1 nucleic acid has the sequence set forth in SEQ ID NO: 3 (GENBANK Accession No.:

NM_020822.3), which is a splicing variant of SEQ ID NO: 1.

In certain embodiments an oligomeric compound complementary to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 is capable of reducing a KCNT1 RNA in a cell. In certain embodiments an oligomeric compound complementary to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 is capable of reducingKCNT1 protein in a cell. In certain embodiments, the cell is *in vitro*. In certain embodiments, the cell is in a subject. In certain embodiments, the oligomeric compound consists of a modified oligonucleotide. In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO:3 is capable of ameliorating one or more symptom or hallmark of a neurological condition when it is introduced to a cell in a subject. In certain embodiments, the neurological condition is epilepsy. In certain embodiments, the one or more symptoms or hallmarks are selected from seizure, brain damage, demyelination, hypotonia, microcephaly, depression, anxiety, and cognitive dysfunction, and combinations thereof

In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 is capable of reducing a detectable amount of KCNT1 RNA in the CSF of a subject when the oligomeric compound is administered to the CSF of the subject. The detectable amount of KCNT1 RNA may be reduced by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%. In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 is capable of reducing a detectable amount of KCNT1 protein in the CSF of the subject when the oligomeric compound is administered to the CSF of the subject. The detectable amount of KCNT1 protein may be reduced by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%.

C. Certain Target Nucleic Acids in Certain Tissues

In certain embodiments, oligomeric compounds comprise or consist of an oligonucleotide comprising a region that is complementary to a target nucleic acid, wherein the target nucleic acid is expressed in a pharmacologically relevant tissue. In certain embodiments, the pharmacologically relevant tissues are the cells and tissues that comprise the central nervous system (CNS). Such tissues include brain tissues, such as, cortex, substantia nigra, striatum, midbrain, and brainstem and spinal cord.

VI. Certain Pharmaceutical Compositions

In certain embodiments, described herein are pharmaceutical compositions comprising one or more oligomeric compounds. In certain embodiments, the one or more oligomeric compounds each consists of a modified oligonucleotide. In certain embodiments, the pharmaceutical composition comprises a pharmaceutically acceptable diluent or carrier. In certain embodiments, a pharmaceutical composition comprises or consists of a sterile saline solution and one or more oligomeric compound. In certain embodiments, the sterile saline is pharmaceutical grade saline. In certain embodiments, a pharmaceutical composition comprises or consists of one or more oligomeric compound and sterile water. In certain

embodiments, the sterile water is pharmaceutical grade water. In certain embodiments, a pharmaceutical composition comprises or consists of one or more oligomeric compound and phosphate-buffered saline (PBS). In certain embodiments, the sterile PBS is pharmaceutical grade PBS. In certain embodiments, a pharmaceutical composition comprises or consists of one or more oligomeric compound and artificial cerebrospinal fluid. In certain embodiments, the artificial cerebrospinal fluid is pharmaceutical grade.

In certain embodiments, a pharmaceutical composition comprises a modified oligonucleotide and artificial cerebrospinal fluid. In certain embodiments, a pharmaceutical composition consists of a modified oligonucleotide and artificial cerebrospinal fluid. In certain embodiments, a pharmaceutical composition consists essentially of a modified oligonucleotide and artificial cerebrospinal fluid. In certain embodiments, the artificial cerebrospinal fluid is pharmaceutical grade.

In certain embodiments, pharmaceutical compositions comprise one or more oligomeric compound and one or more excipients. In certain embodiments, excipients are selected from water, salt solutions, alcohol, polyethylene glycols, gelatin, lactose, amylase, magnesium stearate, talc, silicic acid, viscous paraffin, hydroxymethylcellulose and polyvinylpyrrolidone.

In certain embodiments, oligomeric compounds may be admixed with pharmaceutically acceptable active and/or inert substances for the preparation of pharmaceutical compositions or formulations. Compositions and methods for the formulation of pharmaceutical compositions depend on a number of criteria, including, but not limited to, route of administration, extent of disease, or dose to be administered.

In certain embodiments, pharmaceutical compositions comprising an oligomeric compound encompass any pharmaceutically acceptable salts of the oligomeric compound, esters of the oligomeric compound, or salts of such esters. In certain embodiments, pharmaceutical compositions comprising oligomeric compounds comprising one or more oligonucleotide, upon administration to a subject, including a human, are capable of providing (directly or indirectly) the biologically active metabolite or residue thereof. Accordingly, for example, the disclosure is also drawn to pharmaceutically acceptable salts of oligomeric compounds, prodrugs, pharmaceutically acceptable salts of such prodrugs, and other bioequivalents. Suitable pharmaceutically acceptable salts include, but are not limited to, sodium and potassium salts. In certain embodiments, prodrugs comprise one or more conjugate group attached to an oligonucleotide, wherein the conjugate group is cleaved by endogenous nucleases within the body.

Lipid moieties have been used in nucleic acid therapies in a variety of methods. In certain such methods, the nucleic acid, such as an oligomeric compound, is introduced into preformed liposomes or lipoplexes made of mixtures of cationic lipids and neutral lipids. In certain methods, DNA complexes with mono- or poly-cationic lipids are formed without the presence of a neutral lipid. In certain embodiments, a lipid moiety is selected to increase distribution of a pharmaceutical agent to a particular cell or tissue. In certain embodiments, a lipid moiety is selected to increase distribution of a pharmaceutical agent to fat tissue.

In certain embodiments, a lipid moiety is selected to increase distribution of a pharmaceutical agent to muscle tissue.

In certain embodiments, pharmaceutical compositions comprise a delivery system. Examples of delivery systems include, but are not limited to, liposomes and emulsions. Certain delivery systems are useful for preparing certain pharmaceutical compositions including those comprising hydrophobic compounds. In certain embodiments, certain organic solvents such as dimethylsulfoxide are used.

In certain embodiments, pharmaceutical compositions comprise one or more tissue-specific delivery molecules designed to deliver the one or more pharmaceutical agents of the present invention to specific tissues or cell types. For example, in certain embodiments, pharmaceutical compositions include liposomes coated with a tissue-specific antibody.

In certain embodiments, pharmaceutical compositions comprise a co-solvent system. Certain of such co-solvent systems comprise, for example, benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. In certain embodiments, such co-solvent systems are used for hydrophobic compounds. A non-limiting example of such a co-solvent system is the VPD co-solvent system, which is a solution of absolute ethanol comprising 3% w/v benzyl alcohol, 8% w/v of the nonpolar surfactant Polysorbate 80™ and 65% w/v polyethylene glycol 300. The proportions of such co-solvent systems may be varied considerably without significantly altering their solubility and toxicity characteristics. Furthermore, the identity of co-solvent components may be varied: for example, other surfactants may be used instead of Polysorbate 80™; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, *e.g.*, polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for dextrose.

In certain embodiments, pharmaceutical compositions are prepared for oral administration. In certain embodiments, pharmaceutical compositions are prepared for buccal administration. In certain embodiments, a pharmaceutical composition is prepared for administration by injection (*e.g.*, intravenous, subcutaneous, intramuscular, intrathecal (IT), intracerebroventricular (ICV), etc.). In certain of such embodiments, a pharmaceutical composition comprises a carrier and is formulated in aqueous solution, such as water or physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. In certain embodiments, other ingredients are included (*e.g.*, ingredients that aid in solubility or serve as preservatives). In certain embodiments, injectable suspensions are prepared using appropriate liquid carriers, suspending agents and the like. Certain pharmaceutical compositions for injection are presented in unit dosage form, *e.g.*, in ampoules or in multi-dose containers. Certain pharmaceutical compositions for injection are suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Certain solvents suitable for use in pharmaceutical compositions for injection include, but are not limited to, lipophilic solvents and fatty oils, such as sesame oil, synthetic fatty acid esters, such as ethyl oleate or triglycerides, and liposomes.

Under certain conditions, certain compounds disclosed herein act as acids. Although such compounds may be drawn or described in protonated (free acid) form, or ionized and in association with a cation (salt) form, aqueous solutions of such compounds exist in equilibrium among such forms. For example, a phosphate linkage of an oligonucleotide in aqueous solution exists in equilibrium among free acid, anion and salt forms. Unless otherwise indicated, compounds described herein are intended to include all such forms. Moreover, certain oligonucleotides have several such linkages, each of which is in equilibrium. Thus, oligonucleotides in solution exist in an ensemble of forms at multiple positions all at equilibrium. The term "oligonucleotide" is intended to include all such forms. Drawn structures necessarily depict a single form. Nevertheless, unless otherwise indicated, such drawings are likewise intended to include corresponding forms. Herein, a structure depicting the free acid of a compound followed by the term "or a salt thereof" expressly includes all such forms that may be fully or partially protonated/de-protonated/in association with a cation. In certain instances, one or more specific cation is identified.

In certain embodiments, modified oligonucleotides or oligomeric compounds are in aqueous solution with sodium. In certain embodiments, modified oligonucleotides or oligomeric compounds are in aqueous solution with potassium. In certain embodiments, modified oligonucleotides or oligomeric compounds are in PBS. In certain embodiments, modified oligonucleotides or oligomeric compounds are in water. In certain such embodiments, the pH of the solution is adjusted with NaOH and/or HCl to achieve a desired pH.

Herein, certain specific doses are described. A dose may be in the form of a dosage unit. For clarity, a dose (or dosage unit) of a modified oligonucleotide or an oligomeric compound in milligrams indicates the mass of the free acid form of the modified oligonucleotide or oligomeric compound. As described above, in aqueous solution, the free acid is in equilibrium with anionic and salt forms. However, for the purpose of calculating dose, it is assumed that the modified oligonucleotide or oligomeric compound exists as a solvent-free, sodium-acetate free, anhydrous, free acid. For example, where a modified oligonucleotide or an oligomeric compound is in solution comprising sodium (e.g., saline), the modified oligonucleotide or oligomeric compound may be partially or fully de-protonated and in association with Na+ ions. However, the mass of the protons is nevertheless counted toward the weight of the dose, and the mass of the Na+ ions are not counted toward the weight of the dose. Thus, for example, a dose, or dosage unit, of 80 mg of Compound No. 1080855 equals the number of fully protonated molecules that weighs 80 mg. This would be equivalent to 85 mg of solvent-free, sodium-acetate free, anhydrous sodiated Compound No. 1080855. When an oligomeric compound comprises a conjugate group, the mass of the conjugate group is included in calculating the dose of such oligomeric compound. If the conjugate group also has an acid, the conjugate group is likewise assumed to be fully protonated for the purpose of calculating dose.

Nonlimiting disclosure and incorporation by reference

Each of the literature and patent publications listed herein is incorporated by reference in its entirety.

While certain compounds, compositions and methods described herein have been described with

specificity in accordance with certain embodiments, the following examples serve only to illustrate the compounds described herein and are not intended to limit the same. Each of the references, GenBank accession numbers, and the like recited in the present application is incorporated herein by reference in its entirety.

Although the sequence listing accompanying this filing identifies each sequence as either "RNA" or "DNA" as required, in reality, those sequences may be modified with any combination of chemical modifications. One of skill in the art will readily appreciate that such designation as "RNA" or "DNA" to describe modified oligonucleotides is, in certain instances, arbitrary. For example, an oligonucleotide comprising a nucleoside comprising a 2'-OH sugar moiety and a thymine base could be described as a DNA having a modified sugar (2'-OH in place of one 2'-H of DNA) or as an RNA having a modified base (thymine (methylated uracil) in place of a uracil of RNA). Accordingly, nucleic acid sequences provided herein, including, but not limited to those in the sequence listing, are intended to encompass nucleic acids containing any combination of natural or modified RNA and/or DNA, including, but not limited to such nucleic acids having modified nucleobases. By way of further example and without limitation, an oligomeric compound having the nucleobase sequence "ATCGATCG" encompasses any oligomeric compounds having such nucleobase sequence, whether modified or unmodified, including, but not limited to, such compounds comprising RNA bases, such as those having sequence "AUCGAUCG" and those having some DNA bases and some RNA bases such as "AUCGATCG" and oligomeric compounds having other modified nucleobases, such as "AT^{m}CGAUCG," wherein ^{m}C indicates a cytosine base comprising a methyl group at the 5-position.

Certain compounds described herein (*e.g.*, modified oligonucleotides) have one or more asymmetric center and thus give rise to enantiomers, diastereomers, and other stereoisomeric configurations that may be defined, in terms of absolute stereochemistry, as (*R*) or (*S*), as α or β such as for sugar anomers, or as (D) or (L), such as for amino acids, etc. Compounds provided herein that are drawn or described as having certain stereoisomeric configurations include only the indicated compounds. Compounds provided herein that are drawn or described with undefined stereochemistry include all such possible isomers, including their stereorandom and optically pure forms, unless specified otherwise. Likewise, tautomeric forms of the compounds herein are also included unless otherwise indicated. Unless otherwise indicated, compounds described herein are intended to include corresponding salt forms.

The compounds described herein include variations in which one or more atoms are replaced with a non-radioactive isotope or radioactive isotope of the indicated element. For example, compounds herein that comprise hydrogen atoms encompass all possible deuterium substitutions for each of the ^{1}H hydrogen atoms. Isotopic substitutions encompassed by the compounds herein include but are not limited to: ^{2}H or ^{3}H in place of ^{1}H, ^{13}C or ^{14}C in place of ^{12}C, ^{15}N in place of ^{14}N, ^{17}O or ^{18}O in place of ^{16}O, and ^{33}S, ^{34}S, ^{35}S, or ^{36}S in place of ^{32}S. In certain embodiments, non-radioactive isotopic substitutions may impart new properties on

the oligomeric compound that are beneficial for use as a therapeutic or research tool. In certain embodiments, radioactive isotopic substitutions may make the compound suitable for research or diagnostic purposes such as imaging.

EXAMPLES

The following examples illustrate certain embodiments of the present disclosure and are not limiting. Moreover, where specific embodiments are provided, the inventors have contemplated generic application of those specific embodiments. For example, disclosure of an oligonucleotide having a particular motif provides reasonable support for additional oligonucleotides having the same or similar motif. And, for example, where a particular high-affinity modification appears at a particular position, other high-affinity modifications at the same position are considered suitable, unless otherwise indicated.

Example 1: Effect of 5-10-5 MOE gapmer modified oligonucleotides on human KCNT1 RNA *in vitro*, single dose

Modified oligonucleotides complementary to human KCNT1 nucleic acid were tested for their effect on KCNT1 RNA levels *in vitro*.

The modified oligonucleotides in the tables below are 5-10-5 MOE gapmers with mixed internucleoside linkages. The gapmers are 20 nucleosides in length, wherein the central gap segment consists of ten 2'-β-D-deoxynucleosides and the 3' and 5' wings each consist of five 2'-MOE nucleosides. The motif for the gapmers is (from 5' to 3'): eeeeddddddddddeeeee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, and 'e' represents a 2'-MOE sugar moiety. The internucleoside linkage motif for the gapmers is (from 5' to 3'): soooossssssssssooss; wherein 's' represents a phosphorothioate internucleoside linkage, and 'o' represents a phosphodiester internucleoside linkage. All cytosine residues are 5-methylcytosines.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the human gene sequence. Each modified oligonucleotide listed in the Tables below is 100% complementary to SEQ ID NO: 1 (GENBANK Accession No. NM_020822.2) or SEQ ID NO: 2 (GENBANK Accession No. NC_000009.12 truncated from nucleotides 135698001 to 135796000). 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular gene sequence.

Cultured SH-SY5Y cells (a neuroblastoma cell line) at a density of 20,000 cells per well were treated with 4,000 nM modified oligonucleotide by electroporation. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and KCNT1 RNA levels were measured by quantitative real-time RTPCR. Human KCNT1 primer probe set RTS39508 (forward sequence GTCAACGTGCAGACCATGT, designated herein as SEQ ID NO: 11; reverse sequence TCGCTCCCTCTTTTCTAGTTTG, designated herein as SEQ ID NO: 12; probe sequence

AGCTCACCCACCCTTCCAACATG, designated herein as SEQ ID NO: 13) was used to measure RNA levels presented in Tables 1-6 and human KCNT1 primer probe set RTS39496 (forward sequence CAGGTGGAGTTCTACGTCAA, designated herein as SEQ ID NO: 14; reverse sequence GAGAAGTTGAACAGCCGGAT, designated herein as SEQ ID NO: 15; probe sequence TGATGAAGAACAGCTTGAGCCGCT, designated herein as SEQ ID NO: 16) was used to measure RNA levels presented in Tables 7-38. KCNT1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of KCNT1 RNA is presented in Tables 1-6 below as percent KCNT1 RNA levels relative to untreated control (UTC) cells. Each table represents results from an individual assay plate. 'ND' indicates that the % UTC is not defined for that particular modified oligonucleotide in that particular experiment due to experimental error. However, activities of selected modified oligonucleotides, including those that are not defined in Example 1, are successfully demonstrated in Example 2.

Table 1. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39508

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID NO
1080685	17	36	4201	4220	AGTGGGAGCCGCCACCTTCT	107	21
1080691	50	69	4234	4253	CTGGCAGCTCGGACCCGACC	114	22
1080697	123	142	4307	4326	GTGTAGCCCCCGCCGCGCGC	83	23
1080703	194	213	16586	16605	GGAGCGCGCCGTCCCCCGCG	43	24
1080709	226	245	16618	16637	CAGGTCGCTCATCTTGAAGC	40	25
1080715	329	348	52098	52117	CGTAGAACTCCACCTGGACC	25	26
1080721	458	477	52991	53010	GGACGCGCACAATGTAGAGC	28	27
1080727	590	609	57145	57164	TCGCCCACAGTGTCATCTTT	33	28
1080733	613	632	58871	58890	TATTATGGCCACGATGACCT	64	29
1080739	709	728	59190	59209	GTTGATCATCTCCAGGACGA	57	30
1080745	953	972	61703	61722	ACAGGTTCTCGCCCGCCCGC	78	31
1080751	1069	1088	61819	61838	GGCCACGCAGATCATGATGA	54	32
1080757	1125	1144	67046	67065	TGCCGCTCCATCCAGAGGTA	37	33
1080763	1229	1248	67150	67169	CGTTCAGGAAGTCCATGAGA	36	34
1080768	1498	1517	70851	70870	GAAGTCCTTCACGGCCCAGG	34	35
1080774	1852	1871	72865	72884	CTTCAGCCCGATGAGGCACA	54	36
1080780	1956	1975	72969	72988	GCCGAGTTCTCCTCCTTGGT	34	37
1080786	2197	2216	74829	74848	CAGGACGGGCGCGATGCTGG	57	38
1080792	2262	2281	74894	74913	ACCTCATCCTCCGACTGGTC	58	39
1080798	2460	2479	79374	79393	AGCTTGTTCTTGAACCCGTA	61	40
1080804	2478	2497	79392	79411	TCTGCCGAGACGATGATCAG	39	41

1080810	2503	2522	79417	79436	GTTGTACAGCCCATTGCCGG	66	42
1080816	2530	2549	79444	79463	GTAGTAGGCCCGCAGTGGCA	42	43
1080822	2971	2990	86079	86098	GATGCTGAAGACGCGGCCGG	50	44
1080828	3078	3097	86595	86614	CAGAGGTACCCCGAGCCCGG	50	45
1080834	3387	3406	88332	88351	TGCAGGCTCTTGCGCCGTAG	53	46
1080840	3462	3481	88407	88426	TGCTGGCTGATCCACTCCGC	44	47
1080846	3525	3544	88470	88489	ATGCGGTTCTTCACCAGCTC	14	48
1080852	3842	3861	94221	94240	CCACCGTGTCCTCACACGCT	23	49
1080858	3875	3894	94254	94273	GTAGAGTGTGCCATCCCCAG	23	50
1080864	4046	4065	94425	94444	AGCCCTGGTCACGAGTTGCG	61	51
1080870	4478	4497	94857	94876	TGCCCCCTAGATGCAGTGGC	44	52
1080876	4493	4512	94872	94891	CCATCTTCCGCCCAATGCCC	35	53
1080882	4502	4521	94881	94900	GGAAATGCACCATCTTCCGC	27	54
1080888	4698	4717	95077	95096	CCGTACAAACCAGTAAGGAA	23	55
1080894	4705	4724	95084	95103	GCGCTGACCGTACAAACCAG	16	56
1080900	N/A	N/A	90128	90147	GGTTTACCCGATTCATGACA	26	57
1080906	N/A	N/A	3591	3610	ACACAGCACCTTTAGACGGG	153	58
1080912	N/A	N/A	6781	6800	ACTGCTCCCTAATATGGGCC	88	59
1080918	N/A	N/A	8833	8852	AAATGACCAACTCACTGGCG	77	60
			37277	37296			
1080924	N/A	N/A	14472	14491	CCTGGCATAGCCAGACACGG	92	61
1080930	N/A	N/A	17507	17526	TGCCGTACCCTACACGCTGG	30	62
1080936	N/A	N/A	18221	18240	ACTTCCTGCCCAATATCGGA	58	63
1080942	N/A	N/A	20077	20096	GGAGGGTCCTCCAAGCGGCT	38	64
1080948	N/A	N/A	23023	23042	TTCACGGCCCCTAAACCACC	74	65
1080954	N/A	N/A	24946	24965	GGAGGATTTCCCACGACATC	47	66
1080960	N/A	N/A	27095	27114	GGCCATTGAGCCACCAAGGG	30	67
1080966	N/A	N/A	29977	29996	CATTTTAACCCTCTTTGCCG	90	68
1080972	N/A	N/A	30914	30933	TCAATCCCGAACACCATGTC	61	69
1080978	N/A	N/A	32653	32672	GGTCCGAAATCCCAAGCCTG	23	70
1080984	N/A	N/A	34972	34991	GTGCCGGAATCCTCACCCTT	51	71
1080990	N/A	N/A	38017	38036	ACCGGGCACAGATCCCACCT	53	72
1080996	N/A	N/A	40434	40453	TCCGTGAGATCCACACTCCA	24	73
1081002	N/A	N/A	45589	45608	GGCTTCTATCTCACACCCGT	34	74
1081008	N/A	N/A	47517	47536	CCGTCTGCTCAAACCATCAG	60	75
1081014	N/A	N/A	49388	49407	GGCGGTACCCAGGGACCACC	58	76
1081020	N/A	N/A	52241	52260	CCAGCCTTCGCCATCGCCAG	33	77
1081026	N/A	N/A	56009	56028	GCGCCTGGCTATTGGGAGCT	25	78
			56073	56092			
1081032	N/A	N/A	60111	60130	ACCTGTGTCTCGGCTGAGGC	26	79
			60153	60172			
			60245	60264			
1081038	N/A	N/A	60194	60213	CGTCTCGGCTGAGGCCCACG	36	80
			60286	60305			
1081044	N/A	N/A	64878	64897	CACCATGGCCATACCCATCG	61	81

1081050	N/A	N/A	66061	66080	GCATTGCACTTATCCAGCGC	27	82
1081056	N/A	N/A	67948	67967	GTCCACCCCAGACGATCCAC	29	83
			68544	68563			
1081062	N/A	N/A	67979	67998	ATGGTCCATCCCAGAAGGTC	34	84
			68118	68137			
1081068	N/A	N/A	68507	68526	AGAGGGTCCACCATGGATGG	50	85
			68563	68582			
1081074	N/A	N/A	68517	68536	GGTCCACCCAAGAGGGTCCA	34	86
			68573	68592			
1081080	N/A	N/A	69967	69986	TGTGCAGGCTGACAGCGGGT	13	87
			70025	70044			
1081086	N/A	N/A	71040	71059	TCCTGCCCCAGACGCACCGT	33	88
			71080	71099			
1081092	N/A	N/A	71173	71192	GTGTGCACACGCGCCCTGCC	18	89
			71293	71312			
1081098	N/A	N/A	72815	72834	TCAGGTACCGCCGCTCACCC	89	90
1081104	N/A	N/A	75842	75861	GGGCTCTTACCCACATACTT	25	91
1081110	N/A	N/A	77408	77427	CGCCAGCCTTACCTTGTCCA	156	92
1081116	N/A	N/A	79137	79156	AGCTGTACCCACAGGCGGCA	69	93
1081122	N/A	N/A	82606	82625	CCGAGCATCCCCCTACGCCT	53	94
1081128	N/A	N/A	84928	84947	GTTCGCCCTTACTCATCAGT	63	95
1081134	N/A	N/A	86431	86450	CACAGGTCCATACCCCACCG	51	96
1081140	N/A	N/A	91100	91119	TCCGAGCACCACAGTGCCCG	76	97
1081146	N/A	N/A	92063	92082	TGCCCGGACCACACGCTTCT	48	98

Table 2. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39508

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID NO
1080686	19	38	4203	4222	CGAGTGGGAGCCGCCACCTT	113	99
1080692	77	96	4261	4280	GCGCCCCGTCAGGGAGTGGC	84	100
1080698	125	144	4309	4328	TGGTGTAGCCCCCGCCGCGC	59	101
1080704	199	218	16591	16610	GTCCAGGAGCGCGCCGTCCC	30	102
1080710	234	253	16626	16645	TCGGAGTCCAGGTCGCTCAT	31	103
1080716	357	376	52126	52145	AGCCGCTCCTTGAAGGTGTT	36	104
1080722	464	483	52997	53016	CGAGCAGGACGCGCACAATG	21	105
1080728	591	610	57146	57165	ATCGCCCACAGTGTCATCTT	32	106
1080734	686	705	59167	59186	ACACGCGGAAGATCTGCTCC	41	107
1080740	760	779	59308	59327	GAACAGGTTCCGCAGCGGCG	20	108
1080746	955	974	61705	61724	GGACAGGTTCTCGCCCGCCC	53	109
1080752	1075	1094	61825	61844	CACGAGGGCCACGCAGATCA	83	110

1080758	1147	1166	67068	67087	GCTGTAGTTGCCCCCTGACT	48	111
1080764	1299	1318	67648	67667	TGGACATCCATCTCCGTGGG	28	112
1080769	1502	1521	70855	70874	GGGCGAAGTCCTTCACGGCC	26	113
1080775	1854	1873	72867	72886	CGCTTCAGCCCGATGAGGCA	52	114
1080781	1957	1976	72970	72989	GGCCGAGTTCTCCTCCTTGG	28	115
1080787	2207	2226	74839	74858	CGGCCAGTTCCAGGACGGGC	55	116
1080793	2266	2285	74898	74917	CGTCACCTCATCCTCCGACT	43	117
1080799	2473	2492	79387	79406	CGAGACGATGATCAGCTTGT	39	118
1080805	2479	2498	79393	79412	CTCTGCCGAGACGATGATCA	40	119
1080811	2504	2523	79418	79437	AGTTGTACAGCCCATTGCCG	42	120
1080817	2542	2561	79456	79475	CTTGCGGGATCTGTAGTAGG	60	121
1080823	3016	3035	86533	86552	GTAGTCCTTCACGAAGGACT	72	122
1080829	3079	3098	86596	86615	ACAGAGGTACCCCGAGCCCG	43	123
1080835	3411	3430	88356	88375	TTGCGGCTCAGCCTCCGGGC	32	124
1080841	3463	3482	88408	88427	CTGCTGGCTGATCCACTCCG	42	125
1080847	3526	3545	88471	88490	CATGCGGTTCTTCACCAGCT	18	126
1080853	3847	3866	94226	94245	TAGTGCCACCGTGTCCTCAC	26	127
1080859	3877	3896	94256	94275	GAGTAGAGTGTGCCATCCCC	15	128
1080865	4369	4388	94748	94767	GACGCACCCCTCTCACATGC	21	129
1080871	4480	4499	94859	94878	AATGCCCCCTAGATGCAGTG	28	130
1080877	4495	4514	94874	94893	CACCATCTTCCGCCCAATGC	24	131
1080883	4583	4602	94962	94981	CCGGAGGCTGAATTGTGCTT	27	132
1080889	4699	4718	95078	95097	ACCGTACAAACCAGTAAGGA	15	133
1080895	N/A	N/A	90121	90140	CCGATTCATGACATCACTGG	20	134
1080901	N/A	N/A	90129	90148	AGGTTTACCCGATTCATGAC	28	135
1080907	N/A	N/A	4599	4618	CCCAGCTTCTTACCAGGTCG	121	136
1080913	N/A	N/A	7382	7401	GGGTACACGATACCCGTTCA	56	137
1080919	N/A	N/A	9148	9167	GCACCGGGCCTTATCTGATC	135	138
1080925	N/A	N/A	14834	14853	GCACACGGCCATAAGCAGGT	86	139
1080931	N/A	N/A	17508	17527	CTGCCGTACCCTACACGCTG	37	140
1080937	N/A	N/A	18644	18663	GCACAGCACGCCAAGACCGC	29	141
1080943	N/A	N/A	20549	20568	CGGCACTTCCACCTTACCCA	27	142
1080949	N/A	N/A	23033	23052	TCCTCGAACCTTCACGGCCC	42	143
1080955	N/A	N/A	25141	25160	TCGGAGAGCCACGCCCGTCA	43	144
1080961	N/A	N/A	27253	27272	ACAGGAATCTTTCGAAGGCC	43	145
1080967	N/A	N/A	30331	30350	CCCTCCAAACAATTATGCGA	67	146
1080973	N/A	N/A	30919	30938	ACAGTTCAATCCCGAACACC	47	147
1080979	N/A	N/A	33660	33679	CTAGGACTATTATACCCAGC	31	148
1080985	N/A	N/A	36054	36073	TCGCTTTGCCTACCGCGAGC	88	149
1080991	N/A	N/A	38455	38474	CCGGCTCAAACCACCGCCAG	46	150
1080997	N/A	N/A	42272	42291	CGGCAGGTTCCCACACGCAA	30	151
1081003	N/A	N/A	45594	45613	GGCACGGCTTCTATCTCACA	41	152
1081009	N/A	N/A	48647	48666	CCCTTTACCTCCCCGTGGAC	59	153
1081015	N/A	N/A	49818	49837	GCTTGTCACCCCACCGGGCA	50	154
1081021	N/A	N/A	52720	52739	GCCCCACCTTACAGGTGCCT	39	155

1081027	N/A	N/A	56052	56071	GAGTGGAGACTCATCCCACC	33	156
	N/A	N/A	56116	56135			
1081033	N/A	N/A	60112	60131	CACCTGTGTCTCGGCTGAGG	44	157
			60154	60173			
			60246	60265			
1081039	N/A	N/A	60978	60997	AGTGGTGACCAGGCCTCGCT	27	158
1081045	N/A	N/A	65270	65289	GCCCACCCTTACCATCGCCA	35	159
1081051	N/A	N/A	66638	66657	GTCAGGAGCCTATGTCTGGG	29	160
1081057	N/A	N/A	67950	67969	TGGTCCACCCCAGACGATCC	23	161
			68546	68565			
1081063	N/A	N/A	68042	68061	CACCCTGGATGGTCCACCCT	37	162
			68363	68382			
1081069	N/A	N/A	68508	68527	AAGAGGGTCCACCATGGATG	43	163
			68564	68583			
1081075	N/A	N/A	68538	68557	CCCAGACGATCCACCCCAGA	64	164
1081081	N/A	N/A	70254	70273	CACCGGTATCCCAGTGCCCC	58	165
1081087	N/A	N/A	71072	71091	CAGACGCACCGTCACCCACG	29	166
			71152	71171			
1081093	N/A	N/A	71174	71193	CGTGTGCACACGCGCCCTGC	21	167
			71294	71313			
1081099	N/A	N/A	72851	72870	GGCACACGCCATACCTGGGC	43	168
1081105	N/A	N/A	75990	76009	CCCCCATGCCCTACTCGGTC	49	169
1081111	N/A	N/A	77628	77647	GGTGCCTCTAACATAGACAC	49	170
1081117	N/A	N/A	79139	79158	ACAGCTGTACCCACAGGCGG	52	171
1081123	N/A	N/A	83317	83336	CGTCTCTGTATATGCCTGGC	50	172
1081129	N/A	N/A	84931	84950	CGGGTTCGCCCTTACTCATC	42	173
1081135	N/A	N/A	87153	87172	GCTGCCCGTATTCTTCCTGA	18	174
1081141	N/A	N/A	91137	91156	CGCAGGCATCCCACTCATGA	89	175
1081147	N/A	N/A	93676	93695	TCCGGCCTTCCTGACCATTC	23	176

Table 3. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39508

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID NO
854697	1354	1373	67703	67722	CTGGAGGTAGATGACCCGCT	48	177
1080687	41	60	4225	4244	CGGACCCGACCCGAGGGAGA	65	178
1080693	79	98	4263	4282	CCGCGCCCCGTCAGGGAGTG	68	179
1080699	127	146	4311	4330	GTTGGTGTAGCCCCCGCCGC	85	180
1080705	208	227	16600	16619	GCCGGCGGTGTCCAGGAGCG	36	181
1080711	237	256	16629	16648	ACCTCGGAGTCCAGGTCGCT	43	182
1080717	358	377	52127	52146	GAGCCGCTCCTTGAAGGTGT	36	183

1080723	517	536	55945	55964	GGAGTAGTTCTGCTTTGGGC	ND	184
1080729	594	613	57149	57168	TGGATCGCCCACAGTGTCAT	41	185
1080735	692	711	59173	59192	CGAAGGACACGCGGAAGATC	34	186
1080741	761	780	59309	59328	TGAACAGGTTCCGCAGCGGC	12	187
1080747	1012	1031	61762	61781	GTCACCGTAGCCCACGGTGG	59	188
1080753	1105	1124	67026	67045	GACGAGCTCCTCGAACTGCA	23	189
1080759	1174	1193	67095	67114	GTGCTTCTCCGTCTGCGCAC	43	190
1080770	1710	1729	72314	72333	ATGCGCTGCCACTGCTCCGG	44	191
1080776	1855	1874	72868	72887	CCGCTTCAGCCCGATGAGGC	40	192
1080782	2163	2182	74795	74814	GAGCCGTTCTCCGTGGGCAG	73	193
1080788	2208	2227	74840	74859	TCGGCCAGTTCCAGGACGGG	60	194
1080794	2318	2337	77310	77329	GAGGGTAGCCCTTCACATAC	24	195
1080800	2474	2493	79388	79407	CCGAGACGATGATCAGCTTG	30	196
1080806	2484	2503	79398	79417	GCCGTCTCTGCCGAGACGAT	ND	197
1080812	2505	2524	79419	79438	AAGTTGTACAGCCCATTGCC	50	198
1080818	2550	2569	79464	79483	TTCAGCTCCTTGCGGGATCT	22	199
1080824	3017	3036	86534	86553	TGTAGTCCTTCACGAAGGAC	56	200
1080830	3107	3126	86766	86785	ACAGGTCGCCCTCGGTGATT	48	201
1080836	3433	3452	88378	88397	CCGGCCTGCCTGCTTGGGCG	45	202
1080842	3484	3503	88429	88448	GCGCCGGTACAGGCTGAGGC	41	203
1080848	3536	3555	88481	88500	CCAGGTGCTTCATGCGGTTC	30	204
1080854	3850	3869	94229	94248	CGCTAGTGCCACCGTGTCCT	22	205
1080860	3933	3952	94312	94331	GGCCCTCCCCCCGCATGAGG	28	206
1080866	4370	4389	94749	94768	GGACGCACCCCTCTCACATG	31	207
1080872	4484	4503	94863	94882	GCCCAATGCCCCCTAGATGC	27	208
1080878	4496	4515	94875	94894	GCACCATCTTCCGCCCAATG	22	209
1080884	4631	4650	95010	95029	CGGGATCTCGCCTTGCTGAG	37	210
1080890	4700	4719	95079	95098	GACCGTACAAACCAGTAAGG	16	211
1080896	N/A	N/A	90124	90143	TACCCGATTCATGACATCAC	19	212
1080902	N/A	N/A	90130	90149	CAGGTTTACCCGATTCATGA	21	213
1080908	N/A	N/A	5393	5412	CCCTTAAAGACCATCCGCCC	41	214
1080914	N/A	N/A	7489	7508	CTGGCGGGCCCCACACATCC	63	215
1080920	N/A	N/A	11384	11403	ATGGATTTTCATCACGGCCT	72	216
1080926	N/A	N/A	16248	16267	GCGCACCACTCCTCCCTGAT	88	217
1080932	N/A	N/A	17509	17528	CCTGCCGTACCCTACACGCT	38	218
1080938	N/A	N/A	18670	18689	CGGCACACAACCCATGTGCC	93	219
1080944	N/A	N/A	20551	20570	AGCGGCACTTCCACCTTACC	ND	220
1080950	N/A	N/A	23042	23061	CCCGACTCCTCCTCGAACCT	48	221
1080956	N/A	N/A	25372	25391	GTGGCATTCCATGTTGACCC	38	222
1080962	N/A	N/A	27294	27313	ACCGTGTTTCTACATAAGCC	ND	223
1080968	N/A	N/A	30452	30471	GCTGTTACATCCGCAGTGAG	36	224
1080974	N/A	N/A	31098	31117	CCGTGTATACCTGTCTCCCC	59	225
1080980	N/A	N/A	34408	34427	ACAACAAGATCCAGGCACCG	41	226
1080986	N/A	N/A	36386	36405	GGAAGGACAATACCTTCGGC	29	227
1080992	N/A	N/A	38458	38477	TGCCCGGCTCAAACCACCGC	23	228

1080998	N/A	N/A	42854	42873	CGCAGCATCCAAACCCACGG	39	229
1081004	N/A	N/A	45699	45718	CGGCACACACTATAGCCTCG	36	230
1081010	N/A	N/A	48773	48792	TCCGCCCTGACCATCGCCCC	38	231
1081016	N/A	N/A	50478	50497	GGCTCCTATCAATCGAATCT	ND	232
1081022	N/A	N/A	53235	53254	GGACCCTTCTCCCTACGCTG	34	233
1081028	N/A	N/A	57238	57257	TGGGTTCCCTACTTACTGAG	23	234
			58128	58147			
1081034	N/A	N/A	60113	60132	ACACCTGTGTCTCGGCTGAG	48	235
			60155	60174			
			60247	60266			
1081040	N/A	N/A	61142	61161	GCCAGGTCCCAGATGCTATC	23	236
1081046	N/A	N/A	65273	65292	GCAGCCCACCCTTACCATCG	45	237
1081052	N/A	N/A	66668	66687	CCGGTCTTCCAGGCACTCGC	19	238
1081058	N/A	N/A	67951	67970	ATGGTCCACCCCAGACGATC	24	239
			68547	68566			
1081064	N/A	N/A	68062	68081	ATGGTCCACCCCAGATGGTC	ND	240
1081070	N/A	N/A	68509	68528	CAAGAGGGTCCACCATGGAT	86	241
			68565	68584			
1081076	N/A	N/A	68649	68668	CCGGACAGTCTACCCCAGAC	22	242
1081082	N/A	N/A	70255	70274	CCACCGGTATCCCAGTGCCC	42	243
1081088	N/A	N/A	71073	71092	CCAGACGCACCGTCACCCAC	48	244
			71153	71172			
1081094	N/A	N/A	71350	71369	ACACAGCTCGCCTAACTGCG	99	245
1081100	N/A	N/A	74164	74183	GGGCAGAGTGCCTACTGCGC	23	246
1081106	N/A	N/A	76774	76793	CCTCGGCATAACACATGGCC	82	247
1081112	N/A	N/A	77773	77792	GATCAGACACCCATGCCGGG	37	248
1081118	N/A	N/A	80495	80514	TCGGCCGGCCACGCCTTACT	30	249
1081124	N/A	N/A	84304	84323	GACTCCTCTCACACACCGGG	53	250
1081130	N/A	N/A	84933	84952	TCCGGGTTCGCCCTTACTCA	73	251
1081136	N/A	N/A	87371	87390	GTGAAGCTGCGATGTTCTGG	22	252
1081142	N/A	N/A	91673	91692	ACCCGCTTCCTAACCCTGCA	38	253
1081148	N/A	N/A	95466	95485	GAGTTCTGTGCCACTGCGGG	9	254

Table 4. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39508

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID NO
1080688	42	61	4226	4245	TCGGACCCGACCCGAGGGAG	125	255
1080694	80	99	4264	4283	TCCGCGCCCCGTCAGGGAGT	56	256
1080700	143	162	4327	4346	CAAACTCGAAGGTCCGGTTG	93	257
1080706	222	241	16614	16633	TCGCTCATCTTGAAGCCGGC	19	258

1080712	238	257	16630	16649	CACCTCGGAGTCCAGGTCGC	42	259
1080718	365	384	52134	52153	ACAGCTTGAGCCGCTCCTTG	38	260
1080724	531	550	55959	55978	GACGAGTCATTGAAGGAGTA	40	261
1080730	595	614	57150	57169	CTGGATCGCCCACAGTGTCA	27	262
1080736	698	717	59179	59198	CCAGGACGAAGGACACGCGG	47	263
1080742	910	929	60490	60509	CCCCGTGAAAACGAGGCACA	46	264
1080748	1036	1055	61786	61805	CGATGGCCAGATCTTGGGCG	43	265
1080754	1106	1125	67027	67046	AGACGAGCTCCTCGAACTGC	46	266
1080760	1175	1194	67096	67115	CGTGCTTCTCCGTCTGCGCA	27	267
1080765	1491	1510	70844	70863	TTCACGGCCCAGGCGCGCAG	71	268
1080771	1764	1783	72368	72387	TTGCTGTCACCCATGCGGAT	39	269
1080777	1888	1907	72901	72920	CCCCGGGTTCAGCAGGATGC	48	270
1080783	2164	2183	74796	74815	CGAGCCGTTCTCCGTGGGCA	30	271
1080789	2210	2229	74842	74861	TGTCGGCCAGTTCCAGGACG	85	272
1080795	2319	2338	77311	77330	GGAGGGTAGCCCTTCACATA	28	273
1080801	2475	2494	79389	79408	GCCGAGACGATGATCAGCTT	36	274
1080807	2486	2505	79400	79419	CGGCCGTCTCTGCCGAGACG	44	275
1080813	2512	2531	79426	79445	CACGATGAAGTTGTACAGCC	28	276
1080819	2689	2708	80708	80727	GTCCGCATAGATGATGCCAC	15	277
1080825	3018	3037	86535	86554	ATGTAGTCCTTCACGAAGGA	38	278
1080831	3114	3133	86773	86792	CGGATCCACAGGTCGCCCTC	25	279
1080837	3458	3477	88403	88422	GGCTGATCCACTCCGCGGCC	53	280
1080843	3522	3541	88467	88486	CGGTTCTTCACCAGCTCGGA	45	281
1080849	3663	3682	94042	94061	GGGTCGGAGCGGATGAGATA	29	282
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	22	283
1080861	3934	3953	94313	94332	TGGCCCTCCCCCCGCATGAG	43	284
1080867	4371	4390	94750	94769	GGGACGCACCCCTCTCACAT	32	285
1080873	4486	4505	94865	94884	CCGCCCAATGCCCCCTAGAT	53	286
1080879	4497	4516	94876	94895	TGCACCATCTTCCGCCCAAT	34	287
1080885	4632	4651	95011	95030	CCGGGATCTCGCCTTGCTGA	46	288
1080891	4702	4721	95081	95100	CTGACCGTACAAACCAGTAA	25	289
1080897	N/A	N/A	90125	90144	TTACCCGATTCATGACATCA	38	290
1080903	N/A	N/A	90131	90150	CCAGGTTTACCCGATTCATG	26	291
1080909	N/A	N/A	6181	6200	GGTTCTGACCACGCTGTTGC	79	292
1080915	N/A	N/A	7601	7620	AAGATGCCCATTTAACCGGG	84	293
1080921	N/A	N/A	11439	11458	AACTTGGAACCTCTACCTGG	71	294
1080927	N/A	N/A	16963	16982	CCTCCGCGCCCCAAGTCGGG	33	295
1080933	N/A	N/A	17641	17660	CCTGACCATTTTCAACCTCG	33	296
1080939	N/A	N/A	19044	19063	TGTCCTATAGACACCAACAC	61	297
1080945	N/A	N/A	21696	21715	ACGAAGCTTCCTCTTGCCTG	51	298
1080951	N/A	N/A	24071	24090	GACACCGTTCACATGTGATG	30	299
1080957	N/A	N/A	25510	25529	CCTTCGGGAGCCACACGCTC	61	300
1080963	N/A	N/A	28340	28359	GGGTACGGCCTCATCCAGGT	45	301
1080969	N/A	N/A	30456	30475	GGTGGCTGTTACATCCGCAG	38	302
1080975	N/A	N/A	31586	31605	GTAACGAACCACCACCAGCC	68	303

1080981	N/A	N/A	34524	34543	AGCCCACACGCCATACAGTT	74	304
1080987	N/A	N/A	36895	36914	CTGCAGGGCCCTTCACCGCG	45	305
1080993	N/A	N/A	38783	38802	CCCGCGCGCCCCTACCTCTG	39	306
1080999	N/A	N/A	43235	43254	CCCGATATAGCCCTAGCTGA	55	307
1081005	N/A	N/A	46620	46639	GCCCCGTCCCTACACGGCTG	55	308
1081011	N/A	N/A	48803	48822	GGCCACTCCTCCTAGGCGGG	47	309
1081017	N/A	N/A	50894	50913	AGTCGGCTGCCTTAGCCCTC	38	310
1081023	N/A	N/A	55659	55678	AGGGTACATCCCACATCTGC	17	311
1081029	N/A	N/A	58506	58525	ACCTGGTTTTCCCCCACGGA	48	312
1081035	N/A	N/A	60114	60133	CACACCTGTGTCTCGGCTGA	45	313
			60156	60175			
			60248	60267			
1081041	N/A	N/A	61207	61226	CGGCACAGCCAGACAAGCGC	43	314
1081047	N/A	N/A	65470	65489	CGGAGGATACATATCTGCTG	33	315
1081053	N/A	N/A	67263	67282	GGGACTTGCCAAGCAGTCCT	72	316
			67384	67403			
1081059	N/A	N/A	67955	67974	CTGAATGGTCCACCCCAGAC	52	317
			68094	68113			
1081065	N/A	N/A	68143	68162	ATCCACCCTGGATGGTCCAC	34	318
			68366	68385			
1081071	N/A	N/A	68513	68532	CACCCAAGAGGGTCCACCAT	85	319
			68569	68588			
1081077	N/A	N/A	68940	68959	GGAACTCTACCTTCAGCCCG	55	320
1081083	N/A	N/A	70954	70973	CAGATACACCATCACCCACG	87	321
1081089	N/A	N/A	71076	71095	GCCCCAGACGCACCGTCACC	26	322
			71156	71175			
1081095	N/A	N/A	71738	71757	GGTGGACCTTCCATCGCTCC	30	323
1081101	N/A	N/A	74408	74427	GGTTGGCTGATTCTGGGCTC	38	324
1081107	N/A	N/A	76923	76942	GGACTTAGCCCCATCAGGGC	19	325
1081113	N/A	N/A	78059	78078	GTGACCTGACAATTGACCCC	67	326
1081119	N/A	N/A	81776	81795	GACCAACTGACCATGCCAGG	53	327
1081125	N/A	N/A	84520	84539	CGGATGAGCCCTTCCTGAGC	60	328
1081131	N/A	N/A	85101	85120	GGGTCATTCTTCAGCGGAGG	50	329
1081137	N/A	N/A	88514	88533	GTGTGCCCTTACCGTAGCCG	34	330
1081143	N/A	N/A	91674	91693	AACCCGCTTCCTAACCCTGC	76	331
1081149	N/A	N/A	96183	96202	TGCGACTCCCCCATGGTGCC	72	332

Table 5. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39508

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID NO

1080689	45	64	4229	4248	AGCTCGGACCCGACCCGAGG	97	333
1080695	81	100	4265	4284	GTCCGCGCCCCGTCAGGGAG	76	334
1080701	146	165	4330	4349	CGTCAAACTCGAAGGTCCGG	102	335
1080707	223	242	16615	16634	GTCGCTCATCTTGAAGCCGG	25	336
1080713	327	346	52096	52115	TAGAACTCCACCTGGACCCT	36	337
1080719	417	436	52950	52969	GAGAAGTTGAACAGCCGGAT	48	338
1080725	535	554	55963	55982	GGAGGACGAGTCATTGAAGG	45	339
1080731	597	616	57152	57171	ACCTGGATCGCCCACAGTGT	31	340
1080737	706	725	59187	59206	GATCATCTCCAGGACGAAGG	43	341
1080743	928	947	61678	61697	GTGCTGGATGCCGCAGGTCC	33	342
1080749	1066	1085	61816	61835	CACGCAGATCATGATGACCA	55	343
1080755	1114	1133	67035	67054	CCAGAGGTAGACGAGCTCCT	33	344
1080761	1210	1229	67131	67150	AAGGTCGATCTTGAGGGAGC	36	345
1080766	1493	1512	70846	70865	CCTTCACGGCCCAGGCGCGC	43	346
1080772	1776	1795	72380	72399	TCGCGGAAGAACTTGCTGTC	50	347
1080778	1954	1973	72967	72986	CGAGTTCTCCTCCTTGGTGA	39	348
1080784	2175	2194	74807	74826	CGCCGGCTGCCCGAGCCGTT	54	349
1080790	2213	2232	74845	74864	AGCTGTCGGCCAGTTCCAGG	56	350
1080796	2454	2473	79368	79387	TTCTTGAACCCGTAGGCCTT	44	351
1080802	2476	2495	79390	79409	TGCCGAGACGATGATCAGCT	31	352
1080808	2490	2509	79404	79423	TTGCCGGCCGTCTCTGCCGA	46	353
1080814	2518	2537	79432	79451	CAGTGGCACGATGAAGTTGT	44	354
1080820	2696	2715	80715	80734	CCAGGTTGTCCGCATAGATG	33	355
1080826	3020	3039	86537	86556	TCATGTAGTCCTTCACGAAG	67	356
1080832	3117	3136	86776	86795	GTGCGGATCCACAGGTCGCC	41	357
1080838	3459	3478	88404	88423	TGGCTGATCCACTCCGCGGC	37	358
1080844	3523	3542	88468	88487	GCGGTTCTTCACCAGCTCGG	18	359
1080850	3732	3751	94111	94130	TTGCAGGACGACAGCTTGTG	50	360
1080856	3859	3878	94238	94257	CCAGGGTCACGCTAGTGCCA	25	361
1080862	4032	4051	94411	94430	GTTGCGGTACATCTGTGTAA	8	362
1080868	4414	4433	94793	94812	CCTTCAGAAAGGTCCTCGGC	29	363
1080874	4491	4510	94870	94889	ATCTTCCGCCCAATGCCCCC	42	364
1080880	4498	4517	94877	94896	ATGCACCATCTTCCGCCCAA	27	365
1080886	4634	4653	95013	95032	GCCCGGGATCTCGCCTTGCT	28	366
1080892	4703	4722	95082	95101	GCTGACCGTACAAACCAGTA	14	367
1080898	N/A	N/A	90126	90145	TTTACCCGATTCATGACATC	46	368
1080904	N/A	N/A	2853	2872	CCCCAGATCGCCAGCCCGTC	76	369
1080910	N/A	N/A	6210	6229	GCACCAAGACCTATGGACTC	87	370
1080916	N/A	N/A	8477	8496	GGCGACGGTGCCAAGGAGGA	64	371
1080922	N/A	N/A	12789	12808	GAGCGCATCACTATTTTCTC	88	372
1080928	N/A	N/A	17266	17285	TGGGCTCATCCTGTTGGTCC	35	373
1080934	N/A	N/A	17803	17822	TAGAATATTCCATTCCCCGC	35	374
1080940	N/A	N/A	19220	19239	CTCATCCTATAGACACCAAC	37	375
			19266	19285			
1080946	N/A	N/A	22380	22399	ACTTCCCCGACCAGCTGAGA	68	376

1080952	N/A	N/A	24243	24262	GCGGGATTCGCCCTCTCAGG	18	377
1080958	N/A	N/A	26459	26478	CCCTCGCCGACCACTGGCCT	24	378
1080964	N/A	N/A	28499	28518	CAGGTTCTACCTACCAAGGG	28	379
1080970	N/A	N/A	30784	30803	ATCACCATAACCAGACCCGG	35	380
1080976	N/A	N/A	31773	31792	TGCAACATTTTCAAGCCTCG	24	381
1080982	N/A	N/A	34618	34637	GCAATGGAAGCCACACTCGA	44	382
1080988	N/A	N/A	37260	37279	GCGCTCCCGATACCTGCCCT	39	383
1080994	N/A	N/A	39863	39882	TTGACCTTAGCCTCAACCGC	65	384
1081000	N/A	N/A	43695	43714	TCGGCCTACGCCAGGCTCTC	57	385
1081006	N/A	N/A	46984	47003	GGGCGCAGCCACACACTCGC	28	386
1081012	N/A	N/A	49047	49066	GGGTGACTTCCCAACTGGCT	41	387
1081018	N/A	N/A	51273	51292	TGGCTCACCTACCGTGGCCA	77	388
1081024	N/A	N/A	55801	55820	GGGCTAACCCCCACATCAGA	38	389
1081030	N/A	N/A	58944	58963	CTGTGAGGTGCCATCCCGGG	68	390
1081036	N/A	N/A	60146	60165	TCTCGGCTGAGGCCCACGGG	38	391
			60192	60211			
			60284	60303			
1081042	N/A	N/A	63494	63513	GGTGAGATTTACGGATTGGG	29	392
1081048	N/A	N/A	65546	65565	ACAATCTCCCCCAAAGCGGC	23	393
1081054	N/A	N/A	67914	67933	CCCGGACGATCCACCCTGGA	45	394
1081060	N/A	N/A	67956	67975	CCTGAATGGTCCACCCCAGA	52	395
			68095	68114			
1081066	N/A	N/A	68154	68173	CACCCTAGACAATCCACCCT	53	396
1081072	N/A	N/A	68515	68534	TCCACCCAAGAGGGTCCACC	29	397
			68571	68590			
1081078	N/A	N/A	69277	69296	ATGGCCTACGCCCTTGCCCT	48	398
1081084	N/A	N/A	71037	71056	TGCCCCAGACGCACCGTCAC	32	399
			71077	71096			
			71157	71176			
1081090	N/A	N/A	71165	71184	ACGCGCCCTGCCCCAGACGC	34	400
			71285	71304			
1081096	N/A	N/A	71768	71787	GACCTCAACCCCCTACTTGG	82	401
1081102	N/A	N/A	74644	74663	CGGCGAGTTCCCAGAGCTCA	43	402
1081108	N/A	N/A	77143	77162	CCGTTCTTCCCTTAACCACC	38	403
1081114	N/A	N/A	78693	78712	CCGGCCACAGATTATAACCC	60	404
1081120	N/A	N/A	81784	81803	GGAGTTCTGACCAACTGACC	63	405
1081126	N/A	N/A	84783	84802	GCATCCAGAATTCCAGCCGT	32	406
1081132	N/A	N/A	86404	86423	GCTCGCCACCCCTCATGCAT	42	407
1081138	N/A	N/A	88517	88536	GCCGTGTGCCCTTACCGTAG	40	408
1081144	N/A	N/A	91686	91705	TGCTCGCCCCCCAACCCGCT	48	409
1081150	N/A	N/A	96608	96627	GGGAGGATTCACAGGCCGCT	41	410

Table 6. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39508

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID NO
1080690	46	65	4230	4249	CAGCTCGGACCCGACCCGAG	74	411
1080696	121	140	4305	4324	GTAGCCCCCGCCGCGCGCCT	53	412
1080702	191	210	16583	16602	GCGCGCCGTCCCCCGCGCAG	76	413
1080708	225	244	16617	16636	AGGTCGCTCATCTTGAAGCC	47	414
1080714	328	347	52097	52116	GTAGAACTCCACCTGGACCC	46	415
1080720	457	476	52990	53009	GACGCGCACAATGTAGAGCA	40	416
1080726	547	566	55975	55994	CCAGTTGATCTCGGAGGACG	50	417
1080732	611	630	58869	58888	TTATGGCCACGATGACCTGG	52	418
1080738	708	727	59189	59208	TTGATCATCTCCAGGACGAA	71	419
1080744	948	967	61698	61717	TTCTCGCCCGCCCGCTCCAG	66	420
1080750	1067	1086	61817	61836	CCACGCAGATCATGATGACC	57	421
1080756	1123	1142	67044	67063	CCGCTCCATCCAGAGGTAGA	52	422
1080762	1214	1233	67135	67154	TGAGAAGGTCGATCTTGAGG	75	423
1080767	1494	1513	70847	70866	TCCTTCACGGCCCAGGCGCG	49	424
1080773	1778	1797	72382	72401	ACTCGCGGAAGAACTTGCTG	45	425
1080779	1955	1974	72968	72987	CCGAGTTCTCCTCCTTGGTG	26	426
1080785	2176	2195	74808	74827	CCGCCGGCTGCCCGAGCCGT	40	427
1080791	2261	2280	74893	74912	CCTCATCCTCCGACTGGTCG	38	428
1080797	2455	2474	79369	79388	GTTCTTGAACCCGTAGGCCT	35	429
1080803	2477	2496	79391	79410	CTGCCGAGACGATGATCAGC	34	430
1080809	2502	2521	79416	79435	TTGTACAGCCCATTGCCGGC	46	431
1080815	2519	2538	79433	79452	GCAGTGGCACGATGAAGTTG	61	432
1080821	2954	2973	86062	86081	CGGCGGCGAACGGCAGGCGG	27	433
1080827	3037	3056	86554	86573	CAGCCGGGTGATGGTGATCA	52	434
1080833	3118	3137	86777	86796	CGTGCGGATCCACAGGTCGC	44	435
1080839	3461	3480	88406	88425	GCTGGCTGATCCACTCCGCG	53	436
1080845	3524	3543	88469	88488	TGCGGTTCTTCACCAGCTCG	48	437
1080851	3840	3859	94219	94238	ACCGTGTCCTCACACGCTCC	19	438
1080857	3861	3880	94240	94259	CCCCAGGGTCACGCTAGTGC	25	439
1080863	4033	4052	94412	94431	AGTTGCGGTACATCTGTGTA	23	440
1080869	4456	4475	94835	94854	GGACAGTTCAGTGTGAAGTA	47	441
1080875	4492	4511	94871	94890	CATCTTCCGCCCAATGCCCC	42	442
1080881	4501	4520	94880	94899	GAAATGCACCATCTTCCGCC	39	443
1080887	4641	4660	95020	95039	AGCCGCCGCCCGGGATCTCG	55	444
1080893	4704	4723	95083	95102	CGCTGACCGTACAAACCAGT	39	445
1080899	N/A	N/A	90127	90146	GTTTACCCGATTCATGACAT	38	446
1080905	N/A	N/A	3435	3454	GGAGAACTGCGATTTCTGTC	88	447

1080911	N/A	N/A	6282	6301	CCCCTCTGAACCATAGCACC	91	448
1080917	N/A	N/A	8832	8851	AATGACCAACTCACTGGCGC	40	449
			37276	37295			
1080923	N/A	N/A	12935	12954	CGCGGGAGCCCCAAACCCAC	63	450
1080929	N/A	N/A	17285	17304	AGCGGATGAATTATTCCCAT	30	451
1080935	N/A	N/A	17804	17823	GTAGAATATTCCATTCCCCG	32	452
1080941	N/A	N/A	19315	19334	TGTCCCATCCTATAGACACC	47	453
1080947	N/A	N/A	22762	22781	CACTCACGCCTTCACGCAGA	52	454
1080953	N/A	N/A	24432	24451	TGGTGGCTTCCTGACGCGGA	48	455
1080959	N/A	N/A	26473	26492	CAGACTGGCCACGCCCCTCG	56	456
1080965	N/A	N/A	29889	29908	CACTCGCCTTTTTAGAGCCC	44	457
1080971	N/A	N/A	30872	30891	TCTCAGATTCACAATCCCGG	30	458
1080977	N/A	N/A	32351	32370	CCCCCTCGCCACGCATGGTT	28	459
1080983	N/A	N/A	34970	34989	GCCGGAATCCTCACCCTTAG	38	460
1080989	N/A	N/A	37589	37608	CCGGCCCGCCCCAAACTCAC	54	461
1080995	N/A	N/A	40432	40451	CGTGAGATCCACACTCCAGA	36	462
1081001	N/A	N/A	44414	44433	GGTGACAACCACACTCGAGG	32	463
1081007	N/A	N/A	47083	47102	GGGAACATCGCCATTCCCAG	78	464
1081013	N/A	N/A	49373	49392	CCACCGGGCCCTAAAAGCAT	83	465
1081019	N/A	N/A	52235	52254	TTCGCCATCGCCAGGCTTGC	40	466
1081025	N/A	N/A	56008	56027	CGCCTGGCTATTGGGAGCTG	40	467
			56072	56091			
1081031	N/A	N/A	59374	59393	GCCCCGGCTTACAATCATGT	63	468
1081037	N/A	N/A	60147	60166	GTCTCGGCTGAGGCCCACGG	30	469
			60193	60212			
			60285	60304			
1081043	N/A	N/A	64874	64893	ATGGCCATACCCATCGATGC	22	470
1081049	N/A	N/A	65596	65615	AAGCAGCCCCAGGGATTGCG	28	471
1081055	N/A	N/A	67917	67936	CACCCCGGACGATCCACCCT	52	472
1081061	N/A	N/A	67958	67977	ACCCTGAATGGTCCACCCCA	49	473
			68097	68116			
1081067	N/A	N/A	68342	68361	GAGATCCATCCCAGATGGTT	58	474
1081073	N/A	N/A	68516	68535	GTCCACCCAAGAGGGTCCAC	29	475
			68572	68591			
1081079	N/A	N/A	69658	69677	GGTGGAGACCCCACCTAGGT	46	476
1081085	N/A	N/A	71038	71057	CTGCCCCAGACGCACCGTCA	21	477
			71078	71097			
			71158	71177			
1081091	N/A	N/A	71166	71185	CACGCGCCCTGCCCCAGACG	73	478
			71286	71305			
1081097	N/A	N/A	72438	72457	CCGGCCTTACTTCTTGTGGG	66	479
1081103	N/A	N/A	74938	74957	GCACTCACTCTACCACGGAG	79	480
1081109	N/A	N/A	77306	77325	GTAGCCCTTCACATACCTGG	64	481
1081115	N/A	N/A	78899	78918	GTGGTTCATTCCAGACTGGA	42	482
1081121	N/A	N/A	81950	81969	GTCCCTTGTCAATACAAGGA	59	483

1081127	N/A	N/A	84926	84945	TCGCCCTTACTCATCAGTGG	50	484
1081133	N/A	N/A	86428	86447	AGGTCCATACCCCACCGGCC	39	485
1081139	N/A	N/A	89027	89046	GGTCCCCACCAGTCTTGTTC	49	486
1081145	N/A	N/A	91719	91738	TCCGACCTTTACTCCAGGCC	21	487
1081151	N/A	N/A	96762	96781	CGGGTGCTCCCTAAACCTGG	71	488

Table 7. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	24	283
1337234	N/A	N/A	18642	18661	ACAGCACGCCAAGACCGCTA	28	489
1337247	N/A	N/A	22973	22992	CGTGCCCCACCCTCACCTTT	33	490
1337271	N/A	N/A	25733	25752	ACTGGCAGAATCATCAGTAA	49	491
1337272	N/A	N/A	31118	31137	AGCGAACTTAATTATATCTC	31	492
1337277	N/A	N/A	67945	67964	CACCCCAGACGATCCACCCT	51	493
1337307	N/A	N/A	48755	48774	CCACACTCCACTCCAAGGCA	31	494
1337319	N/A	N/A	19177	19196	CTCCCATCCTATACACACCA	41	495
1337323	N/A	N/A	47075	47094	CGCCATTCCCAGAGTCCACA	31	496
1337325	N/A	N/A	66012	66031	GCCTTGCCACACAAAACAGT	43	497
1337327	N/A	N/A	87839	87858	AGCACATCCTGGCCTTGCCC	12	498
1337332	N/A	N/A	54378	54397	GGTTCTGCCCTCTTCTGACC	9	499
1337337	N/A	N/A	19881	19900	GACTCACCCAACCCTACCAT	58	500
1337378	N/A	N/A	42262	42281	CCACACGCAACAAAGGCACC	40	501
1337473	N/A	N/A	33706	33725	GATGACGGTCCCATGCTGAT	30	502
1337479	N/A	N/A	44857	44876	CTCTCACACCTCTAAGAGCC	68	503
1337515	N/A	N/A	40232	40251	GCGAGGCCACCCATGTGAAA	48	504
1337557	N/A	N/A	31679	31698	AGCTGAACCACCCACAGAGA	61	505
1337565	N/A	N/A	73927	73946	CACCGTGTAACAACACCCCA	36	506
1337570	N/A	N/A	22293	22312	ACCGCAACCCCTTCTGCTTG	32	507
1337582	N/A	N/A	18187	18206	CTGCCGTTTTCAAGAATTAA	28	508
1337624	N/A	N/A	34958	34977	ACCCTTAGCCCTCATCAGGA	45	509
1337658	N/A	N/A	17714	17733	GACTCTAGTTACAAACATGA	30	510
1337674	N/A	N/A	48074	48093	ACGATCCATTTTCCCCTGCA	28	511
1337696	N/A	N/A	86209	86228	AGAGGGAGTCCTATCATTCA	32	512
1337729	N/A	N/A	29630	29649	CCTGGTGCCACACCTCCCTT	31	513
1337790	N/A	N/A	37484	37503	CCTCCATGCACCCGTGCCAC	31	514
1337831	N/A	N/A	62061	62080	TCACGGGACTCCATCATTAC	37	515
1337853	N/A	N/A	76382	76401	CGGACACACAACATACGCAA	61	516
1337856	N/A	N/A	32675	32694	GTTTTAAGCACACCATCCCG	57	517
1337871	N/A	N/A	93318	93337	CTTCATAGCAACCCATGCCT	36	518

1337874	N/A	N/A	68280	68299	CACCCTGGACAGTCTACCCT	43	519
1337896	N/A	N/A	62937	62956	GAAAGCCACACACAACTGGC	27	520
1337952	N/A	N/A	81978	81997	GGCAGGCCCCTTCCCTCTCA	36	521
1337988	N/A	N/A	55656	55675	GTACATCCCACATCTGCGGG	21	522
1337990	N/A	N/A	24539	24558	GGCATAAACACACTTACACC	35	523
1338022	N/A	N/A	21423	21442	CCCCCGACATACACAGCATC	40	524
1338028	N/A	N/A	39245	39264	ACCAGCCCAAGCATACCCCA	43	525
1338062	N/A	N/A	27209	27228	GGAGTACTCTCCACAGACCC	23	526
1338153	N/A	N/A	78619	78638	GGAGGTCCCCTCCGTGGCCG	53	527
1338221	N/A	N/A	89346	89365	GCCCATGGCTTCATCAACGG	24	528
1338284	N/A	N/A	82786	82805	GAACACAGAATCCTGTGAAC	51	529
1338312	N/A	N/A	53236	53255	GGGACCCTTCTCCCTACGCT	14	530
1338327	N/A	N/A	71160	71179	CCCTGCCCCAGACGCACCGT	26	531
1338371	N/A	N/A	75708	75727	TTGACCCCACCCCAGAGGCA	56	532
1338380	N/A	N/A	58395	58414	ACCCAGTCATGAACTAGGTC	25	533
1338411	N/A	N/A	68885	68904	GCCCCTGTTCTATTTTGAGC	64	534
1338472	N/A	N/A	43184	43203	TCTACTCTGCCCAAGGCCCT	52	535
1338475	3837	3856	94216	94235	GTGTCCTCACACGCTCCTCC	15	536
1338539	N/A	N/A	77536	77555	CCTTGCAGAATTCTTGCAGC	41	537
1338584	N/A	N/A	87032	87051	TAGCAAAGCTGATCTAGCCC	16	538
1338668	N/A	N/A	45674	45693	AGACGCATCCATTTCCTCCA	28	539
1338714	N/A	N/A	50484	50503	GGCACTGGCTCCTATCAATC	21	540
1338732	N/A	N/A	30479	30498	GGGCTTTTCCCAGGCAGGCC	30	541
1338757	N/A	N/A	40855	40874	TAATCAGCTCCCAATCCCTC	59	542
1338790	N/A	N/A	92433	92452	CTGTGTCCACACCTGCGGGA	30	543
1338877	4746	4765	95125	95144	CTTCATGCCTCCAGAATGCA	28	544
1338944	N/A	N/A	51865	51884	TGAAGATTCCTCCCCGCAGC	59	545
1338988	N/A	N/A	49201	49220	ACCAGACCCCAGAATCTCCT	42	546
1339065	N/A	N/A	84233	84252	ACCAGCAGCATCCTTAATAA	48	547
1339137	N/A	N/A	72442	72461	CAGCCCGGCCTTACTTCTTG	38	548
1339151	N/A	N/A	27805	27824	CCCAGGCAAACCGCCCAGCA	20	549
1339156	N/A	N/A	91716	91735	GACCTTTACTCCAGGCCTCA	13	550
1339160	N/A	N/A	90703	90722	ACGAAGGTCACCATCCACCT	19	551
1339168	N/A	N/A	23662	23681	TTGGACACCATCCCGGGCCT	16	552
1339180	4265	4284	94644	94663	CAGAGTGCAGAACAGCAGCC	41	553
1339217	N/A	N/A	69820	69839	GCCCTGTTCTCTGAAGCAAC	26	554
1339277	N/A	N/A	65182	65201	ATCACTGTCCCAATCACCCC	58	555
1339289	4507	4526	94886	94905	TCCATGGAAATGCACCATCT	23	556
1339330	N/A	N/A	60779	60798	GGGCCAGTCCCCTTCTCTAC	21	557
1339365	N/A	N/A	36572	36591	CAAGAGAACATCTGTGCCGT	32	558
1339417	N/A	N/A	57078	57097	CAGTAGGGCACCACAGCCAC	67	559
1339423	N/A	N/A	58942	58961	GTGAGGTGCCATCCCGGGCA	29	560
1339454	N/A	N/A	85145	85164	GGCGGTACATCCACGGGCTC	39	561

1339481	N/A	N/A	56447	56466	GGTGCCTTCCTTTGCCGTAA	13	562
1339523	N/A	N/A	20544	20563	CTTCCACCTTACCCAGACCT	37	563
1339569	N/A	N/A	32356	32375	GTGGTCCCCCTCGCCACGCA	26	564
1339621	N/A	N/A	79249	79268	AGACCCCTCACCAAACATCC	51	565

Table 8. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	30	283
1337226	N/A	N/A	37418	37437	CGGCAGGTCCCTGACAGGCA	12	566
1337228	N/A	N/A	93317	93336	TTCATAGCAACCCATGCCTA	59	567
1337243	N/A	N/A	57076	57095	GTAGGGCACCACAGCCACTA	56	568
1337267	N/A	N/A	56391	56410	GAGACGGGCTTCCTTGCATC	27	569
1337329	N/A	N/A	60574	60593	GCATCTGTATCCCCTCGCCC	12	570
1337365	N/A	N/A	82776	82795	TCCTGTGAACTTCCTCCCCT	55	571
1337400	N/A	N/A	50482	50501	CACTGGCTCCTATCAATCGA	50	572
1337409	N/A	N/A	68260	68279	AGATGGTCCACCCCACATGA	44	573
1337462	N/A	N/A	34887	34906	CCAGGGCTGACCCTTGGACT	47	574
1337506	N/A	N/A	76381	76400	GGACACACAACATACGCAAC	69	575
1337528	N/A	N/A	73718	73737	CCATGGGCCTCCACCTGCTC	62	576
1337575	N/A	N/A	90700	90719	AAGGTCACCATCCACCTGGC	18	577
1337595	N/A	N/A	49164	49183	CAGCACGGCCTCCCCGAGCT	35	578
1337598	N/A	N/A	51825	51844	AGTCTGGGCCCTCCAGGCCG	55	579
1337622	N/A	N/A	19121	19140	ACACACCAACACCACAGGGC	22	580
			19165	19184			
1337673	N/A	N/A	68884	68903	CCCCTGTTCTATTTTGAGCC	42	581
1337677	N/A	N/A	67941	67960	CCAGACGATCCACCCTAAAT	51	582
1337684	N/A	N/A	22968	22987	CCCACCCTCACCTTTGGGTC	50	583
1337708	N/A	N/A	91714	91733	CCTTTACTCCAGGCCTCAGT	76	584
1337816	N/A	N/A	27208	27227	GAGTACTCTCCACAGACCCC	35	585
1337925	N/A	N/A	29628	29647	TGGTGCCACACCTCCCTTCA	46	586
1337956	N/A	N/A	78566	78585	ACTGGAAACCATCCACAGAT	56	587
1337975	N/A	N/A	54376	54395	TTCTGCCCTCTTCTGACCTA	23	588
1338018	N/A	N/A	93878	93897	CACAGGTGCTACTCACACAA	53	589
1338027	4745	4764	95124	95143	TTCATGCCTCCAGAATGCAT	31	590
1338042	N/A	N/A	18184	18203	CCGTTTTCAAGAATTAACCA	19	591
1338060	N/A	N/A	43150	43169	GAGGAAGCCACCACCTGTCA	49	592
1338124	N/A	N/A	17646	17665	TGTGTCCTGACCATTTTCAA	26	593
1338160	N/A	N/A	42252	42271	CAAAGGCACCCCCTTATCTC	66	594

1338161	N/A	N/A	22247	22266	GAGAGAAGCCTCTCTCTGTT	44	595
1338269	N/A	N/A	75543	75562	ACTTGGCCCCAAACCTAGGC	39	596
1338324	N/A	N/A	62935	62954	AAGCCACACACAACTGGCTT	66	597
1338369	N/A	N/A	58383	58402	ACTAGGTCACCCACCCAGGA	52	598
1338422	N/A	N/A	55655	55674	TACATCCCACATCTGCGGGA	23	599
1338464	N/A	N/A	87027	87046	AAGCTGATCTAGCCCAGGTC	28	600
1338477	N/A	N/A	66011	66030	CCTTGCCACACAAAACAGTT	53	601
1338483	N/A	N/A	85116	85135	CCGTGGCCAACTCTCGGGTC	50	602
1338523	N/A	N/A	47069	47088	TCCCAGAGTCCACACCCGGC	38	603
1338533	N/A	N/A	53183	53202	TGGCTTTTTCCATCCTGGGA	8	604
1338553	N/A	N/A	71083	71102	GCATCCTGCCCCAGACGCAC	32	605
1338579	N/A	N/A	40139	40158	GCTACAGCTCCCATGCTGCA	41	606
1338676	N/A	N/A	31675	31694	GAACCACCCACAGAGAGGCC	43	607
1338677	N/A	N/A	92432	92451	TGTGTCCACACCTGCGGGAT	29	608
1338698	4503	4522	94882	94901	TGGAAATGCACCATCTTCCG	22	609
1338706	N/A	N/A	39169	39188	GGCTTCGGCCTCACTCACCT	32	610
1338721	N/A	N/A	58927	58946	GGGCAGGCACTCACTTTGTA	67	611
1338726	N/A	N/A	23651	23670	CCCGGGCCTTTCCTGCTCCA	31	612
1338753	N/A	N/A	21375	21394	GAAGCCGCACCTCCACTGCC	46	613
1338771	N/A	N/A	32673	32692	TTTAAGCACACCATCCCGGA	65	614
1338793	N/A	N/A	48754	48773	CACACTCCACTCCAAGGCAA	74	615
1338825	N/A	N/A	27739	27758	GCTGAGGGTCCCAAACCCAG	35	616
1338845	N/A	N/A	72437	72456	CGGCCTTACTTCTTGTGGGC	50	617
1338852	N/A	N/A	45673	45692	GACGCATCCATTTCCTCCAC	31	618
1338905	N/A	N/A	36489	36508	AGGATCTTCGCAACTTGCTG	38	619
1338915	N/A	N/A	79245	79264	CCCTCACCAAACATCCCCCG	84	620
1338943	N/A	N/A	32279	32298	ATTTGGCCCACCACACACGG	66	621
1338969	N/A	N/A	87774	87793	AGCCCTGATCCCTCTTGCAA	19	622
1338983	4264	4283	94643	94662	AGAGTGCAGAACAGCAGCCC	24	623
1339093	N/A	N/A	65181	65200	TCACTGTCCCAATCACCCCC	69	624
1339109	N/A	N/A	40854	40873	AATCAGCTCCCAATCCCTCC	82	625
1339133	N/A	N/A	33704	33723	TGACGGTCCCATGCTGATCA	37	626
1339167	N/A	N/A	48034	48053	GCGATCTGTCTTCACGAGTC	33	627
1339170	N/A	N/A	25732	25751	CTGGCAGAATCATCAGTAAC	74	628
1339194	N/A	N/A	31117	31136	GCGAACTTAATTATATCTCC	16	629
1339212	N/A	N/A	89345	89364	CCCATGGCTTCATCAACGGA	46	630
1339228	N/A	N/A	81929	81948	GCAGTGGTTATACTGAACCT	42	631
1339262	N/A	N/A	44846	44865	CTAAGAGCCCTTGTCTGCCA	63	632
1339388	N/A	N/A	20528	20547	ACCTGAGACACCCCCATGGC	70	633
1339451	N/A	N/A	30453	30472	GGCTGTTACATCCGCAGTGA	16	634
1339467	N/A	N/A	69811	69830	TCTGAAGCAACCCCCCAGCT	63	635
1339471	N/A	N/A	19854	19873	GAAGCAAGCCCCTTTGGGCA	30	636
1339491	N/A	N/A	62059	62078	ACGGGACTCCATCATTACCC	15	637

1339558	N/A	N/A	18574	18593	GGAGTGAGTCCCAGTGGTTA	56	638
1339564	N/A	N/A	86207	86226	AGGGAGTCCTATCATTCAGA	33	639
1339578	N/A	N/A	77410	77429	GCCGCCAGCCTTACCTTGTC	80	640
1339626	N/A	N/A	24534	24553	AAACACACTTACACCCATTC	33	641
1339630	N/A	N/A	84232	84251	CCAGCAGCATCCTTAATAAT	61	642

Table 9. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	21	283
1337246	N/A	N/A	65180	65199	CACTGTCCCAATCACCCCCA	51	643
1337258	N/A	N/A	19136	19155	TCCCTCCTGTCCTATACACA	56	644
1337259	623	642	58881	58900	CCAGGAAGCTTATTATGGCC	19	645
1337266	N/A	N/A	55630	55649	GGTAGCCCCAACCCAACAGC	17	646
1337417	N/A	N/A	92410	92429	GACGGCCTGACACCTGCCCC	25	647
1337494	N/A	N/A	30386	30405	CCGCTGGCTCTTTTCTGCCC	34	648
1337654	N/A	N/A	81925	81944	TGGTTATACTGAACCTGTTT	28	649
1337688	4500	4519	94879	94898	AAATGCACCATCTTCCGCCC	33	650
1337702	4744	4763	95123	95142	TCATGCCTCCAGAATGCATC	20	651
1337728	N/A	N/A	54372	54391	GCCCTCTTCTGACCTAGACA	23	652
1337760	N/A	N/A	67938	67957	GACGATCCACCCTAAATGGT	33	653
1337775	N/A	N/A	27199	27218	CCACAGACCCCTCCTTCTGA	44	654
1337794	N/A	N/A	53182	53201	GGCTTTTTCCATCCTGGGAC	14	655
1337801	N/A	N/A	68883	68902	CCCTGTTCTATTTTGAGCCT	52	656
1337808	N/A	N/A	69810	69829	CTGAAGCAACCCCCCAGCTT	65	657
1337819	N/A	N/A	22967	22986	CCACCCTCACCTTTGGGTCA	54	658
1337833	N/A	N/A	46983	47002	GGCGCAGCCACACACTCGCC	47	659
1338021	N/A	N/A	29627	29646	GGTGCCACACCTCCCTTCAA	44	660
1338053	N/A	N/A	86206	86225	GGGAGTCCTATCATTCAGAA	38	661
1338129	N/A	N/A	24533	24552	AACACACTTACACCCATTCC	28	662
1338163	N/A	N/A	83786	83805	TGGCAGAGCATCTCACTGAC	58	663
1338193	N/A	N/A	49144	49163	CTGTTGTTCTCCCCTCCGCT	42	664
1338266	N/A	N/A	40138	40157	CTACAGCTCCCATGCTGCAC	51	665
1338292	N/A	N/A	78190	78209	GTGGTTTGCTTTCCTGATCT	24	666
1338314	N/A	N/A	58348	58367	GGCCTGTGCACTCTCCACCC	48	667
1338316	N/A	N/A	40739	40758	TGCAGCACCCATAAGTGGGC	54	668
1338339	N/A	N/A	21372	21391	GCCGCACCTCCACTGCCACA	44	669
1338487	N/A	N/A	90682	90701	GCCTGGGCAGCCATAAAGCC	39	670
1338514	N/A	N/A	85115	85134	CGTGGCCAACTCTCGGGTCA	76	671

1338561	N/A	N/A	45672	45691	ACGCATCCATTTCCTCCACA	49	672
1338607	N/A	N/A	79244	79263	CCTCACCAAACATCCCCCGT	72	673
1338672	N/A	N/A	48753	48772	ACACTCCACTCCAAGGCAAC	66	674
1338679	N/A	N/A	32658	32677	CCGGAGGTCCGAAATCCCAA	22	675
1338699	N/A	N/A	77409	77428	CCGCCAGCCTTACCTTGTCC	95	676
1338709	N/A	N/A	18069	18088	GAGAGCCTCCCAGCCACGCA	37	677
1338764	N/A	N/A	60573	60592	CATCTGTATCCCCTCGCCCG	25	678
1338775	N/A	N/A	89299	89318	GATGAGCTTCTCTCCACGCC	36	679
1338803	N/A	N/A	34864	34883	GTGAGACCTCTTGATTGCCC	53	680
1338822	N/A	N/A	91688	91707	TCTGCTCGCCCCCCAACCCG	58	681
1338867	N/A	N/A	44823	44842	AGACAGTTCCTCCCTTGCAA	47	682
1338903	N/A	N/A	82775	82794	CCTGTGAACTTCCTCCCCTT	47	683
1338942	N/A	N/A	56380	56399	CCTTGCATCTCTCACTGGGC	26	684
1338964	N/A	N/A	50481	50500	ACTGGCTCCTATCAATCGAA	25	685
1338992	N/A	N/A	31674	31693	AACCACCCACAGAGAGGCCA	45	686
1339024	N/A	N/A	71081	71100	ATCCTGCCCCAGACGCACCG	28	687
1339033	N/A	N/A	23650	23669	CCGGGCCTTTCCTGCTCCAA	38	688
1339046	N/A	N/A	68257	68276	TGGTCCACCCCACATGATCT	28	689
1339115	N/A	N/A	93316	93335	TCATAGCAACCCATGCCTAT	53	690
1339128	N/A	N/A	33699	33718	GTCCCATGCTGATCAAGTTC	19	691
1339131	N/A	N/A	25730	25749	GGCAGAATCATCAGTAACAA	36	692
1339173	N/A	N/A	62926	62945	ACAACTGGCTTCTTCTAGAA	43	693
1339177	N/A	N/A	76187	76206	ACACAATACCACTCAGACAC	100	694
1339222	N/A	N/A	93877	93896	ACAGGTGCTACTCACACAAT	48	695
1339249	N/A	N/A	75542	75561	CTTGGCCCCAAACCTAGGCC	81	696
1339298	N/A	N/A	20527	20546	CCTGAGACACCCCCATGGCC	46	697
1339323	N/A	N/A	86927	86946	TGTGGGTCACACAGGACAGG	26	698
			86984	87003			
1339355	N/A	N/A	31116	31135	CGAACTTAATTATATCTCCC	26	699
1339358	N/A	N/A	73621	73640	GCCACTGCGACCTCATTCCG	49	700
1339372	N/A	N/A	18554	18573	AGGAGATTCCTTCTAGGGTA	17	701
1339396	N/A	N/A	22119	22138	CTTCTGCACCCATTCCTGCT	47	702
1339426	1719	1738	72323	72342	CGCCCATACATGCGCTGCCA	28	703
1339465	N/A	N/A	57072	57091	GGCACCACAGCCACTAGTGT	56	704
1339469	N/A	N/A	42250	42269	AAGGCACCCCCTTATCTCGG	52	705
1339470	N/A	N/A	17644	17663	TGTCCTGACCATTTTCAACC	25	706
1339478	N/A	N/A	51692	51711	TCAGGACACCGCAAGTGCTC	44	707
1339479	N/A	N/A	62058	62077	CGGGACTCCATCATTACCCA	14	708
1339530	N/A	N/A	65998	66017	AACAGTTTCCACAGCTGGGA	35	709
1339571	N/A	N/A	39124	39143	CCTGTCTCCCCCAAAGTGGC	55	710
1339574	N/A	N/A	27738	27757	CTGAGGGTCCCAAACCCAGC	41	711
1339595	N/A	N/A	43135	43154	TGTCAGATGTCCCACAGCCT	57	712
1339606	N/A	N/A	32277	32296	TTGGCCCACCACACACGGCA	44	713

1339617	N/A	N/A	36426	36445	ATGTTTGTCACAGAAAGTCC	39	714
1339619	N/A	N/A	48033	48052	CGATCTGTCTTCACGAGTCA	29	715
1339628	N/A	N/A	87773	87792	GCCCTGATCCCTCTTGCAAA	31	716
1339635	4263	4282	94642	94661	GAGTGCAGAACAGCAGCCCT	34	717
1339642	N/A	N/A	19853	19872	AAGCAAGCCCCTTTGGGCAA	72	718
1339647	N/A	N/A	37384	37403	TTCTTCAGCACCCATGCTGA	60	719

Table 10. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	24	283
1337233	N/A	N/A	83763	83782	CGTGTATGCCATCTCCACCT	37	720
1337268	N/A	N/A	31114	31133	AACTTAATTATATCTCCCGT	39	721
1337297	N/A	N/A	30385	30404	CGCTGGCTCTTTTCTGCCCC	47	722
1337301	N/A	N/A	65976	65995	TGCTCAAGACTCCAGGGCGA	36	723
1337316	N/A	N/A	36385	36404	GAAGGACAATACCTTCGGCA	47	724
1337392	N/A	N/A	29508	29527	CCTTGACTAATCACTGTGGA	46	725
1337420	N/A	N/A	43061	43080	GTAGAGGATCCACCCAGGGA	63	726
1337483	622	641	58880	58899	CAGGAAGCTTATTATGGCCA	18	727
1337510	N/A	N/A	48748	48767	CCACTCCAAGGCAACACCCA	47	728
1337516	N/A	N/A	77309	77328	AGGGTAGCCCTTCACATACC	31	729
1337632	N/A	N/A	34717	34736	GCAGACAAAGAACCCGGCCA	48	730
1337665	N/A	N/A	73620	73639	CCACTGCGACCTCATTCCGC	47	731
1337681	N/A	N/A	27059	27078	GTCATGTGTCCACCACACGC	30	732
1337694	N/A	N/A	78189	78208	TGGTTTGCTTTCCTGATCTC	38	733
1337698	N/A	N/A	22118	22137	TTCTGCACCCATTCCTGCTC	90	734
1337704	N/A	N/A	93874	93893	GGTGCTACTCACACAATGTC	39	735
1337709	N/A	N/A	44808	44827	TGCAAAGCACTTACTGAGAC	62	736
1337758	N/A	N/A	45595	45614	GGGCACGGCTTCTATCTCAC	44	737
1337779	N/A	N/A	58199	58218	GTCCTCAGCACTCACTGAAC	32	738
1337803	N/A	N/A	53181	53200	GCTTTTTCCATCCTGGGACA	18	739
1337916	N/A	N/A	87772	87791	CCCTGATCCCTCTTGCAAAC	29	740
1337946	N/A	N/A	50480	50499	CTGGCTCCTATCAATCGAAT	37	741
1338050	N/A	N/A	51681	51700	CAAGTGCTCAGAACATGCCG	39	742
1338056	N/A	N/A	69806	69825	AGCAACCCCCCAGCTTGTCC	40	743
1338059	N/A	N/A	23641	23660	TCCTGCTCCAATAAACCAGA	54	744
1338079	N/A	N/A	57070	57089	CACCACAGCCACTAGTGTCC	65	745
1338089	N/A	N/A	62057	62076	GGGACTCCATCATTACCCAC	31	746
1338132	N/A	N/A	75541	75560	TTGGCCCCAAACCTAGGCCA	84	747

1338165	N/A	N/A	47908	47927	GGCCCAAGCCTCCTTGCTGC	81	748
1338185	N/A	N/A	71075	71094	CCCCAGACGCACCGTCACCC	15	749
			71155	71174			
1338192	N/A	N/A	25701	25720	GACACGGCACTTCCCGGGAC	36	750
1338206	N/A	N/A	90676	90695	GCAGCCATAAAGCCTGCCTA	38	751
1338229	N/A	N/A	65034	65053	GCTTGTCCCACTCAGGGCCT	16	752
1338243	N/A	N/A	20525	20544	TGAGACACCCCCATGGCCAA	61	753
1338291	4743	4762	95122	95141	CATGCCTCCAGAATGCATCC	31	754
1338334	N/A	N/A	18410	18429	TCATTGTGAAATCCCATGCC	51	755
1338374	N/A	N/A	46982	47001	GCGCAGCCACACACTCGCCA	49	756
1338401	N/A	N/A	32255	32274	TCCACGGAACTCCATGGGTC	32	757
1338424	N/A	N/A	81840	81859	GTACTAAGAGCTACTGGCCA	52	758
1338559	4499	4518	94878	94897	AATGCACCATCTTCCGCCCA	43	759
1338566	N/A	N/A	37300	37319	GCTGAGCCGCCATCATGCTC	38	760
1338573	N/A	N/A	91687	91706	CTGCTCGCCCCCCAACCCGC	50	761
1338577	N/A	N/A	92409	92428	ACGGCCTGACACCTGCCCCT	29	762
1338582	N/A	N/A	24532	24551	ACACACTTACACCCATTCCA	39	763
1338589	N/A	N/A	85104	85123	CTCGGGTCATTCTTCAGCGG	64	764
1338615	N/A	N/A	54305	54324	ATGCCAGGCCCCCTTGTGAC	32	765
1338643	N/A	N/A	18006	18025	AGGGAGATAAACTAAACTCT	69	766
1338651	N/A	N/A	40738	40757	GCAGCACCCATAAGTGGGCA	60	767
1338658	N/A	N/A	62925	62944	CAACTGGCTTCTTCTAGAAC	68	768
1338762	N/A	N/A	22942	22961	GGCCACACCCTTCCTCCTGA	74	769
1338855	N/A	N/A	33690	33709	TGATCAAGTTCTAATGGGAA	57	770
1338864	N/A	N/A	72184	72203	TGGCATGGATCCCCTCCCTA	36	771
1338911	N/A	N/A	93301	93320	CCTATGGTATCCACAGACCC	27	772
1338948	N/A	N/A	17643	17662	GTCCTGACCATTTTCAACCT	34	773
1338950	N/A	N/A	55629	55648	GTAGCCCCAACCCAACAGCA	32	774
1339010	N/A	N/A	42248	42267	GGCACCCCCTTATCTCGGGC	38	775
1339028	N/A	N/A	19821	19840	GAAGAGAAACCCTTCAGGCC	36	776
1339045	N/A	N/A	27736	27755	GAGGGTCCCAAACCCAGCAA	41	777
1339055	N/A	N/A	86959	86978	CCACAGTCCCAGCCCCCGGA	24	778
1339107	N/A	N/A	89298	89317	ATGAGCTTCTCTCCACGCCA	47	779
1339108	N/A	N/A	76135	76154	CCAGACACACATCACATATC	96	780
1339162	N/A	N/A	19092	19111	TCCCTCCCGTCCTATAGACA	59	781
1339182	N/A	N/A	21370	21389	CGCACCTCCACTGCCACAGA	39	782
1339250	N/A	N/A	39106	39125	GCGCTGGCACCAACAAGATC	54	783
1339266	N/A	N/A	82774	82793	CTGTGAACTTCCTCCCCTTC	59	784
1339292	N/A	N/A	31638	31657	GGTGGAAACTTCTGCAGGAC	49	785
1339305	N/A	N/A	60572	60591	ATCTGTATCCCCTCGCCCGG	55	786
1339320	N/A	N/A	40137	40156	TACAGCTCCCATGCTGCACT	53	787
1339378	4062	4081	94441	94460	CGTTGCCCTCCCAGCCAGCC	35	788
1339420	N/A	N/A	79242	79261	TCACCAAACATCCCCCGTGA	75	789

1339453	N/A	N/A	68874	68893	ATTTTGAGCCTCCCTAGAAC	87	790
1339476	N/A	N/A	67937	67956	ACGATCCACCCTAAATGGTC	47	791
1339525	N/A	N/A	56379	56398	CTTGCATCTCTCACTGGGCT	21	792
1339538	N/A	N/A	49143	49162	TGTTGTTCTCCCCTCCGCTC	44	793
1339567	N/A	N/A	32655	32674	GAGGTCCGAAATCCCAAGCC	39	794
1339573	N/A	N/A	68256	68275	GGTCCACCCCACATGATCTA	23	795
1339593	N/A	N/A	86205	86224	GGAGTCCTATCATTCAGAAC	61	796

Table 11. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	19	283
1080862	4032	4051	94411	94430	GTTGCGGTACATCTGTGTAA	14	362
1080878	4496	4515	94875	94894	GCACCATCTTCCGCCCAATG	13	209
1337245	N/A	N/A	30373	30392	TCTGCCCCACATAGAAACCA	31	797
1337250	N/A	N/A	86199	86218	CTATCATTCAGAACAGGGAC	32	798
1337269	N/A	N/A	44807	44826	GCAAAGCACTTACTGAGACA	46	799
1337276	N/A	N/A	45593	45612	GCACGGCTTCTATCTCACAC	27	800
1337279	N/A	N/A	62055	62074	GACTCCATCATTACCCACCA	14	801
1337388	N/A	N/A	72183	72202	GGCATGGATCCCCTCCCTAT	26	802
1337425	N/A	N/A	79229	79248	CCCGTGAACACCCAGCCGTT	54	803
1337434	N/A	N/A	23640	23659	CCTGCTCCAATAAACCAGAC	27	804
1337472	N/A	N/A	62924	62943	AACTGGCTTCTTCTAGAACA	30	805
1337487	N/A	N/A	86884	86903	GGCTGCCCCAGAACCTCCGA	22	806
1337488	N/A	N/A	56330	56349	GGCTGGGAACTCACAATTCT	13	807
1337493	N/A	N/A	18409	18428	CATTGTGAAATCCCATGCCA	54	808
1337513	N/A	N/A	28635	28654	ACAGAATTAATTAGCTAATC	109	809
1337522	N/A	N/A	89294	89313	GCTTCTCTCCACGCCAGGCA	31	810
1337534	N/A	N/A	57058	57077	TAGTGTCCCCCAGCCACCCT	49	811
1337578	N/A	N/A	65912	65931	CTGTCAGACACCCCAGGGCT	22	812
1337583	N/A	N/A	85103	85122	TCGGGTCATTCTTCAGCGGA	40	813
1337584	N/A	N/A	40682	40701	AGCAAGTGCCCTCCCCCGAC	52	814
1337603	N/A	N/A	64957	64976	GAGGGACCCCACTGTGGACA	16	815
1337644	621	640	58879	58898	AGGAAGCTTATTATGGCCAC	25	816
1337667	N/A	N/A	43059	43078	AGAGGATCCACCCAGGGACT	40	817
1337686	N/A	N/A	87767	87786	ATCCCTCTTGCAAACACACC	16	818
1337732	N/A	N/A	78185	78204	TTGCTTTCCTGATCTCAACA	35	819
1337740	N/A	N/A	33664	33683	AGGTCTAGGACTATTATACC	27	820
1337752	N/A	N/A	76083	76102	TTGACACACAACACACATTA	78	821

1337770	N/A	N/A	77308	77327	GGGTAGCCCTTCACATACCT	18	822
1337798	N/A	N/A	49142	49161	GTTGTTCTCCCCTCCGCTCC	70	823
1337815	N/A	N/A	91677	91696	CCCAACCCGCTTCCTAACCC	72	824
1337837	N/A	N/A	17574	17593	CGGATTTGCTAGCTGAGCCC	13	825
1337967	N/A	N/A	22926	22945	CTGACTGTCCCCCTCTGTTT	61	826
1337991	N/A	N/A	38852	38871	ACGCAGGTGCAGCCCAGCCA	39	827
1338041	N/A	N/A	75528	75547	TAGGCCAGGACAACAACTCA	49	828
1338066	N/A	N/A	50453	50472	TTTGATGTCACTGCCTGGCC	59	829
1338072	N/A	N/A	55618	55637	CCAACAGCAACACACTGGTT	29	830
1338118	N/A	N/A	32654	32673	AGGTCCGAAATCCCAAGCCT	26	831
1338212	N/A	N/A	31556	31575	CAGCAGCACCCACTTATCAC	39	832
1338222	4739	4758	95118	95137	CCTCCAGAATGCATCCATTT	18	833
1338237	N/A	N/A	47905	47924	CCAAGCCTCCTTGCTGCGGC	15	834
1338256	N/A	N/A	27058	27077	TCATGTGTCCACCACACGCC	33	835
1338268	N/A	N/A	67936	67955	CGATCCACCCTAAATGGTCC	28	836
1338313	N/A	N/A	58147	58166	CTTCAGCATTCACTGAGCCT	7	837
1338375	N/A	N/A	60571	60590	TCTGTATCCCCTCGCCCGGC	22	838
1338459	N/A	N/A	18005	18024	GGGAGATAAACTAAACTCTT	44	839
1338525	N/A	N/A	42216	42235	CCCCAGGCTAACATGCTGAA	53	840
1338560	N/A	N/A	21309	21328	CCGTCAGGACCCAAGCCCTC	48	841
1338619	N/A	N/A	48744	48763	TCCAAGGCAACACCCAGCCA	63	842
1338700	N/A	N/A	31113	31132	ACTTAATTATATCTCCCGTG	25	843
1338766	N/A	N/A	19692	19711	TAGGGCACCCTCTCTTACAT	70	844
1338797	N/A	N/A	73619	73638	CACTGCGACCTCATTCCGCC	51	845
1338819	N/A	N/A	92408	92427	CGGCCTGACACCTGCCCCTC	19	846
1338833	N/A	N/A	8841	8860	TGCTCAGAAAATGACCAACT	36	847
			37285	37304			
1338907	N/A	N/A	93873	93892	GTGCTACTCACACAATGTCA	54	848
1338917	N/A	N/A	82773	82792	TGTGAACTTCCTCCCCTTCC	62	849
1339030	N/A	N/A	54205	54224	CAGGCCTTCTCTCCAGGGAA	10	850
1339044	N/A	N/A	27697	27716	TGGGAACCTCCTTAGTGGCC	49	851
1339048	N/A	N/A	36362	36381	AGCAGCAGTCCCAGAAGCCC	17	852
1339070	N/A	N/A	51582	51601	GCTATGGGCCACTGCAGCCT	33	853
1339082	N/A	N/A	71041	71060	GTCCTGCCCCAGACGCACCG	21	854
1339118	N/A	N/A	24530	24549	ACACTTACACCCATTCCATT	37	855
1339121	N/A	N/A	69795	69814	AGCTTGTCCCTAAGTTGGCC	20	856
1339163	N/A	N/A	25671	25690	GCTCCGGACACCCACCAGGA	27	857
1339283	N/A	N/A	90645	90664	TTGGAGTCCCCACCCCTGCA	36	858
1339300	N/A	N/A	46981	47000	CGCAGCCACACACTCGCCAC	50	859
1339331	N/A	N/A	81829	81848	TACTGGCCAACCTATGTGGA	37	860
1339332	N/A	N/A	32254	32273	CCACGGAACTCCATGGGTCC	31	861
1339336	N/A	N/A	68853	68872	TGACAAAGATTTCCCTAGAC	59	862
1339342	N/A	N/A	20449	20468	CACACCAGCCCTTCCGTCCA	47	863

1339356	N/A	N/A	53032	53051	CGTGGCCCACCATCCGATGC	46	864
1339427	N/A	N/A	83762	83781	GTGTATGCCATCTCCACCTC	32	865
1339477	N/A	N/A	22117	22136	TCTGCACCCATTCCTGCTCC	44	866
1339480	N/A	N/A	34648	34667	GGCACTGTGTCAACTTGATA	20	867
1339582	N/A	N/A	40095	40114	CTGGGCAGAACCTGCTATCC	46	868
1339585	N/A	N/A	93286	93305	GACCCCTGCACACTCACTCA	37	869
1339586	N/A	N/A	68252	68271	CACCCCACATGATCTACACT	70	870
1339648	N/A	N/A	19051	19070	CCCCTCCTGTCCTATAGACA	53	871

Table 12. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	14	283
1337217	N/A	N/A	31554	31573	GCAGCACCCACTTATCACTT	34	872
1337220	N/A	N/A	93871	93890	GCTACTCACACAATGTCACT	49	873
1337264	N/A	N/A	46951	46970	GCCCGTCTCACCTCTGCCAG	43	874
1337298	N/A	N/A	78154	78173	GAGAAGCTGCTAACTCCAGA	43	875
1337304	N/A	N/A	60560	60579	TCGCCCGGCCCTGCTTGCCT	14	876
1337383	N/A	N/A	77305	77324	TAGCCCTTCACATACCTGGG	53	877
1337393	N/A	N/A	18979	18998	GGGCCAGGTCCACTCCCATC	16	878
1337439	N/A	N/A	38781	38800	CGCGCGCCCCTACCTCTGGC	38	879
1337463	N/A	N/A	33662	33681	GTCTAGGACTATTATACCCA	40	880
1337618	N/A	N/A	56329	56348	GCTGGGAACTCACAATTCTC	14	881
1337640	N/A	N/A	65841	65860	GCACGGCAACCCTCCAGGGC	13	882
1337641	N/A	N/A	56972	56991	AAAGGAGCCTACCTTGCCTT	23	883
1337648	4031	4050	94410	94429	TTGCGGTACATCTGTGTAAA	12	884
1337726	N/A	N/A	71039	71058	CCTGCCCCAGACGCACCGTC	19	885
			71079	71098			
			71159	71178			
1337727	N/A	N/A	93284	93303	CCCCTGCACACTCACTCATA	56	886
1337750	N/A	N/A	64896	64915	GGGCTGTCGGTCACTTGTCA	20	887
1337787	N/A	N/A	8838	8857	TCAGAAAATGACCAACTCAC	45	888
			37282	37301			
1337842	N/A	N/A	82772	82791	GTGAACTTCCTCCCCTTCCG	46	889
1337851	N/A	N/A	86881	86900	TGCCCCAGAACCTCCGAGGT	49	890
1337860	N/A	N/A	87764	87783	CCTCTTGCAAACACACCCTT	29	891
1337864	1598	1617	71960	71979	CGTACTTGCACTCCTCCTCA	23	892
1337905	N/A	N/A	25667	25686	CGGACACCCACCAGGAGAGC	42	893
1338005	N/A	N/A	62923	62942	ACTGGCTTCTTCTAGAACAC	11	894

1338020	N/A	N/A	62051	62070	CCATCATTACCCACCATGCT	38	895
1338075	N/A	N/A	20425	20444	CCAGGACCCCATCCCAGTGT	63	896
1338077	N/A	N/A	17526	17545	ACAGTGACAACCCCGACCCT	59	897
1338107	N/A	N/A	67935	67954	GATCCACCCTAAATGGTCCA	13	898
1338130	N/A	N/A	24525	24544	TACACCCATTCCATTTCAGC	32	899
1338131	N/A	N/A	55617	55636	CAACAGCAACACACTGGTTC	19	900
1338150	N/A	N/A	27696	27715	GGGAACCTCCTTAGTGGCCC	37	901
1338169	N/A	N/A	73618	73637	ACTGCGACCTCATTCCGCCA	34	902
1338178	N/A	N/A	40087	40106	AACCTGCTATCCCTATGGGC	29	903
1338181	N/A	N/A	42157	42176	AGACGAGGCCTTTAAAGCGG	34	904
1338211	N/A	N/A	47853	47872	TCCGCTAGCTCCTCAGAGTC	52	905
1338213	N/A	N/A	76082	76101	TGACACACAACACACATTAC	66	906
1338232	N/A	N/A	32243	32262	CATGGGTCCACACCTGATGC	20	907
1338271	N/A	N/A	53031	53050	GTGGCCCACCATCCGATGCC	28	908
1338294	N/A	N/A	50430	50449	GGCTGGTGACCCCAACATCT	28	909
1338333	N/A	N/A	57240	57259	CCTGGGTTCCCTACTTACTG	10	910
			58130	58149			
1338340	N/A	N/A	45592	45611	CACGGCTTCTATCTCACACC	36	911
1338341	N/A	N/A	83760	83779	GTATGCCATCTCCACCTCCT	28	912
1338352	N/A	N/A	34588	34607	AGCCTGTTCATCTCAGCAGC	48	913
1338355	N/A	N/A	58739	58758	GCCTTGACCCTCACTCCCAT	35	914
1338399	N/A	N/A	91676	91695	CCAACCCGCTTCCTAACCCT	64	915
1338420	N/A	N/A	48742	48761	CAAGGCAACACCCAGCCAGC	36	916
1338427	N/A	N/A	54145	54164	GCAGGGTTCACCCCGATGGC	12	917
1338488	N/A	N/A	28627	28646	AATTAGCTAATCATCAGGTT	65	918
1338519	4494	4513	94873	94892	ACCATCTTCCGCCCAATGCC	46	919
1338535	N/A	N/A	18004	18023	GGAGATAAACTAAACTCTTC	37	920
1338575	N/A	N/A	75525	75544	GCCAGGACAACAACTCAGGA	29	921
1338581	N/A	N/A	18405	18424	GTGAAATCCCATGCCAGCTT	31	922
1338663	N/A	N/A	69794	69813	GCTTGTCCCTAAGTTGGCCA	21	923
1338686	N/A	N/A	21215	21234	AGTCTGTGTCCTCCAAGGGC	14	924
1338781	N/A	N/A	40681	40700	GCAAGTGCCCTCCCCCGACA	52	925
1338812	N/A	N/A	68249	68268	CCCACATGATCTACACTGGA	49	926
1338839	N/A	N/A	81828	81847	ACTGGCCAACCTATGTGGAA	42	927
1338846	N/A	N/A	85971	85990	GCCGAGGTCCCTCCAGTGGC	53	928
1338952	N/A	N/A	23639	23658	CTGCTCCAATAAACCAGACC	43	929
1338996	N/A	N/A	21991	22010	TTGTGGTCCACTTCTCAGCT	27	930
1339076	N/A	N/A	85025	85044	CACGGAGGCCACACTTCCCC	80	931
1339125	N/A	N/A	36189	36208	AGAGGCTCGACCCTATGGCT	37	932
1339155	N/A	N/A	44774	44793	GCTGAAATCTTCTACAGGAA	49	933
1339181	N/A	N/A	27056	27075	ATGTGTCCACCACACGCCCC	23	934
1339223	N/A	N/A	31092	31111	ATACCTGTCTCCCCATTCCT	29	935
1339225	N/A	N/A	90619	90638	CCAGGCTTCACCGAGCTCCT	31	936

1339227	N/A	N/A	92377	92396	GCTCTTTTCCCAAAACCCAT	16	937
1339235	N/A	N/A	42961	42980	AGCTCTGTGCAAACAAGGTC	39	938
1339288	N/A	N/A	79224	79243	GAACACCCAGCCGTTAGCCT	32	939
1339395	N/A	N/A	30341	30360	CCGATGTTCTCCCTCCAAAC	47	940
1339455	4736	4755	95115	95134	CCAGAATGCATCCATTTAAT	17	941
1339457	N/A	N/A	51532	51551	GAAGTGGTCATCCCTGCACC	33	942
1339502	N/A	N/A	68852	68871	GACAAAGATTTCCCTAGACT	43	943
1339518	N/A	N/A	32564	32583	CGGTGACCACCACCCTCCCC	48	944
1339521	N/A	N/A	49141	49160	TTGTTCTCCCCTCCGCTCCG	65	945
1339549	N/A	N/A	19689	19708	GGCACCCTCTCTTACATCCA	69	946
1339557	N/A	N/A	22925	22944	TGACTGTCCCCCTCTGTTTC	60	947
1339602	N/A	N/A	89256	89275	AGCCCAAGCACACTTCCCAC	39	948

Table 13. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	33	283
1081085	N/A	N/A	71038	71057	CTGCCCCAGACGCACCGTCA	17	477
			71078	71097			
			71158	71177			
1337229	N/A	N/A	24524	24543	ACACCCATTCCATTTCAGCT	27	949
1337280	N/A	N/A	57239	57258	CTGGGTTCCCTACTTACTGA	35	950
			58129	58148			
1337291	N/A	N/A	90413	90432	GGGCAGTCGCCACTCTGCCT	57	951
1337347	N/A	N/A	62049	62068	ATCATTACCCACCATGCTGA	44	952
1337468	N/A	N/A	36188	36207	GAGGCTCGACCCTATGGCTA	65	953
1337507	N/A	N/A	86756	86775	CTCGGTGATTTTCATCTGCA	45	954
1337526	N/A	N/A	81783	81802	GAGTTCTGACCAACTGACCA	44	955
1337536	N/A	N/A	19687	19706	CACCCTCTCTTACATCCAGT	60	956
1337577	N/A	N/A	82738	82757	GAGCACACCCCTCTGCCGGC	38	957
1337607	N/A	N/A	31091	31110	TACCTGTCTCCCCATTCCTC	50	958
1337615	N/A	N/A	77208	77227	TCGAGGGCACCCACTCCACC	54	959
1337646	N/A	N/A	45591	45610	ACGGCTTCTATCTCACACCC	31	960
1337653	N/A	N/A	50429	50448	GCTGGTGACCCCAACATCTC	35	961
1337662	N/A	N/A	73616	73635	TGCGACCTCATTCCGCCAAC	38	962
1337670	N/A	N/A	32526	32545	ATCGCTCCAGTCCTTGCTTC	45	963
1337714	N/A	N/A	60551	60570	CCTGCTTGCCTCTCGGGCCC	24	964
1337806	N/A	N/A	64886	64905	TCACTTGTCACCATGGCCAT	38	965
1337850	N/A	N/A	32242	32261	ATGGGTCCACACCTGATGCT	45	966

1337886	N/A	N/A	46950	46969	CCCGTCTCACCTCTGCCAGT	73	967
1337937	N/A	N/A	83743	83762	CCTCCCTTTTTCCTTCCGGA	45	968
1337942	N/A	N/A	33661	33680	TCTAGGACTATTATACCCAG	39	969
1337951	N/A	N/A	31551	31570	GCACCCACTTATCACTTCTC	39	970
1338004	N/A	N/A	79217	79236	CAGCCGTTAGCCTCTCGGCC	59	971
1338082	N/A	N/A	78150	78169	AGCTGCTAACTCCAGAAGGA	38	972
1338087	N/A	N/A	54123	54142	GATGGTGACAACCACACCAC	23	973
1338099	1597	1616	71959	71978	GTACTTGCACTCCTCCTCAC	59	974
1338103	N/A	N/A	17505	17524	CCGTACCCTACACGCTGGAA	28	975
1338139	N/A	N/A	85970	85989	CCGAGGTCCCTCCAGTGGCA	65	976
1338158	N/A	N/A	38452	38471	GCTCAAACCACCGCCAGGAC	37	977
1338188	N/A	N/A	42156	42175	GACGAGGCCTTTAAAGCGGT	25	978
1338228	N/A	N/A	51530	51549	AGTGGTCATCCCTGCACCCA	51	979
1338231	N/A	N/A	30329	30348	CTCCAAACAATTATGCGATT	50	980
1338270	N/A	N/A	40629	40648	TGGAGACCTCTCCTCTGCTT	56	981
1338276	N/A	N/A	55511	55530	GAGCTGCCTTGAACAAGGCT	32	982
1338304	N/A	N/A	68234	68253	CTGGATGGTCCACCCTGAAC	40	983
1338343	N/A	N/A	92374	92393	CTTTTCCCAAAACCCATGGT	52	984
1338348	N/A	N/A	67927	67946	CTAAATGGTCCACCCCGGAC	61	985
1338367	N/A	N/A	85024	85043	ACGGAGGCCACACTTCCCCC	49	986
1338398	N/A	N/A	8836	8855	AGAAAATGACCAACTCACTG	59	987
			37280	37299			
1338440	N/A	N/A	18978	18997	GGCCAGGTCCACTCCCATCC	47	988
1338462	N/A	N/A	44771	44790	GAAATCTTCTACAGGAAGCC	49	989
1338479	N/A	N/A	47745	47764	CCGGCTGTTCCCCTCCACCT	36	990
1338492	N/A	N/A	21990	22009	TGTGGTCCACTTCTCAGCTT	30	991
1338521	N/A	N/A	69721	69740	CTGGATTTGTCCATACTCCC	57	992
1338537	3982	4001	94361	94380	TAGGTTAAAAAACTCTCCTC	27	993
1338555	N/A	N/A	68851	68870	ACAAAGATTTCCCTAGACTT	70	994
1338556	N/A	N/A	42940	42959	GTCGGCTGCACAAACCCTGC	30	995
1338574	N/A	N/A	93255	93274	GCATGCCGTCCTCCACATCC	27	996
1338604	N/A	N/A	87666	87685	CTGGGTGGCACCTTCAGAAA	33	997
1338641	4490	4509	94869	94888	TCTTCCGCCCAATGCCCCCT	39	998
1338649	N/A	N/A	23637	23656	GCTCCAATAAACCAGACCTT	35	999
1338656	N/A	N/A	27589	27608	AACTGAGTGCCCAAAACTAC	45	1000
1338660	N/A	N/A	56327	56346	TGGGAACTCACAATTCTCAA	19	1001
1338684	N/A	N/A	18003	18022	GAGATAAACTAAACTCTTCA	62	1002
1338687	N/A	N/A	20424	20443	CAGGACCCCATCCCAGTGTC	42	1003
1338746	N/A	N/A	91670	91689	CGCTTCCTAACCCTGCAGGC	42	1004
1338758	4735	4754	95114	95133	CAGAATGCATCCATTTAATA	30	1005
1338798	N/A	N/A	93688	93707	GAGCTGAGTCTTTCCGGCCT	44	1006
1338849	N/A	N/A	89251	89270	AAGCACACTTCCCACCACAA	35	1007
1338863	N/A	N/A	25665	25684	GACACCCACCAGGAGAGCCA	68	1008

1338887	N/A	N/A	53029	53048	GGCCCACCATCCGATGCCCA	25	1009
1338977	N/A	N/A	18400	18419	ATCCCATGCCAGCTTCTCCT	52	1010
1338990	N/A	N/A	28549	28568	GTCCGTAGCAGAACTTGGCT	25	1011
1339023	N/A	N/A	62903	62922	AGAGACTCGCTCATCAGCGA	38	1012
1339057	N/A	N/A	56971	56990	AAGGAGCCTACCTTGCCTTT	32	1013
1339080	N/A	N/A	75342	75361	CCCAGCTCCATCCTGATTCA	65	1014
1339172	N/A	N/A	22918	22937	CCCCCTCTGTTTCAAAGCTC	54	1015
1339209	N/A	N/A	48740	48759	AGGCAACACCCAGCCAGCTC	55	1016
1339265	N/A	N/A	40086	40105	ACCTGCTATCCCTATGGGCC	45	1017
1339285	N/A	N/A	58736	58755	TTGACCCTCACTCCCATGTC	62	1018
1339385	N/A	N/A	49046	49065	GGTGACTTCCCAACTGGCTC	48	1019
1339443	N/A	N/A	76013	76032	GACACACCCCCCTTGCACAC	56	1020
1339450	N/A	N/A	27055	27074	TGTGTCCACCACACGCCCCC	38	1021
1339516	N/A	N/A	21032	21051	ATGCTGCTCCATGGGAGCAC	63	1022
1339607	N/A	N/A	65839	65858	ACGGCAACCCTCCAGGGCCG	50	1023
1339653	N/A	N/A	34555	34574	GGAGACCACAGAACTCCAGA	41	1024

Table 14. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	34	283
1337227	N/A	N/A	78102	78121	CTACTGACCCCAGCTTGCCA	79	1025
1337248	N/A	N/A	75247	75266	GCCTGACAGCCCCTGTGCCA	34	1026
1337290	N/A	N/A	87662	87681	GTGGCACCTTCAGAAAGGCC	22	1027
1337326	N/A	N/A	93679	93698	CTTTCCGGCCTTCCTGACCA	34	1028
1337331	N/A	N/A	68815	68834	GAGCTCGCAAAAGGCTGCCC	55	1029
1337338	N/A	N/A	36129	36148	AACTGCCCTTTTAGAGAGCA	50	1030
1337342	N/A	N/A	40628	40647	GGAGACCTCTCCTCTGCTTC	39	1031
1337346	N/A	N/A	21952	21971	TGGTGTTGCTCAACTCCAGA	27	1032
1337351	N/A	N/A	85019	85038	GGCCACACTTCCCCCCGGAA	54	1033
1337358	N/A	N/A	21014	21033	ACCCGAGACACCATCTGGTA	63	1034
1337359	N/A	N/A	25529	25548	CGCACAGGCACAAAATGCCC	41	1035
1337363	N/A	N/A	93254	93273	CATGCCGTCCTCCACATCCA	24	1036
1337386	N/A	N/A	44738	44757	GGGCATCAACCAGAATGCGG	50	1037
1337427	N/A	N/A	68232	68251	GGATGGTCCACCCTGAACAG	47	1038
1337428	N/A	N/A	23623	23642	GACCTTGACTCAATCATGCA	22	1039
1337500	N/A	N/A	18368	18387	GGCATGGTTCTCTCTAGGCG	12	1040
1337587	N/A	N/A	82605	82624	CGAGCATCCCCCTACGCCTC	47	1041
1337626	N/A	N/A	81774	81793	CCAACTGACCATGCCAGGAC	19	1042

1337647	N/A	N/A	89248	89267	CACACTTCCCACCACAAGGC	33	1043
1337741	N/A	N/A	47744	47763	CGGCTGTTCCCCTCCACCTG	47	1044
1337768	N/A	N/A	34551	34570	ACCACAGAACTCCAGAAGCA	43	1045
1337796	N/A	N/A	48694	48713	CCCCCAACCCTCCATCGGTC	63	1046
1337804	N/A	N/A	27588	27607	ACTGAGTGCCCAAAACTACA	53	1047
1337813	4733	4752	95112	95131	GAATGCATCCATTTAATAGA	30	1048
1337823	N/A	N/A	71036	71055	GCCCCAGACGCACCGTCACA	26	1049
1337877	N/A	N/A	92299	92318	AGGGAGACACACCCTCCCCA	69	1050
1337955	N/A	N/A	83740	83759	CCCTTTTTCCTTCCGGAGTC	37	1051
1337989	N/A	N/A	27048	27067	ACCACACGCCCCCCCACGCA	60	1052
1338104	N/A	N/A	45590	45609	CGGCTTCTATCTCACACCCG	42	1053
1338145	N/A	N/A	62900	62919	GACTCGCTCATCAGCGAGAA	65	1054
1338148	N/A	N/A	20423	20442	AGGACCCCATCCCAGTGTCC	76	1055
1338168	N/A	N/A	38123	38142	TTGCCTGTCCTCACCAGGGT	26	1056
1338171	N/A	N/A	50428	50447	CTGGTGACCCCAACATCTCC	24	1057
1338183	N/A	N/A	69720	69739	TGGATTTGTCCATACTCCCA	49	1058
1338287	N/A	N/A	31550	31569	CACCCACTTATCACTTCTCA	44	1059
1338298	N/A	N/A	56324	56343	GAACTCACAATTCTCAAACT	44	1060
1338315	N/A	N/A	58108	58127	CCTGTCTGTCTTCAGCATTC	17	1061
1338323	N/A	N/A	75989	76008	CCCCATGCCCTACTCGGTCT	55	1062
1338383	N/A	N/A	85840	85859	CATGTGTGCATACACCGGCA	39	1063
1338388	N/A	N/A	24523	24542	CACCCATTCCATTTCAGCTG	26	1064
1338396	N/A	N/A	58735	58754	TGACCCTCACTCCCATGTCA	25	1065
1338430	N/A	N/A	73607	73626	ATTCCGCCAACTCCTGGCCC	42	1066
1338432	N/A	N/A	19684	19703	CCTCTCTTACATCCAGTCGA	52	1067
1338433	N/A	N/A	17441	17460	CGTGAGTCCTCAGAGCACTT	23	1068
1338435	1596	1615	71958	71977	TACTTGCACTCCTCCTCACA	47	1069
1338508	N/A	N/A	31082	31101	CCCCATTCCTCCTTTGTATA	45	1070
1338546	N/A	N/A	18001	18020	GATAAACTAAACTCTTCACC	53	1071
1338626	4489	4508	94868	94887	CTTCCGCCCAATGCCCCCTA	25	1072
1338629	N/A	N/A	51520	51539	CCTGCACCCACCTCGCAGGC	104	1073
1338634	N/A	N/A	42938	42957	CGGCTGCACAAACCCTGCCA	47	1074
1338638	N/A	N/A	86755	86774	TCGGTGATTTTCATCTGCAG	77	1075
1338675	N/A	N/A	65787	65806	CCGTAGTGACCCTAAAAGTC	49	1076
1338716	N/A	N/A	49045	49064	GTGACTTCCCAACTGGCTCT	60	1077
1338755	N/A	N/A	28519	28538	GCCTCGCTTTACCCTCCCAA	41	1078
1338789	N/A	N/A	33659	33678	TAGGACTATTATACCCAGCC	18	1079
1338800	N/A	N/A	54120	54139	GGTGACAACCACACCACACA	13	1080
1338828	N/A	N/A	40085	40104	CCTGCTATCCCTATGGGCCC	28	1081
1338869	N/A	N/A	62036	62055	ATGCTGAGCACCACCGGACC	31	1082
1338881	N/A	N/A	42155	42174	ACGAGGCCTTTAAAGCGGTC	37	1083
1338882	N/A	N/A	32210	32229	TCCAGGGAACCCCTTTCCTT	35	1084
1338923	N/A	N/A	90397	90416	GCCTGGCGGCCAACAGCACC	22	1085

1338961	N/A	N/A	18974	18993	AGGTCCACTCCCATCCTTCA	28	1086
1339007	N/A	N/A	22916	22935	CCCTCTGTTTCAAAGCTCCA	27	1087
1339060	N/A	N/A	64877	64896	ACCATGGCCATACCCATCGA	48	1088
1339063	N/A	N/A	56924	56943	GAAGGTTCCCCAAGAGAGGA	29	1089
1339067	N/A	N/A	79215	79234	GCCGTTAGCCTCTCGGCCCA	39	1090
1339073	N/A	N/A	91669	91688	GCTTCCTAACCCTGCAGGCC	14	1091
1339099	N/A	N/A	30187	30206	GCTACGCTTCCTTGGAGGCC	27	1092
1339280	N/A	N/A	37259	37278	CGCTCCCGATACCTGCCCTA	48	1093
1339340	N/A	N/A	32517	32536	GTCCTTGCTTCCCCTGCTCA	42	1094
1339380*	N/A	N/A	52941	52960	AACAGCCGGATCCTCAGGCC	13	1095
1339431	N/A	N/A	55469	55488	AGAGGAAGCTCCTATCCCCA	10	1096
1339437	3981	4000	94360	94379	AGGTTAAAAAACTCTCCTCA	17	1097
1339482	N/A	N/A	67913	67932	CCGGACGATCCACCCTGGAC	53	1098
1339529	N/A	N/A	60517	60536	GGTGCTCACACTGACGGCCG	16	1099
1339601	N/A	N/A	46847	46866	CCGGTGAGACTCATGGGCAT	36	1100
1339616	N/A	N/A	77206	77225	GAGGGCACCCACTCCACCCA	80	1101

Table 15. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	12	283
1337219	N/A	N/A	67912	67931	CGGACGATCCACCCTGGACA	38	1102
1337242	N/A	N/A	58099	58118	CTTCAGCATTCACTAAAGTC	20	1103
1337315	N/A	N/A	71035	71054	CCCCAGACGCACCGTCACAC	17	1104
1337373	N/A	N/A	75172	75191	TAGCCCAGCACACCCCATCT	67	1105
1337410	N/A	N/A	85018	85037	GCCACACTTCCCCCCGGAAC	40	1106
1337430	N/A	N/A	64873	64892	TGGCCATACCCATCGATGCA	23	1107
1337436	N/A	N/A	61928	61947	TGCCACAGCCTCAGTGGCAC	54	1108
1337530	N/A	N/A	55425	55444	CCTAAGCTGCTTCTGAGGAC	20	1109
1337546	N/A	N/A	46782	46801	TCAGACAGTCCCTTGTGTAC	56	1110
1337558	N/A	N/A	73504	73523	GTTGAGCTGCCAACCGGTCC	55	1111
1337573	N/A	N/A	49017	49036	CCGTCCAGCCCCACTCTACC	49	1112
1337594	N/A	N/A	82586	82605	CAGGCTGGCATCTCTAAGGC	39	1113
1337600	N/A	N/A	47687	47706	GGACAGGGACCAACTCCCGG	29	1114
1337617	N/A	N/A	32500	32519	TCATCTCCTTCTCCAGCGAC	33	1115
1337671	N/A	N/A	56819	56838	CCTGCAGCCCATGACACTAC	38	1116
1337682	N/A	N/A	24465	24484	GCATTGGGAATTACAACCTG	27	1117
1337683	N/A	N/A	71775	71794	GTCTGTGGACCTCAACCCCC	10	1118
1337685	N/A	N/A	93628	93647	AGCCAGGGCCCATCCCTGAC	36	1119

1337722	N/A	N/A	42154	42173	CGAGGCCTTTAAAGCGGTCA	10	1120
1337737	N/A	N/A	75979	75998	TACTCGGTCTTTCTCCTCCC	33	1121
1337814	N/A	N/A	92217	92236	GAGGGCAGCTCTAGTAGGTT	13	1122
1337866	N/A	N/A	68228	68247	GGTCCACCCTGAACAGTCCA	20	1123
1337878	N/A	N/A	51436	51455	ACTGGTTCCCAGACACCCCT	35	1124
1337882	N/A	N/A	85836	85855	TGTGCATACACCGGCAGGCC	20	1125
1337931	N/A	N/A	18973	18992	GGTCCACTCCCATCCTTCAC	22	1126
1337977	N/A	N/A	69657	69676	GTGGAGACCCCACCTAGGTG	28	1127
1338039	N/A	N/A	65786	65805	CGTAGTGACCCTAAAAGTCC	28	1128
1338121	N/A	N/A	89247	89266	ACACTTCCCACCACAAGGCG	50	1129
1338138	N/A	N/A	93253	93272	ATGCCGTCCTCCACATCCAC	35	1130
1338152	N/A	N/A	26994	27013	CGCTGCTTCCACCAAGATTA	27	1131
1338167	N/A	N/A	48686	48705	CCTCCATCGGTCATAGGCCT	35	1132
1338175*	N/A	N/A	52795	52814	ACGCAGAGCTCTGTGTGCCC	20	1133
1338210	N/A	N/A	31547	31566	CCACTTATCACTTCTCAGTT	32	1134
1338223	N/A	N/A	60406	60425	GTGGAAGTCATTCTGTGGAA	58	1135
1338230	N/A	N/A	30076	30095	TCACACGGCCATCTCCTTCT	55	1136
1338253	N/A	N/A	27586	27605	TGAGTGCCCAAAACTACAGC	36	1137
1338259	N/A	N/A	68747	68766	GGCTGCTCCACAGTGGGTAT	22	1138
1338275	N/A	N/A	40002	40021	GATCACTGCCCTCCCCCTTC	37	1139
1338356	N/A	N/A	33658	33677	AGGACTATTATACCCAGCCA	13	1140
1338359	N/A	N/A	77205	77224	AGGGCACCCACTCCACCCAC	66	1141
1338397	N/A	N/A	58731	58750	CCTCACTCCCATGTCAGGAC	52	1142
1338442	N/A	N/A	54119	54138	GTGACAACCACACCACACAC	17	1143
1338450	N/A	N/A	22912	22931	CTGTTTCAAAGCTCCAGCTA	22	1144
1338453	N/A	N/A	17996	18015	ACTAAACTCTTCACCTGGGC	10	1145
1338500	N/A	N/A	37255	37274	CCCGATACCTGCCCTAGCGC	26	1146
1338512	N/A	N/A	36128	36147	ACTGCCCTTTTAGAGAGCAC	23	1147
1338530	N/A	N/A	38112	38131	CACCAGGGTCCTCACCCCCC	45	1148
1338543	N/A	N/A	79200	79219	GCCCACAGCCCTTTCACGGC	35	1149
1338578	N/A	N/A	19680	19699	TCTTACATCCAGTCGAGGCA	66	1150
1338635	N/A	N/A	78101	78120	TACTGACCCCAGCTTGCCAT	31	1151
1338744	N/A	N/A	91627	91646	GCTCTTGGCATCCACGGTCA	20	1152
1338759	N/A	N/A	21013	21032	CCCGAGACACCATCTGGTAA	23	1153
1338784	N/A	N/A	90386	90405	AACAGCACCTTGACTAGCAC	16	1154
1338802	4483	4502	94862	94881	CCCAATGCCCCCTAGATGCA	22	1155
1338823	N/A	N/A	62812	62831	GGCCGACAACCAGATGGAAA	13	1156
1338830	N/A	N/A	25528	25547	GCACAGGCACAAAATGCCCC	15	1157
1338844	N/A	N/A	42937	42956	GGCTGCACAAACCCTGCCAA	41	1158
1338866	N/A	N/A	20392	20411	CCTAAGGGCTTTCTCACCCA	47	1159
1338868	N/A	N/A	86752	86771	GTGATTTTCATCTGCAGGGT	50	1160
1338872	N/A	N/A	32209	32228	CCAGGGAACCCCTTTCCTTG	19	1161
1338970	4730	4749	95109	95128	TGCATCCATTTAATAGAAGT	18	1162

1338972	N/A	N/A	45588	45607	GCTTCTATCTCACACCCGTC	40	1163
1338989	N/A	N/A	31081	31100	CCCATTCCTCCTTTGTATAA	53	1164
1339003	N/A	N/A	50406	50425	AAGTGATTAAAACATTCGAT	63	1165
1339043	N/A	N/A	17424	17443	CTTGCCTTCACTTGCAGGCA	36	1166
1339083	N/A	N/A	81748	81767	CCTTGGCCTCCAGATACGGC	57	1167
1339202	N/A	N/A	40627	40646	GAGACCTCTCCTCTGCTTCA	36	1168
1339239	N/A	N/A	23620	23639	CTTGACTCAATCATGCAGGT	21	1169
1339312	N/A	N/A	56322	56341	ACTCACAATTCTCAAACTGC	10	1170
1339444	N/A	N/A	28518	28537	CCTCGCTTTACCCTCCCAAC	33	1171
1339463	N/A	N/A	18367	18386	GCATGGTTCTCTCTAGGCGG	29	1172
1339487	N/A	N/A	83705	83724	TCTTTATCCTTCCACTGGGC	52	1173
1339489	N/A	N/A	34550	34569	CCACAGAACTCCAGAAGCAA	57	1174
1339492	N/A	N/A	44413	44432	GTGACAACCACACTCGAGGA	44	1175
1339511	N/A	N/A	87564	87583	CACCTGGTGTCCAAACTCAC	40	1176
1339614	3980	3999	94359	94378	GGTTAAAAAACTCTCCTCAC	22	1177
1339658	N/A	N/A	21950	21969	GTGTTGCTCAACTCCAGAGA	32	1178

Table 16. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	20	283
1337237	N/A	N/A	73460	73479	CACTTGGACACAGTGAGCAA	33	1179
1337310	N/A	N/A	56320	56339	TCACAATTCTCAAACTGCTC	22	1180
1337334	N/A	N/A	25484	25503	TGCACAAGAACTTCCTGCCA	18	1181
1337387	N/A	N/A	61916	61935	AGTGGCACCCTCCCTCTACT	26	1182
1337418	N/A	N/A	27584	27603	AGTGCCCAAAACTACAGCGG	30	1183
1337437	N/A	N/A	26993	27012	GCTGCTTCCACCAAGATTAC	48	1184
1337484	N/A	N/A	48648	48667	TCCCTTTACCTCCCCGTGGA	63	1185
1337492	N/A	N/A	20386	20405	GGCTTTCTCACCCAGAGCCG	39	1186
1337495	N/A	N/A	85820	85839	GGCCTGAACCAGCTCTATCT	47	1187
1337542	4729	4748	95108	95127	GCATCCATTTAATAGAAGTT	6	1188
1337551	N/A	N/A	86668	86687	GGCAGGTGCCCATCCACCCA	37	1189
1337620	N/A	N/A	71774	71793	TCTGTGGACCTCAACCCCCT	31	1190
1337687	N/A	N/A	62789	62808	GCGCACGGCCCCATCTGAAC	21	1191
1337703	N/A	N/A	81747	81766	CTTGGCCTCCAGATACGGCC	72	1192
1337723	3979	3998	94358	94377	GTTAAAAAACTCTCCTCACT	26	1193
1337738	N/A	N/A	68218	68237	GAACAGTCCATCCCAGATGA	38	1194
1337743	N/A	N/A	79199	79218	CCCACAGCCCTTTCACGGCC	54	1195

1337827	N/A	N/A	40471	40490	CCACACCTGCCTCTCGGCTC	17	1196
1337838	N/A	N/A	31056	31075	GGCCTTAGTCCTATTGAATT	32	1197
1337844	N/A	N/A	32176	32195	AGGCTGCAATTCAACACTGC	25	1198
1337900	N/A	N/A	37222	37241	GCTGAGTAAGGAAAATCCCC	23	1199
1337908	N/A	N/A	58027	58046	GGTCCCCTGTTTACTGATCC	21	1200
1337909	N/A	N/A	77145	77164	GCCCGTTCTTCCCTTAACCA	33	1201
1337919	N/A	N/A	50392	50411	TTCGATGTTTCCCAAAGCTC	13	1202
1337957	N/A	N/A	23529	23548	ATGGCCGGCACCCTCCCCCG	30	1203
1337976	N/A	N/A	69583	69602	GAGACATTCACCCAGGGCTG	11	1204
1338002	N/A	N/A	55408	55427	GACAAGCGGCCCCCAAGCCA	21	1205
1338003	N/A	N/A	67911	67930	GGACGATCCACCCTGGACAG	28	1206
1338010	N/A	N/A	87563	87582	ACCTGGTGTCCAAACTCACA	15	1207
1338046	N/A	N/A	56790	56809	CAAAGCTTCTCCTCTCTGGA	24	1208
1338051	N/A	N/A	58720	58739	TGTCAGGACAGTCTTAGCCA	22	1209
1338094	N/A	N/A	24460	24479	GGGAATTACAACCTGAAGCC	18	1210
1338135	N/A	N/A	34530	34549	GCGGAGAGCCCACACGCCAT	41	1211
1338176	N/A	N/A	17368	17387	GCTGGGTGTTTACCCAAGAC	26	1212
1338195	N/A	N/A	75978	75997	ACTCGGTCTTTCTCCTCCCA	32	1213
1338199	N/A	N/A	64871	64890	GCCATACCCATCGATGCAAT	16	1214
1338202	N/A	N/A	51420	51439	CCCTCAACCCCCATGCACGC	50	1215
1338215	N/A	N/A	92164	92183	GTGACGAGCACCCAGTGGGA	10	1216
1338225	N/A	N/A	89246	89265	CACTTCCCACCACAAGGCGC	36	1217
1338226	N/A	N/A	84998	85017	CAGAACTCGATTCACAGGTA	20	1218
1338303	N/A	N/A	54079	54098	CGCCTGAGCACTCTTACGCA	20	1219
1338328	N/A	N/A	18924	18943	TCTGAGGCCATCTTGAGGGA	49	1220
1338387	N/A	N/A	44396	44415	GGAGAGGGCCACCCTTCAGC	41	1221
1338392	N/A	N/A	68641	68660	TCTACCCCAGACAATCCACC	56	1222
1338460	N/A	N/A	21949	21968	TGTTGCTCAACTCCAGAGAA	43	1223
1338627	N/A	N/A	41902	41921	GCAAACACCCCTGAAAGACA	41	1224
1338724	N/A	N/A	18354	18373	TAGGCGGACAGCAAAAGCCT	36	1225
1338760*	N/A	N/A	52750	52769	TGGGTCAGCCTCCAAGAGGC	21	1226
1338786	N/A	N/A	17995	18014	CTAAACTCTTCACCTGGGCA	28	1227
1338854	N/A	N/A	82585	82604	AGGCTGGCATCTCTAAGGCA	22	1228
1338861	N/A	N/A	42857	42876	ATCCGCAGCATCCAAACCCA	41	1229
1338934	N/A	N/A	65777	65796	CCTAAAAGTCCTATCTGCCC	28	1230
1338939	N/A	N/A	46672	46691	CCATGGCGAACAACTTGTCC	29	1231
1338941	N/A	N/A	19669	19688	GTCGAGGCAATTTCTCAGGA	26	1232
1338960	N/A	N/A	93626	93645	CCAGGGCCCATCCCTGACCG	65	1233
1339027	N/A	N/A	33551	33570	GTTGGGAGAAAAACAACCAC	24	1234
1339031	N/A	N/A	35848	35867	TTATGACACCCATTCTGGAC	67	1235
1339040	N/A	N/A	31546	31565	CACTTATCACTTCTCAGTTC	38	1236
1339072	N/A	N/A	90380	90399	ACCTTGACTAGCACAAGCCC	15	1237
1339085	N/A	N/A	75168	75187	CCAGCACACCCCATCTCAGT	50	1238

1339111	N/A	N/A	47625	47644	GCTGAGATAGAAACAATGGC	31	1239
1339135	N/A	N/A	22909	22928	TTTCAAAGCTCCAGCTACAC	45	1240
1339165	N/A	N/A	60122	60141	CCCACGGCCACACCTGTGTC	49	1241
1339189	N/A	N/A	49015	49034	GTCCAGCCCCACTCTACCCT	65	1242
1339190	N/A	N/A	91618	91637	ATCCACGGTCACTCCCGCCT	32	1243
1339216	4481	4500	94860	94879	CAATGCCCCCTAGATGCAGT	20	1244
1339221	N/A	N/A	78078	78097	ATCCAAGTAAACATCGCCAG	43	1245
1339297	N/A	N/A	71033	71052	CCAGACGCACCGTCACACAT	29	1246
1339346	N/A	N/A	20985	21004	GAGGGTCCACCATCAGGTCC	31	1247
1339392	N/A	N/A	38104	38123	TCCTCACCCCCCAATTCCTA	44	1248
1339447	N/A	N/A	39987	40006	CCTTCCCCCCACGCCAGCAT	51	1249
1339468	N/A	N/A	32491	32510	TCTCCAGCGACTCTGAACCT	24	1250
1339552	N/A	N/A	83704	83723	CTTTATCCTTCCACTGGGCC	47	1251
1339566	N/A	N/A	28517	28536	CTCGCTTTACCCTCCCAACA	35	1252
1339579	N/A	N/A	30068	30087	CCATCTCCTTCTGCCTGTTA	42	1253
1339588	N/A	N/A	93252	93271	TGCCGTCCTCCACATCCACA	24	1254
1339644	N/A	N/A	45587	45606	CTTCTATCTCACACCCGTCA	34	1255

Table 17. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	29	283
1337254	N/A	N/A	19579	19598	GGCAGAAGCCCCCAACTCAC	48	1256
1337263	N/A	N/A	56789	56808	AAAGCTTCTCCTCTCTGGAC	45	1257
1337275	N/A	N/A	51275	51294	CGTGGCTCACCTACCGTGGC	68	1258
1337285	N/A	N/A	93251	93270	GCCGTCCTCCACATCCACAC	19	1259
1337317	N/A	N/A	67897	67916	GGACAGTCCACCTAGATGGT	34	1260
1337344	N/A	N/A	39980	39999	CCCACGCCAGCATCCAGGAA	55	1261
1337372	N/A	N/A	18345	18364	AGCAAAAGCCTCTGCTGTCC	57	1262
1337398	N/A	N/A	48585	48604	CTGGCAAGACCACGAAGCCA	71	1263
1337447	N/A	N/A	64826	64845	GTTCCGTGAATTTCCCTGAA	18	1264
1337485	N/A	N/A	34528	34547	GGAGAGCCCACACGCCATAC	50	1265
1337540	N/A	N/A	86667	86686	GCAGGTGCCCATCCACCCAC	68	1266
1337560	N/A	N/A	79198	79217	CCACAGCCCTTTCACGGCCT	77	1267
1337589	N/A	N/A	65776	65795	CTAAAAGTCCTATCTGCCCA	26	1268
1337602	N/A	N/A	47623	47642	TGAGATAGAAACAATGGCCT	34	1269
1337625	3976	3995	94355	94374	AAAAAACTCTCCTCACTAGC	33	1270
1337693	N/A	N/A	17993	18012	AAACTCTTCACCTGGGCATT	28	1271
1337712	N/A	N/A	32489	32508	TCCAGCGACTCTGAACCTCT	37	1272

1337753	N/A	N/A	32175	32194	GGCTGCAATTCAACACTGCC	40	1273
1337791	N/A	N/A	40470	40489	CACACCTGCCTCTCGGCTCT	54	1274
1337845	N/A	N/A	93625	93644	CAGGGCCCATCCCTGACCGA	38	1275
1337880	N/A	N/A	85812	85831	CCAGCTCTATCTTCCCAGAC	35	1276
1337899	N/A	N/A	54078	54097	GCCTGAGCACTCTTACGCAT	9	1277
1337910	N/A	N/A	68217	68236	AACAGTCCATCCCAGATGAC	51	1278
1337934	N/A	N/A	26990	27009	GCTTCCACCAAGATTACCCT	29	1279
1337959	N/A	N/A	46331	46350	TCATGGTGCCCACCCCCACA	71	1280
1337965	N/A	N/A	41854	41873	ACACAGCCCCACCCCTGCGG	54	1281
1337998	N/A	N/A	90301	90320	GAGGCCTTGCCCAACAGGGC	72	1282
1338030	N/A	N/A	49008	49027	CCCACTCTACCCTCTGGCAT	77	1283
1338063*	N/A	N/A	52674	52693	AGGCCACTCCACTTCTTGGA	47	1284
1338064	N/A	N/A	71771	71790	GTGGACCTCAACCCCCTACT	38	1285
1338101	N/A	N/A	28514	28533	GCTTTACCCTCCCAACAGGT	44	1286
1338134	N/A	N/A	82506	82525	AACTGACTCCAGGATCCCTA	33	1287
1338143	N/A	N/A	22908	22927	TTCAAAGCTCCAGCTACACC	44	1288
1338196	4721	4740	95100	95119	TTAATAGAAGTTTCCAGCGC	31	1289
1338318	N/A	N/A	69374	69393	GCAGGGAACCCCACCACATC	72	1290
1338350	N/A	N/A	92130	92149	GGCCACCAGCTCATTTCACT	33	1291
1338463	N/A	N/A	75166	75185	AGCACACCCCATCTCAGTGA	45	1292
1338468	N/A	N/A	77142	77161	CGTTCTTCCCTTAACCACCT	31	1293
1338481	N/A	N/A	42856	42875	TCCGCAGCATCCAAACCCAC	34	1294
1338489	N/A	N/A	31055	31074	GCCTTAGTCCTATTGAATTA	64	1295
1338499	N/A	N/A	50391	50410	TCGATGTTTCCCAAAGCTCA	47	1296
1338504	N/A	N/A	55398	55417	CCCCAAGCCACCTGGAACCA	12	1297
1338548	N/A	N/A	23466	23485	GGCCATTTCTCAGGCTGGCC	66	1298
1338592	N/A	N/A	91605	91624	CCCGCCTGAATCCCCCACGC	41	1299
1338674	N/A	N/A	68632	68651	GACAATCCACCCCAGAGGGT	49	1300
1338705	N/A	N/A	37184	37203	GGTCTGAGCACACGCTCCTA	29	1301
1338730	N/A	N/A	75977	75996	CTCGGTCTTTCTCCTCCCAC	33	1302
1338748	N/A	N/A	89245	89264	ACTTCCCACCACAAGGCGCA	43	1303
1338897	N/A	N/A	78077	78096	TCCAAGTAAACATCGCCAGT	59	1304
1339016	N/A	N/A	58716	58735	AGGACAGTCTTAGCCACCAA	28	1305
1339039	N/A	N/A	25349	25368	GATGGACGATATCTCCTGGA	22	1306
1339053	N/A	N/A	35847	35866	TATGACACCCATTCTGGACA	63	1307
1339059	N/A	N/A	81746	81765	TTGGCCTCCAGATACGGCCA	120	1308
1339088	N/A	N/A	44395	44414	GAGAGGGCCACCCTTCAGCC	54	1309
1339158	N/A	N/A	33536	33555	ACCACAGCCACCTCAAAGAT	106	1310
1339198	N/A	N/A	45586	45605	TTCTATCTCACACCCGTCAC	66	1311
1339200	N/A	N/A	38102	38121	CTCACCCCCCAATTCCTACC	70	1312
1339205	N/A	N/A	70733	70752	AGGTCTCTTCCCTCAGGGAC	70	1313
1339244	N/A	N/A	29998	30017	TGTGCATAACACAAATATTG	58	1314
1339275	N/A	N/A	20957	20976	AGTGAGCTCCCAACTCTGTC	41	1315

1339318	N/A	N/A	87559	87578	GGTGTCCAAACTCACAGGCT	13	1316
1339325	N/A	N/A	84987	85006	TCACAGGTAAAAGACACGAC	71	1317
1339393	N/A	N/A	73446	73465	GAGCAATGCCCACAAAGGTG	39	1318
1339404	4425	4444	94804	94823	GTCTTCTGCTTCCTTCAGAA	28	1319
1339405	N/A	N/A	83567	83586	TAAATTGGCATTAATGTCTT	90	1320
1339414	N/A	N/A	62788	62807	CGCACGGCCCCATCTGAACT	28	1321
1339430	N/A	N/A	20350	20369	GGGCTCAGCCCTTTCAGACC	50	1322
1339434	N/A	N/A	61913	61932	GGCACCCTCCCTCTACTGGC	33	1323
1339436	N/A	N/A	27583	27602	GTGCCCAAAACTACAGCGGT	20	1324
1339456	N/A	N/A	60121	60140	CCACGGCCACACCTGTGTCT	23	1325
1339488	N/A	N/A	24451	24470	AACCTGAAGCCCAAACGGTT	70	1326
1339533	N/A	N/A	57933	57952	GTCACCTGTTTTACTGAGCC	34	1327
1339609	N/A	N/A	17365	17384	GGGTGTTTACCCAAGACAGC	22	1328
1339624	N/A	N/A	31514	31533	GTCTGCGCACAGCTGAGCTT	34	1329
1339639	N/A	N/A	56319	56338	CACAATTCTCAAACTGCTCC	14	1330
1339649	N/A	N/A	18869	18888	CCGAAGCTCTAATCCCTGGC	32	1331
1339660	N/A	N/A	21948	21967	GTTGCTCAACTCCAGAGAAC	44	1332

Table 18. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	15	283
1080891	4702	4721	95081	95100	CTGACCGTACAAACCAGTAA	18	289
1337256	N/A	N/A	48584	48603	TGGCAAGACCACGAAGCCAA	99	1333
1337339	N/A	N/A	50382	50401	CCCAAAGCTCACAACACTCA	66	1334
1337353	N/A	N/A	51274	51293	GTGGCTCACCTACCGTGGCC	95	1335
1337366	N/A	N/A	78024	78043	GGCTGGCCCCACATGCAGGC	58	1336
1337404	N/A	N/A	83424	83443	CCCTGGTGCCTTCTACAGGC	52	1337
1337537	N/A	N/A	32487	32506	CAGCGACTCTGAACCTCTGC	30	1338
1337547	N/A	N/A	28513	28532	CTTTACCCTCCCAACAGGTT	62	1339
1337554	N/A	N/A	82500	82519	CTCCAGGATCCCTATGGGCT	31	1340
1337588	N/A	N/A	79156	79175	AGGCACCACCAGATGCCACA	78	1341
1337604	N/A	N/A	75975	75994	CGGTCTTTCTCCTCCCACCA	36	1342
1337619	3975	3994	94354	94373	AAAAACTCTCCTCACTAGCC	28	1343
1337669	N/A	N/A	20349	20368	GGCTCAGCCCTTTCAGACCT	56	1344
1337742	N/A	N/A	55336	55355	TGTCCCAGACCATCATCGAT	23	1345
1337748	4368	4387	94747	94766	ACGCACCCCTCTCACATGCC	24	1346
1337793*	N/A	N/A	52607	52626	GGGAAACCCCCCAAGTCCTC	39	1347
1337824	N/A	N/A	38101	38120	TCACCCCCCAATTCCTACCT	67	1348

1337881	N/A	N/A	71770	71789	TGGACCTCAACCCCCTACTT	52	1349
1337888	N/A	N/A	91604	91623	CCGCCTGAATCCCCCACGCC	59	1350
1337903	N/A	N/A	87558	87577	GTGTCCAAACTCACAGGCTA	19	1351
1337950	N/A	N/A	29997	30016	GTGCATAACACAAATATTGC	18	1352
1337958	N/A	N/A	26984	27003	ACCAAGATTACCCTCAGGAT	27	1353
1338007	N/A	N/A	75165	75184	GCACACCCCATCTCAGTGAC	28	1354
1338009	N/A	N/A	35846	35865	ATGACACCCATTCTGGACAT	50	1355
1338029	N/A	N/A	61912	61931	GCACCCTCCCTCTACTGGCA	21	1356
1338098	N/A	N/A	18335	18354	TCTGCTGTCCACTCCTGAAC	99	1357
1338142	N/A	N/A	32174	32193	GCTGCAATTCAACACTGCCT	54	1358
1338154	N/A	N/A	39904	39923	CGGAGGCTGCCCATTAGCTG	99	1359
1338220	N/A	N/A	41785	41804	AAACAGGTGCATTCTAGGGT	41	1360
1338250	N/A	N/A	64779	64798	ACCTGGTGCACCTGGAGTCA	25	1361
1338265	N/A	N/A	44338	44357	GCCCTGCTCAGCACGAAGCC	53	1362
1338325	N/A	N/A	93154	93173	TGGACAGGCCATTCCCACTC	34	1363
1338357	N/A	N/A	34523	34542	GCCCACACGCCATACAGTTA	61	1364
1338393	N/A	N/A	56290	56309	GGACATTCCCAGCATTGACC	22	1365
1338415	N/A	N/A	18868	18887	CGAAGCTCTAATCCCTGGCC	43	1366
1338507	N/A	N/A	84986	85005	CACAGGTAAAAGACACGACA	61	1367
1338513	N/A	N/A	23450	23469	GGCCGTGTCCTCCCAAGCCT	27	1368
1338516	N/A	N/A	58711	58730	AGTCTTAGCCACCAAGGCCT	56	1369
1338528	N/A	N/A	59994	60013	GGACGGGTCCCCATCTTGCC	70	1370
1338557	N/A	N/A	17363	17382	GTGTTTACCCAAGACAGCTA	34	1371
1338680	N/A	N/A	69373	69392	CAGGGAACCCCACCACATCA	41	1372
1338710	N/A	N/A	45577	45596	ACACCCGTCACCCTCTGCAC	64	1373
1338727	N/A	N/A	47599	47618	GTCCCAGGCTTCTCTTGGGA	61	1374
1338731	N/A	N/A	24384	24403	GTGTTCTGTTTTACACTAAT	10	1375
1338756	N/A	N/A	40431	40450	GTGAGATCCACACTCCAGAA	36	1376
1338761	N/A	N/A	27582	27601	TGCCCAAAACTACAGCGGTC	25	1377
1338769	N/A	N/A	90160	90179	CGCCAGGGCAGAATTACCTT	29	1378
1338811	N/A	N/A	73444	73463	GCAATGCCCACAAAGGTGGC	65	1379
1338815	N/A	N/A	19578	19597	GCAGAAGCCCCCAACTCACT	46	1380
1338899	N/A	N/A	22907	22926	TCAAAGCTCCAGCTACACCT	49	1381
1338900	N/A	N/A	21947	21966	TTGCTCAACTCCAGAGAACC	53	1382
1338908	N/A	N/A	31009	31028	CCTTAATTACCTCTAAAGAA	55	1383
1338938	N/A	N/A	81680	81699	TCCCAGTGCCTCACACGCGG	49	1384
1338959	N/A	N/A	85811	85830	CAGCTCTATCTTCCCAGACA	51	1385
1338982	N/A	N/A	56788	56807	AAGCTTCTCCTCTCTGGACA	33	1386
1339005	N/A	N/A	57932	57951	TCACCTGTTTTACTGAGCCT	6	1387
1339029	N/A	N/A	92129	92148	GCCACCAGCTCATTTCACTC	24	1388
1339052	N/A	N/A	49007	49026	CCACTCTACCCTCTGGCATC	58	1389
1339120	N/A	N/A	17965	17984	GGTGGGCTCATTATTAGAGC	32	1390
1339150	N/A	N/A	42853	42872	GCAGCATCCAAACCCACGGT	39	1391

1339161	N/A	N/A	46246	46265	CAACAGTTCTCCCTGCTGAC	63	1392
1339187	N/A	N/A	86662	86681	TGCCCATCCACCCACTTGGA	70	1393
1339208	N/A	N/A	68619	68638	AGAGGGTCCACCCCAGACAG	28	1394
1339215	1415	1434	70613	70632	AGCAGGCCTCCCCATTGTCC	29	1395
1339251	N/A	N/A	65765	65784	ATCTGCCCAGAACCTCGCCA	19	1396
1339267	N/A	N/A	31486	31505	GCAGAGGGTCCCATGAGGCT	26	1397
1339343	N/A	N/A	54077	54096	CCTGAGCACTCTTACGCATA	20	1398
1339368	N/A	N/A	89082	89101	CCCCAAAGTCTCCCCCCTAC	50	1399
1339375	N/A	N/A	33534	33553	CACAGCCACCTCAAAGATGA	72	1400
1339403	N/A	N/A	25322	25341	GCAGGACAATTTCTAGGTAC	29	1401
1339498	N/A	N/A	77137	77156	TTCCCTTAACCACCTGTGCA	79	1402
1339507	N/A	N/A	67895	67914	ACAGTCCACCTAGATGGTCC	21	1403
1339527	N/A	N/A	93614	93633	CCTGACCGACACCTGTCCCA	32	1404
1339537	N/A	N/A	62787	62806	GCACGGCCCCATCTGAACTC	18	1405
1339541	N/A	N/A	68214	68233	AGTCCATCCCAGATGACCCA	44	1406
1339659	N/A	N/A	20956	20975	GTGAGCTCCCAACTCTGTCC	30	1407
1339664	N/A	N/A	37179	37198	GAGCACACGCTCCTATGCAT	63	1408

Table 19. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	31	283
1080888	4698	4717	95077	95096	CCGTACAAACCAGTAAGGAA	31	55
1337224	N/A	N/A	73379	73398	CAGAGAGACTCCACCTGTCC	72	1409
1337241	N/A	N/A	44316	44335	CCCAGGCCCCATGTGTGGTC	33	1410
1337261	N/A	N/A	75959	75978	ACCACAGCCTAGACCAGGCT	35	1411
1337278	N/A	N/A	68178	68197	CTGGACAGTTCACCCCAGAT	23	1412
1337320	N/A	N/A	64141	64160	GTCTTACTTCTTAATGGAGA	10	1413
1337361	N/A	N/A	65622	65641	GGCTGAGGTTTCTACAGCCA	59	1414
1337362	N/A	N/A	50378	50397	AAGCTCACAACACTCAGGGT	36	1415
1337368	N/A	N/A	29984	30003	ATATTGCCATTTTAACCCTC	36	1416
1337370	N/A	N/A	78006	78025	GCAGAGTCCCACCACCAAGA	63	1417
1337397	N/A	N/A	93149	93168	AGGCCATTCCCACTCGCTGT	32	1418
1337443	N/A	N/A	86660	86679	CCCATCCACCCACTTGGACA	88	1419
1337454	N/A	N/A	20945	20964	ACTCTGTCCACTTCCTCCAC	39	1420
1337466	N/A	N/A	19542	19561	GAAAGTTGCCCACTCCTGTA	63	1421
1337469	N/A	N/A	84930	84949	GGGTTCGCCCTTACTCATCA	33	1422
1337478	N/A	N/A	24379	24398	CTGTTTTACACTAATGCGGG	68	1423
1337548	4366	4385	94745	94764	GCACCCCTCTCACATGCCCG	46	1424

1337574	3973	3992	94352	94371	AAACTCTCCTCACTAGCCTG	28	1425
1337597	N/A	N/A	75151	75170	AGTGACACTCAAAAGTGCTC	43	1426
1337610	N/A	N/A	55302	55321	CCAAGGAGACCTCACTGCTC	29	1427
1337639	N/A	N/A	58690	58709	TGGCTGACCCCCGCCAGGGC	34	1428
1337724	N/A	N/A	51141	51160	GATGCGGGCCAGGCTAGGCC	21	1429
1337746	N/A	N/A	18851	18870	GCCACTCTCCCTCCAATAGA	43	1430
1337747	N/A	N/A	68605	68624	AGACAGTCCACCCTGGATGA	45	1431
1337756	N/A	N/A	85807	85826	TCTATCTTCCCAGACACACT	66	1432
1337759	N/A	N/A	46174	46193	TAGTCATACACAGATGGCCA	73	1433
1337788	N/A	N/A	59991	60010	CGGGTCCCCATCTTGCCTAC	57	1434
1337836	N/A	N/A	38019	38038	GCACCGGGCACAGATCCCAC	35	1435
1337857	N/A	N/A	56703	56722	CCGGGCTCCCATGAATGTCC	33	1436
1337902	N/A	N/A	30947	30966	GGGCTTTGATATATAAATCT	42	1437
1337935	N/A	N/A	41399	41418	GCCAAGGAACATCAGGGCGA	55	1438
1337943	N/A	N/A	82467	82486	TGGCCGGAACACACTTTCAC	59	1439
1338037	1413	1432	70611	70630	CAGGCCTCCCCATTGTCCAT	45	1440
1338119	N/A	N/A	22825	22844	GCCCTAGCTTCCCCAGAGCA	27	1441
1338123	N/A	N/A	26982	27001	CAAGATTACCCTCAGGATCA	52	1442
1338238	N/A	N/A	35744	35763	GTCTGAGACCCATCTGGGTC	74	1443
1338267	N/A	N/A	42771	42790	TCTCTGCCAGCCCTAACTTA	58	1444
1338272	N/A	N/A	37095	37114	AGCACGAGTACCCTCTGCCA	36	1445
1338307	N/A	N/A	33509	33528	AGCTGCTAAAAGAAATGCCA	26	1446
1338311	N/A	N/A	71765	71784	CTCAACCCCCTACTTGGTCT	57	1447
1338372	N/A	N/A	45575	45594	ACCCGTCACCCTCTGCACCA	40	1448
1338412	N/A	N/A	87549	87568	CTCACAGGCTACTCCCCCCA	35	1449
1338485	N/A	N/A	62452	62471	GGTCCCCTCCTTCTCCCATC	22	1450
1338495	N/A	N/A	77110	77129	ACGCTCCTCCAGCTGAGCCT	53	1451
1338538	N/A	N/A	32172	32191	TGCAATTCAACACTGCCTTA	29	1452
1338564	N/A	N/A	54043	54062	TTTGAGGAAATCTACGGGTA	28	1453
1338583	N/A	N/A	91599	91618	TGAATCCCCCACGCCAGGCC	34	1454
1338609	N/A	N/A	79136	79155	GCTGTACCCACAGGCGGCAC	68	1455
1338632	N/A	N/A	47565	47584	ACAGGCTCCATTGAGAGGCT	52	1456
1338637	N/A	N/A	23309	23328	ATGTTAAATATAACCACCCC	70	1457
1338645	N/A	N/A	93542	93561	CCCGCACCCACCTCTGGTGC	75	1458
1338719	N/A	N/A	56054	56073	TGGAGTGGAGACTCATCCCA	18	1459
	N/A	N/A	56118	56137			
1338813	N/A	N/A	17945	17964	ACTGAGTTCAACAAGATGAA	28	1460
1338860*	N/A	N/A	52340	52359	GCCCCACTCACCATGCAGAC	47	1461
1338862	N/A	N/A	27568	27587	GCGGTCTCTTCTCTCTGTTC	23	1462
1338913	N/A	N/A	17281	17300	GATGAATTATTCCCATGGGC	31	1463
1338924	N/A	N/A	57904	57923	CCTTGGCATTCACTGAGCCT	19	1464
1338984	N/A	N/A	25293	25312	TCCTGACACCCCACCAACGC	85	1465
1339015	N/A	N/A	18333	18352	TGCTGTCCACTCCTGAACAC	83	1466

1339021	N/A	N/A	89016	89035	GTCTTGTTCTCTGCGAGAAC	13	1467
1339066	1068	1087	61818	61837	GCCACGCAGATCATGATGAC	54	1468
1339087	N/A	N/A	39852	39871	CTCAACCGCCTCTTCTGCAA	86	1469
1339095	N/A	N/A	20260	20279	CACACGGCTCCTGTGAGTCA	31	1470
1339169	N/A	N/A	31410	31429	CCCAGGCTCATTCCCGCCAT	50	1471
1339179	N/A	N/A	48970	48989	CGAGGCAGAATTCTCCATTC	34	1472
1339206	N/A	N/A	83413	83432	TCTACAGGCTCCTTGCATGC	47	1473
1339271	N/A	N/A	69371	69390	GGGAACCCCACCACATCACT	56	1474
1339413	N/A	N/A	21945	21964	GCTCAACTCCAGAGAACCAA	49	1475
1339432	N/A	N/A	92126	92145	ACCAGCTCATTTCACTCCGG	21	1476
1339500	N/A	N/A	28502	28521	CAACAGGTTCTACCTACCAA	93	1477
1339509	N/A	N/A	32484	32503	CGACTCTGAACCTCTGCCTC	70	1478
1339553	N/A	N/A	90156	90175	AGGGCAGAATTACCTTGCAA	33	1479
1339560	N/A	N/A	40425	40444	TCCACACTCCAGAAGAACAA	49	1480
1339565	N/A	N/A	67852	67871	TCTCATGGCTCTCATTGGCC	41	1481
1339575	N/A	N/A	34509	34528	CAGTTATGACTCAATGAGCC	48	1482
1339618	N/A	N/A	81636	81655	TCCTGGTTCCACCATCAAGA	63	1483
1339622	N/A	N/A	48514	48533	GCAACCCTGCCCATTGCCAG	70	1484

Table 20. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	18	283
1337222	N/A	N/A	19455	19474	GGGCTGGACACCAGCCGACC	65	1485
1337239	N/A	N/A	48943	48962	CACCAGGCCAACCATCCCCC	57	1486
1337318	N/A	N/A	85691	85710	CTTGCCATCCCGAAATTCCA	33	1487
1337348	N/A	N/A	29976	29995	ATTTTAACCCTCTTTGCCGC	58	1488
1337452	N/A	N/A	64019	64038	TGCACATCCCGATTTGGCCC	36	1489
1337457	N/A	N/A	84790	84809	GTGATTTGCATCCAGAATTC	47	1490
1337517	N/A	N/A	71575	71594	TGGTCCCTGCCCATAGAGGT	36	1491
1337538	N/A	N/A	18845	18864	CTCCCTCCAATAGAACCTCA	36	1492
1337649	N/A	N/A	90107	90126	CACTGGCTGTTAAATTTGCT	18	1493
1337668	N/A	N/A	20940	20959	GTCCACTTCCTCCACCGGGC	23	1494
1337680	N/A	N/A	83316	83335	GTCTCTGTATATGCCTGGCC	65	1495
1337690	N/A	N/A	32086	32105	GCACAGCTCCCATGGATGAA	19	1496
1337697	N/A	N/A	56025	56044	GGTCCCAGGCCTCTGAGCGC	10	1497
			56089	56108			
			56153	56172			
1337700	N/A	N/A	76996	77015	GGTGCCGAACCTTAAGGACC	41	1498

1337725	N/A	N/A	27518	27537	GCAGGTCCACCCTCCCCCGC	25	1499
1337771	N/A	N/A	37927	37946	TAACCGTTCCCTTCCATGTC	41	1500
1337777	N/A	N/A	55294	55313	ACCTCACTGCTCACAAGGCC	18	1501
1337784*	N/A	N/A	52238	52257	GCCTTCGCCATCGCCAGGCT	14	1502
1337795	N/A	N/A	86406	86425	GGGCTCGCCACCCCTCATGC	43	1503
1337855	N/A	N/A	21896	21915	GCTAATGAAACAGCCTGGTC	43	1504
1337978	N/A	N/A	78952	78971	CTTGGTTTCCAATCATCATT	36	1505
1337981	N/A	N/A	32439	32458	TTGGCTCACCCAGATCATCC	31	1506
1337992	N/A	N/A	58649	58668	AACCATGGTCCTCCTGGGCC	38	1507
1337997	N/A	N/A	17841	17860	CTCTTGGTTCACACAACCAA	17	1508
1338015	N/A	N/A	67431	67450	GGGCTGCCACCCTCACTGAA	51	1509
1338071	N/A	N/A	62366	62385	GCCCAAGCACTTCACACCCT	26	1510
1338078	N/A	N/A	68133	68152	GATGGTCCACACTAAATGGT	48	1511
1338085	N/A	N/A	69098	69117	CACTATGCCACTAAGGACAC	60	1512
1338088	N/A	N/A	33378	33397	AGGTAAGCATTTAAACCTTG	34	1513
1338109	N/A	N/A	37048	37067	ATGGAAGCCCCCTTCAACCC	324	1514
1338189	N/A	N/A	24230	24249	TCTCAGGGTCTCCCTGGATA	50	1515
1338200	N/A	N/A	28397	28416	AGCTCAGGCCACCCAAGACT	43	1516
1338204	N/A	N/A	31389	31408	TGCGGAATCCCCTCCTGCAC	47	1517
1338283	N/A	N/A	93415	93434	TCTGTTCACCTCACATGCAT	45	1518
1338301	N/A	N/A	20129	20148	GGGATGGCTTCTAATGGCAG	24	1519
1338308	N/A	N/A	26886	26905	CAGGGTCATCCTCGAAGCCA	25	1520
1338332	N/A	N/A	77995	78014	CCACCAAGAAACATCGCAGA	52	1521
1338351	N/A	N/A	91344	91363	GCTCCGCTTGAATCTAAACA	15	1522
1338402	N/A	N/A	73267	73286	GTCTCCCGCCCTGCCTGGTC	21	1523
1338467	N/A	N/A	17257	17276	CCTGTTGGTCCTTAACTGAA	30	1524
1338474	N/A	N/A	34425	34444	ACCAGCACAGCAAAGGCACA	36	1525
1338520	N/A	N/A	82454	82473	CTTTCACTCTCCATCGGGTT	31	1526
1338536	N/A	N/A	88950	88969	GCTGGCCCAACTCTAGCTGA	26	1527
1338562	N/A	N/A	23101	23120	CACCCTTCCCAAACTCAGCT	45	1528
1338631	N/A	N/A	30920	30939	CACAGTTCAATCCCGAACAC	23	1529
1338639	N/A	N/A	75847	75866	GCCTTGGGCTCTTACCCACA	31	1530
1338683	N/A	N/A	47511	47530	GCTCAAACCATCAGGACCCA	20	1531
1338690	N/A	N/A	92120	92139	TCATTTCACTCCGGCAGGCA	15	1532
1338725	N/A	N/A	42691	42710	CTCGCTGTCAACACACGAAC	38	1533
1338773	N/A	N/A	35706	35725	TCTGAAGCCCCAAACTAGCT	63	1534
1338776	N/A	N/A	93094	93113	GCATCAGCCCAGAGCACCCC	22	1535
1338779	N/A	N/A	44272	44291	TGAGCTCCACCTCATGCCGA	22	1536
1338795	N/A	N/A	56670	56689	GGTCGGGCTATCTAACCCAC	12	1537
1338806	N/A	N/A	59651	59670	GGGTTTGTCACACCCTTCAC	22	1538
1338817	N/A	N/A	65553	65572	GCATGGGACAATCTCCCCCA	19	1539
1338835	N/A	N/A	74943	74962	AGGCAGCACTCACTCTACCA	62	1540
1338840	N/A	N/A	50285	50304	TAGAGTCCCAGCACCTGCCT	32	1541

1338865	N/A	N/A	18306	18325	TACAGCATTACAATTTGATC	23	1542
1338871	4363	4382	94742	94761	CCCCTCTCACATGCCCGGCT	28	1543
1338895	N/A	N/A	68551	68570	ATGGATGGTCCACCCCAGAC	17	1544
1338914	N/A	N/A	51100	51119	AGGAAAACTCCAATGCTGCC	56	1545
1338918	N/A	N/A	61485	61504	TCTGTCCCCAAGCTCTGCCG	21	1546
1338949	3938	3957	94317	94336	GAGCTGGCCCTCCCCCCGCA	32	1547
1339004	N/A	N/A	57690	57709	GGCCTGGTTTCCCTATTTAC	26	1548
1339013	N/A	N/A	39660	39679	CCTGATGAAACTTCAGCCCT	41	1549
1339037	N/A	N/A	40417	40436	CCAGAAGAACAAACCTACCA	58	1550
1339129	N/A	N/A	45288	45307	CAAAGCCTCTTCCATTTGAC	68	1551
1339149	4695	4714	95074	95093	TACAAACCAGTAAGGAACCA	19	1552
1339246	N/A	N/A	41167	41186	TGAGCTCCTCAGCATGGGCC	25	1553
			50778	50797			
1339278	N/A	N/A	53948	53967	CTGGAGACACCATCTTCGGA	13	1554
1339367	N/A	N/A	25089	25108	TCAGCCTTCACTCACACAGT	40	1555
1339373	N/A	N/A	70358	70377	AGTGGGCATCCCCATACTGC	62	1556
1339397	N/A	N/A	22735	22754	GGCTCAGTGCCCTTCAGGGA	26	1557
1339535	N/A	N/A	81460	81479	GCTGCTCACCTTTTCTAGTT	66	1558
1339544	N/A	N/A	87544	87563	AGGCTACTCCCCCCAGGCCT	41	1559
1339594	N/A	N/A	46150	46169	GGGAAGCTCCACACCAGCTC	42	1560
1339665	N/A	N/A	48469	48488	AGTTCCTCCCCAGACACCGT	34	1561

Table 21. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	23	283
1337253	2743	2762	80762	80781	CATGTAGTCCTCCTCGGCGC	28	1562
1337270	N/A	N/A	22602	22621	GCAAAGCTCCCTCTGGAGGA	53	1563
1337295	N/A	N/A	32420	32439	CACGATAATTTCCCATCTTC	27	1564
1337305	N/A	N/A	71519	71538	TGACCCTGCCTTCACTGACC	66	1565
1337384	N/A	N/A	20104	20123	GGCATCAGACCCCACCCCAA	30	1566
1337489	N/A	N/A	63575	63594	AAAGCAGGTCCCCCTGCACC	43	1567
1337511	N/A	N/A	39659	39678	CTGATGAAACTTCAGCCCTC	54	1568
1337533	2002	2021	73015	73034	CGAGAAGGCCCTCTTCTTCC	49	1569
1337545	N/A	N/A	86405	86424	GGCTCGCCACCCCTCATGCA	37	1570
1337586	N/A	N/A	69090	69109	CACTAAGGACACATTCAGGC	34	1571
1337591	N/A	N/A	90106	90125	ACTGGCTGTTAAATTTGCTA	18	1572
1337611	N/A	N/A	37926	37945	AACCGTTCCCTTCCATGTCA	43	1573
1337638	N/A	N/A	87543	87562	GGCTACTCCCCCCAGGCCTC	25	1574

1337676	N/A	N/A	25085	25104	CCTTCACTCACACAGTGGCC	36	1575
1337707	N/A	N/A	83281	83300	GGCATCTGTCCCACATGGAC	45	1576
1337776	N/A	N/A	28339	28358	GGTACGGCCTCATCCAGGTC	38	1577
1337846	N/A	N/A	59649	59668	GTTTGTCACACCCTTCACTT	38	1578
1337917	N/A	N/A	18840	18859	TCCAATAGAACCTCACTGTA	51	1579
1337984	N/A	N/A	31388	31407	GCGGAATCCCCTCCTGCACA	48	1580
1338036	N/A	N/A	56053	56072	GGAGTGGAGACTCATCCCAC	17	1581
	N/A	N/A	56117	56136			
1338073	N/A	N/A	27516	27535	AGGTCCACCCTCCCCCGCAA	41	1582
1338105	N/A	N/A	33373	33392	AGCATTTAAACCTTGGTGGA	26	1583
1338108	N/A	N/A	17839	17858	CTTGGTTCACACAACCAAAT	41	1584
1338147	N/A	N/A	56669	56688	GTCGGGCTATCTAACCCACA	12	1585
1338205	N/A	N/A	21895	21914	CTAATGAAACAGCCTGGTCA	78	1586
1338236	N/A	N/A	17256	17275	CTGTTGGTCCTTAACTGAAA	26	1587
1338242	N/A	N/A	62364	62383	CCAAGCACTTCACACCCTGA	32	1588
1338254	N/A	N/A	45287	45306	AAAGCCTCTTCCATTTGACC	59	1589
1338274	N/A	N/A	92110	92129	CCGGCAGGCACAGACTGGCC	26	1590
1338290	N/A	N/A	77994	78013	CACCAAGAAACATCGCAGAC	70	1591
1338296	N/A	N/A	37047	37066	TGGAAGCCCCCTTCAACCCT	48	1592
1338331	N/A	N/A	51004	51023	GCACATGTCCCCCTAAACGG	55	1593
1338426	N/A	N/A	18305	18324	ACAGCATTACAATTTGATCA	37	1594
1338443	N/A	N/A	34417	34436	AGCAAAGGCACAACAAGATC	83	1595
1338449	N/A	N/A	35705	35724	CTGAAGCCCCAAACTAGCTG	49	1596
1338451	4362	4381	94741	94760	CCCTCTCACATGCCCGGCTT	27	1597
1338456	N/A	N/A	23098	23117	CCTTCCCAAACTCAGCTCCA	67	1598
1338497	N/A	N/A	42690	42709	TCGCTGTCAACACACGAACA	36	1599
1338506	N/A	N/A	40416	40435	CAGAAGAACAAACCTACCAA	69	1600
1338540	N/A	N/A	67276	67295	CTGAGAGGACTCAGGGACTT	31	1601
	N/A	N/A	67397	67416			
1338544	N/A	N/A	85690	85709	TTGCCATCCCGAAATTCCAA	59	1602
1338608	3937	3956	94316	94335	AGCTGGCCCTCCCCCCGCAT	32	1603
1338622	N/A	N/A	48400	48419	CTTTGAGGCCCCTTGACCTC	65	1604
1338702	N/A	N/A	58560	58579	GAGCGGCTATCCCGCTGCCC	110	1605
1338735	N/A	N/A	44244	44263	AGGCTGTCCCCTTGTCTCCA	40	1606
1338747	N/A	N/A	49819	49838	GGCTTGTCACCCCACCGGGC	55	1607
1338751	N/A	N/A	68549	68568	GGATGGTCCACCCCAGACGA	15	1608
1338792	N/A	N/A	46107	46126	GGGCCCACCATAGCCCTGCA	62	1609
1338816	N/A	N/A	76995	77014	GTGCCGAACCTTAAGGACCC	47	1610
1338843	N/A	N/A	57689	57708	GCCTGGTTTCCCTATTTACT	13	1611
1338847	N/A	N/A	84781	84800	ATCCAGAATTCCAGCCGTAC	44	1612
1338896	N/A	N/A	70357	70376	GTGGGCATCCCCATACTGCC	61	1613
1338936	N/A	N/A	55266	55285	TGGCCAGCTCCTCTTGTCTT	10	1614
1338955	N/A	N/A	53947	53966	TGGAGACACCATCTTCGGAA	28	1615

1338956	N/A	N/A	24175	24194	CGCTTGAGTCATAAAGACGC	39	1616
1338971*	N/A	N/A	52174	52193	CAGGCACCCCACTCACTCGA	58	1617
1338973	N/A	N/A	74942	74961	GGCAGCACTCACTCTACCAC	52	1618
1338987	N/A	N/A	47465	47484	CTTCGACTCACCGTGGCTCC	34	1619
1338998	N/A	N/A	41165	41184	AGCTCCTCAGCATGGGCCCC	50	1620
	N/A	N/A	50776	50795			
1339006	N/A	N/A	75846	75865	CCTTGGGCTCTTACCCACAT	46	1621
1339019	N/A	N/A	29975	29994	TTTTAACCCTCTTTGCCGCC	71	1622
1339038	N/A	N/A	65552	65571	CATGGGACAATCTCCCCCAA	34	1623
1339058	N/A	N/A	93398	93417	CATGCATGCCTTCATCTACA	22	1624
1339077	N/A	N/A	48942	48961	ACCAGGCCAACCATCCCCCA	59	1625
1339166	N/A	N/A	26816	26835	GAGGAAGCTCCAATCCAGGT	43	1626
1339211	4681	4700	95060	95079	GAACCAGCAGCAAAGGACGC	42	1627
1339226	N/A	N/A	78951	78970	TTGGTTTCCAATCATCATTT	31	1628
1339339	N/A	N/A	30913	30932	CAATCCCGAACACCATGTCA	61	1629
1339347	N/A	N/A	88946	88965	GCCCAACTCTAGCTGATGCC	23	1630
1339351	N/A	N/A	91317	91336	GCAGCTCCCCAGCCCCAGAA	15	1631
1339472	N/A	N/A	68132	68151	ATGGTCCACACTAAATGGTC	40	1632
1339496	N/A	N/A	61469	61488	GCCGGAGCCACCTCCTGCCT	16	1633
1339501	N/A	N/A	93068	93087	GCAGCTCATCCCTCCGAGAA	26	1634
1339526	N/A	N/A	31908	31927	CCACAGGCCACCTTGAGGTG	56	1635
1339577	N/A	N/A	19431	19450	GCCCCCCACCTTCCAGATCT	40	1636
1339605	N/A	N/A	82338	82357	CCACGGTGTCACAATCCTGC	38	1637
1339655	N/A	N/A	20846	20865	GCCGAGCTCTTCTCTGTCCA	25	1638

Table 22. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	26	283
1337255	N/A	N/A	56666	56685	GGGCTATCTAACCCACAGCC	28	1639
1337274	N/A	N/A	74939	74958	AGCACTCACTCTACCACGGA	68	1640
1337314	N/A	N/A	62360	62379	GCACTTCACACCCTGAGGCA	18	1641
1337324	N/A	N/A	85684	85703	TCCCGAAATTCCAAATCCTC	51	1642
1337349*	N/A	N/A	52173	52192	AGGCACCCCACTCACTCGAT	52	1643
1337385	N/A	N/A	24174	24193	GCTTGAGTCATAAAGACGCA	32	1644
1337403	N/A	N/A	31837	31856	CCATCAGGCCATCTTTGACA	55	1645
1337421	N/A	N/A	27358	27377	GATCTGAGCCCCTCGGTCCA	22	1646
1337445	N/A	N/A	23051	23070	GCATGGTTCCCCGACTCCTC	23	1647
1337470	N/A	N/A	56051	56070	AGTGGAGACTCATCCCACCC	29	1648

			56115	56134			
1337512	N/A	N/A	76922	76941	GACTTAGCCCCATCAGGGCC	83	1649
1337520	N/A	N/A	57688	57707	CCTGGTTTCCCTATTTACTG	26	1650
1337543	N/A	N/A	39612	39631	GCCCATCTCCCCATGCTTGT	52	1651
1337581	N/A	N/A	48392	48411	CCCCTTGACCTCCTCCTGGC	41	1652
1337593	N/A	N/A	51003	51022	CACATGTCCCCCTAAACGGC	85	1653
1337661	N/A	N/A	47384	47403	TCTCCGCTTCCTGTCAGGGC	53	1654
1337695	N/A	N/A	53932	53951	CGGAAGGACATTCAGAGAAA	33	1655
1337705	N/A	N/A	37924	37943	CCGTTCCCTTCCATGTCACA	42	1656
1337713	N/A	N/A	84746	84765	GTGAAATTCCAGAACAACTT	77	1657
1337719	N/A	N/A	80638	80657	GGATGCGGCCCACTCCCCAC	66	1658
1337745	N/A	N/A	20841	20860	GCTCTTCTCTGTCCAAGGCC	34	1659
1337757	N/A	N/A	34411	34430	GGCACAACAAGATCCAGGCA	15	1660
1337762	N/A	N/A	86403	86422	CTCGCCACCCCTCATGCATA	41	1661
1337797	N/A	N/A	40414	40433	GAAGAACAAACCTACCAAGT	59	1662
1337811	N/A	N/A	28083	28102	TTGCCGGCCCTTCTGTGGAT	38	1663
1337812	N/A	N/A	93067	93086	CAGCTCATCCCTCCGAGAAC	20	1664
1337865	N/A	N/A	42685	42704	GTCAACACACGAACAGAACC	47	1665
1337913	N/A	N/A	67268	67287	ACTCAGGGACTTGCCAAGCA	55	1666
			67389	67408			
1337921	N/A	N/A	29966	29985	TCTTTGCCGCCCTCTTTTAA	46	1667
1337985	N/A	N/A	58505	58524	CCTGGTTTTCCCCCACGGAA	35	1668
1338033	N/A	N/A	59648	59667	TTTGTCACACCCTTCACTTT	65	1669
1338035	N/A	N/A	37046	37065	GGAAGCCCCCTTCAACCCTC	47	1670
1338054	N/A	N/A	83280	83299	GCATCTGTCCCACATGGACC	69	1671
1338068	N/A	N/A	26739	26758	GCTAGGGATCCCAATGAAAT	25	1672
1338084	N/A	N/A	63574	63593	AAGCAGGTCCCCCTGCACCT	29	1673
1338116	4638	4657	95017	95036	CGCCGCCCGGGATCTCGCCT	21	1674
1338122	N/A	N/A	68131	68150	TGGTCCACACTAAATGGTCC	43	1675
1338172	N/A	N/A	20079	20098	CAGGAGGGTCCTCCAAGCGG	37	1676
1338235	N/A	N/A	17145	17164	GGACAAGCTCCCTCATTGAA	42	1677
1338239	N/A	N/A	49817	49836	CTTGTCACCCCACCGGGCAT	51	1678
1338353	N/A	N/A	90105	90124	CTGGCTGTTAAATTTGCTAC	38	1679
1338358	N/A	N/A	44119	44138	GACCTGGACACACCACCCTC	75	1680
1338378	N/A	N/A	22469	22488	GAGGAGGGCACTTATGCAAT	23	1681
1338461	N/A	N/A	45952	45971	GCTTCAGGCCCACTGCCAAC	69	1682
1338491	N/A	N/A	55251	55270	GTCTTTTCTTTCAACTGATC	8	1683
1338563	3935	3954	94314	94333	CTGGCCCTCCCCCCGCATGA	35	1684
1338593	N/A	N/A	78949	78968	GGTTTCCAATCATCATTTTC	59	1685
1338603	N/A	N/A	25084	25103	CTTCACTCACACAGTGGCCG	39	1686
1338711	N/A	N/A	88516	88535	CCGTGTGCCCTTACCGTAGC	29	1687
1338722	N/A	N/A	45286	45305	AAGCCTCTTCCATTTGACCT	41	1688
1338742	N/A	N/A	87522	87541	GCTTCCCCACCACCAGTGCA	18	1689

1338750	N/A	N/A	75845	75864	CTTGGGCTCTTACCCACATA	64	1690
1338774	N/A	N/A	70354	70373	GGCATCCCCATACTGCCCCC	36	1691
1338827	N/A	N/A	21813	21832	AAGGCGGCCACTCCCTTCCC	35	1692
1338876	N/A	N/A	18297	18316	ACAATTTGATCAACCACAGC	56	1693
1338909	N/A	N/A	18838	18857	CAATAGAACCTCACTGTATA	70	1694
1338966	2000	2019	73013	73032	AGAAGGCCCTCTTCTTCCGC	30	1695
1339036	N/A	N/A	65547	65566	GACAATCTCCCCCAAAGCGG	27	1696
1339051	N/A	N/A	82337	82356	CACGGTGTCACAATCCTGCA	71	1697
1339096	N/A	N/A	69087	69106	TAAGGACACATTCAGGCTCC	53	1698
1339134	N/A	N/A	77983	78002	ATCGCAGACCCACCTGCCAC	55	1699
1339138	N/A	N/A	32419	32438	ACGATAATTTCCCATCTTCA	42	1700
1339191	N/A	N/A	71499	71518	CCAGGATCCCAGCATAAGAC	25	1701
1339263	N/A	N/A	33359	33378	GGTGGAGTAAAAACAATGAT	52	1702
1339309	N/A	N/A	35667	35686	GGTACAGCCTGAAACTGGCC	26	1703
1339322	N/A	N/A	61467	61486	CGGAGCCACCTCCTGCCTGA	27	1704
1339329	N/A	N/A	68548	68567	GATGGTCCACCCCAGACGAT	23	1705
1339357	N/A	N/A	19331	19350	AGCTAAGTCCCCTCCCTGTC	85	1706
1339377	N/A	N/A	48941	48960	CCAGGCCAACCATCCCCCAC	53	1707
1339445	N/A	N/A	17835	17854	GTTCACACAACCAAATGTTA	46	1708
1339508	N/A	N/A	93396	93415	TGCATGCCTTCATCTACACC	29	1709
1339531	N/A	N/A	30873	30892	GTCTCAGATTCACAATCCCG	24	1710
1339580	N/A	N/A	92109	92128	CGGCAGGCACAGACTGGCCC	32	1711
1339583	N/A	N/A	40974	40993	GCTCAGGGCCTCCTGATGCA	59	1712
1339603	4353	4372	94732	94751	ATGCCCGGCTTCCCCGGGCC	75	1713
1339615	N/A	N/A	31360	31379	GAGGACCCCCTTTCTTGCTG	52	1714
1339663	N/A	N/A	91291	91310	CACCGTCACCCTCCCGGGCA	30	1715

Table 23. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	33	283
1337281	N/A	N/A	23050	23069	CATGGTTCCCCGACTCCTCC	29	1716
1337287	N/A	N/A	37916	37935	TTCCATGTCACAGACGCGGC	29	1717
1337288	N/A	N/A	21812	21831	AGGCGGCCACTCCCTTCCCA	46	1718
1337299	N/A	N/A	65509	65528	GCCAACCCCTCCACTTCCGA	21	1719
1337442	3882	3901	94261	94280	ATGGTGAGTAGAGTGTGCCA	23	1720
1337465	N/A	N/A	20063	20082	GCGGCTGATCCCCTCCTCCA	49	1721
1337482	N/A	N/A	93395	93414	GCATGCCTTCATCTACACCT	16	1722
1337539	N/A	N/A	74626	74645	CAGGTGAACACAGTCAGCTC	31	1723

1337580	N/A	N/A	76921	76940	ACTTAGCCCCATCAGGGCCT	59	1724
1337592	N/A	N/A	62326	62345	GCCTCCACCTTTCCCACTGA	39	1725
1337636	N/A	N/A	57687	57706	CTGGTTTCCCTATTTACTGA	29	1726
1337730	N/A	N/A	28040	28059	GTCTCTTGCCCTGACAGGCC	40	1727
1337751	N/A	N/A	24117	24136	TCACGGACCCTCCTCCATGC	73	1728
1337772	N/A	N/A	26736	26755	AGGGATCCCAATGAAATACA	72	1729
1337778	N/A	N/A	49771	49790	GGGACAAGCCTCCCACAGAC	88	1730
1337789	N/A	N/A	71498	71517	CAGGATCCCAGCATAAGACT	36	1731
1337818	N/A	N/A	85683	85702	CCCGAAATTCCAAATCCTCC	41	1732
1337825	N/A	N/A	24945	24964	GAGGATTTCCCACGACATCT	2	1733
1337843	N/A	N/A	50908	50927	CGTCTGCTCCTATCAGTCGG	32	1734
1337849	N/A	N/A	61400	61419	CGGCGAATTCCCCGGAGCCT	35	1735
1337852	N/A	N/A	86402	86421	TCGCCACCCCTCATGCATAC	60	1736
1337854	N/A	N/A	48940	48959	CAGGCCAACCATCCCCCACC	99	1737
1337859	N/A	N/A	45285	45304	AGCCTCTTCCATTTGACCTA	45	1738
1337890	N/A	N/A	56049	56068	TGGAGACTCATCCCACCCCA	28	1739
			56113	56132			
1337907	N/A	N/A	40936	40955	GCCCTGTCCCCCCATTGGGC	77	1740
1337924	N/A	N/A	47241	47260	GGGCTAGGAAGAACCTGCCT	70	1741
1337971	N/A	N/A	33311	33330	ACACTGTGATCCAAAATGAA	70	1742
1338019	N/A	N/A	30792	30811	GTTTGTGAATCACCATAACC	35	1743
1338031	N/A	N/A	59645	59664	GTCACACCCTTCACTTTGTC	29	1744
1338044	N/A	N/A	40410	40429	AACAAACCTACCAAGTCCTC	51	1745
1338049	N/A	N/A	31836	31855	CATCAGGCCATCTTTGACAC	61	1746
1338110	N/A	N/A	67980	67999	AATGGTCCATCCCAGAAGGT	41	1747
			68119	68138			
1338141	N/A	N/A	87487	87506	CAACAGCCTTCTCTGAGCCG	35	1748
1338162	N/A	N/A	82335	82354	CGGTGTCACAATCCTGCAGC	44	1749
1338197	N/A	N/A	91775	91794	GGCAGGGCCACCTCGCCCCT	52	1750
1338295	N/A	N/A	44115	44134	TGGACACACCACCCTCCACC	49	1751
1338310	N/A	N/A	89952	89971	GAGTCGGTCACCAGAAAGGC	31	1752
1338317	4352	4371	94731	94750	TGCCCGGCTTCCCCGGGCCC	79	1753
1338326	N/A	N/A	75844	75863	TTGGGCTCTTACCCACATAC	34	1754
1338382	1999	2018	73012	73031	GAAGGCCCTCTTCTTCCGCT	25	1755
1338418	N/A	N/A	22461	22480	CACTTATGCAATCCCAGGCT	30	1756
1338439	N/A	N/A	17144	17163	GACAAGCTCCCTCATTGAAT	45	1757
1338454	N/A	N/A	93066	93085	AGCTCATCCCTCCGAGAACA	26	1758
1338502*	N/A	N/A	52172	52191	GGCACCCCACTCACTCGATC	57	1759
1338549	N/A	N/A	35666	35685	GTACAGCCTGAAACTGGCCA	53	1760
1338572	N/A	N/A	19330	19349	GCTAAGTCCCCTCCCTGTCC	75	1761
1338621	N/A	N/A	80490	80509	CGGCCACGCCTTACTTGTCC	47	1762
1338625	N/A	N/A	18827	18846	CACTGTATACTTCATTTCCA	86	1763
1338650	N/A	N/A	53772	53791	GGGCTGGTCCCCAAAGACAT	12	1764

1338681	N/A	N/A	91290	91309	ACCGTCACCCTCCCGGGCAT	27	1765
1338708	N/A	N/A	42680	42699	CACACGAACAGAACCTGCAC	88	1766
1338799	N/A	N/A	39502	39521	GACATGTGCCCACACCAGGC	44	1767
1338814	N/A	N/A	56665	56684	GGCTATCTAACCCACAGCCC	69	1768
1338831	N/A	N/A	32415	32434	TAATTTCCCATCTTCAAGGC	73	1769
1338920	N/A	N/A	67265	67284	CAGGGACTTGCCAAGCAGTC	58	1770
			67386	67405			
1338993	N/A	N/A	58504	58523	CTGGTTTTCCCCCACGGAAC	65	1771
1338997	N/A	N/A	34376	34395	GGACACTTCCACTGGAGGAT	50	1772
1339018	N/A	N/A	88515	88534	CGTGTGCCCTTACCGTAGCC	40	1773
1339110	N/A	N/A	27350	27369	CCCCTCGGTCCAGAATGGCC	16	1774
1339112	N/A	N/A	31255	31274	GTTCAGTTCCCTGCTGCCTC	26	1775
1339124	N/A	N/A	29960	29979	CCGCCCTCTTTTAAGGACTT	27	1776
1339130	4619	4638	94998	95017	TTGCTGAGAAGATCCTCTCT	27	1777
1339157	N/A	N/A	48391	48410	CCCTTGACCTCCTCCTGGCA	58	1778
1339213	N/A	N/A	17834	17853	TTCACACAACCAAATGTTAT	54	1779
1339268	N/A	N/A	77982	78001	TCGCAGACCCACCTGCCACC	51	1780
1339308	N/A	N/A	63553	63572	AGGATGAGTCCTCATTTGCA	11	1781
1339338	N/A	N/A	18295	18314	AATTTGATCAACCACAGCCA	29	1782
1339360	N/A	N/A	55240	55259	CAACTGATCCACTTTCCCCT	16	1783
1339381	N/A	N/A	83279	83298	CATCTGTCCCACATGGACCC	60	1784
1339399	N/A	N/A	45950	45969	TTCAGGCCCACTGCCAACCC	60	1785
1339406	N/A	N/A	84689	84708	CAGGAAACAAGAACCACGAC	35	1786
1339410	N/A	N/A	69034	69053	GGAGTGTCCCAGAAAGTGCA	47	1787
1339448	N/A	N/A	70328	70347	CCCAACCCACATCACAGTGT	49	1788
1339461	N/A	N/A	37045	37064	GAAGCCCCCTTCAACCCTCC	54	1789
1339576	N/A	N/A	20808	20827	GCTGTGGTGACTCACTGCCA	35	1790
1339589	N/A	N/A	67947	67966	TCCACCCCAGACGATCCACC	27	1791
			68543	68562			
1339597	N/A	N/A	78897	78916	GGTTCATTCCAGACTGGAGC	33	1792

Table 24. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	15	283
1080859	3877	3896	94256	94275	GAGTAGAGTGTGCCATCCCC	13	128
1337244	N/A	N/A	40935	40954	CCCTGTCCCCCCATTGGGCA	47	1793
1337262	N/A	N/A	24944	24963	AGGATTTCCCACGACATCTT	20	1794
1337313	N/A	N/A	58502	58521	GGTTTTCCCCCACGGAACCC	51	1795

1337356	N/A	N/A	50896	50915	TCAGTCGGCTGCCTTAGCCC	8	1796
1337367	N/A	N/A	48939	48958	AGGCCAACCATCCCCCACCA	54	1797
1337474	N/A	N/A	62166	62185	GCCGGCTGTCCACCTTGACC	46	1798
1337505	N/A	N/A	55206	55225	TTGTTGCAAACTAAGTGCCC	6	1799
1337521	N/A	N/A	68080	68099	CCAGACAGTCCATCCTAGAT	22	1800
1337523	N/A	N/A	45278	45297	TCCATTTGACCTACATCTTA	38	1801
1337555	N/A	N/A	53762	53781	CCAAAGACATGACTCAGGAC	23	1802
1337568*	N/A	N/A	52171	52190	GCACCCCACTCACTCGATCT	36	1803
1337621	N/A	N/A	19319	19338	TCCCTGTCCCATCCTATAGA	52	1804
1337655	N/A	N/A	31823	31842	TTGACACGGGCAACCAGGAC	27	1805
1337678	N/A	N/A	74568	74587	GAGGAGCTTCAATCTATGCC	40	1806
1337701	N/A	N/A	61271	61290	GGTCTGGCCCTCTACCCCCA	14	1807
1337720	N/A	N/A	40384	40403	GGAGCCTGCCCTACTCATCT	23	1808
1337754	N/A	N/A	30789	30808	TGTGAATCACCATAACCAGA	15	1809
1337781	N/A	N/A	37705	37724	CAGGGATCTGTCTCTATTTC	30	1810
1337986	N/A	N/A	78861	78880	GTGGCTGGAACATCTCCGGT	31	1811
1338008	N/A	N/A	89951	89970	AGTCGGTCACCAGAAAGGCA	11	1812
1338026	N/A	N/A	49770	49789	GGACAAGCCTCCCACAGACC	58	1813
1338048	N/A	N/A	82334	82353	GGTGTCACAATCCTGCAGCC	33	1814
1338055	N/A	N/A	31244	31263	TGCTGCCTCCAGTCACTTCA	27	1815
1338076	N/A	N/A	92954	92973	ACAGCCCCCCCATCATCTCA	28	1816
1338091	N/A	N/A	18294	18313	ATTTGATCAACCACAGCCAC	39	1817
1338146	N/A	N/A	23046	23065	GTTCCCCGACTCCTCCTCGA	30	1818
1338151	N/A	N/A	17808	17827	TCTGGTAGAATATTCCATTC	8	1819
1338209	N/A	N/A	56664	56683	GCTATCTAACCCACAGCCCC	23	1820
1338233	N/A	N/A	76874	76893	GGTAGGGCCCTCACTGCTGC	13	1821
1338281	N/A	N/A	22460	22479	ACTTATGCAATCCCAGGCTC	23	1822
1338289	N/A	N/A	87461	87480	GGCCGACACATCCGTGGGAC	28	1823
1338299	N/A	N/A	35154	35173	GGCTGCACTAACCCAGGACA	26	1824
1338322	N/A	N/A	68541	68560	CACCCCAGACGATCCACCCC	48	1825
1338376	1998	2017	73011	73030	AAGGCCCTCTTCTTCCGCTT	19	1826
1338413	N/A	N/A	48390	48409	CCTTGACCTCCTCCTGGCAC	59	1827
1338437	4617	4636	94996	95015	GCTGAGAAGATCCTCTCTCT	13	1828
1338446	N/A	N/A	86379	86398	CACACAGAACCACCAGGTCC	31	1829
1338470	N/A	N/A	91739	91758	TGACTCCTCCACCCAGACCC	49	1830
1338480	N/A	N/A	45928	45947	GGGCCAGCTATTCTGAGCCT	55	1831
1338624	3275	3294	88220	88239	CCCGTGTGTCCTCACAGTCC	10	1832
1338648	N/A	N/A	27349	27368	CCCTCGGTCCAGAATGGCCT	28	1833
1338701	N/A	N/A	33280	33299	CGACTGAGATTCTAACGCGA	30	1834
1338723	N/A	N/A	29931	29950	GTTTTGGGCCAGGATGGCCT	26	1835
1338739	4350	4369	94729	94748	CCCGGCTTCCCCGGGCCCTT	21	1836
1338752	N/A	N/A	84684	84703	AACAAGAACCACGACAGGGC	45	1837
1338810	N/A	N/A	26731	26750	TCCCAATGAAATACATGACA	42	1838

1338834	N/A	N/A	37039	37058	CCCTTCAACCCTCCTGTGGA	50	1839
1338912	N/A	N/A	91266	91285	GCCGAGCCCAGGAAATGCCT	12	1840
1339008	N/A	N/A	69033	69052	GAGTGTCCCAGAAAGTGCAC	27	1841
1339042	N/A	N/A	44039	44058	CAGTTGTCCCAGACTGGCCA	27	1842
1339049	N/A	N/A	19951	19970	GTCAGCATCCTGATTTCCCT	12	1843
1339050	N/A	N/A	17143	17162	ACAAGCTCCCTCATTGAATA	37	1844
1339069	N/A	N/A	67264	67283	AGGGACTTGCCAAGCAGTCC	59	1845
			67385	67404			
1339074	N/A	N/A	75843	75862	TGGGCTCTTACCCACATACT	15	1846
1339100	N/A	N/A	71469	71488	GAGTTTGGACCCCCTAGGTC	18	1847
1339127	N/A	N/A	55985	56004	TGTGGACTCACCAGTTGATC	15	1848
1339143	N/A	N/A	77981	78000	CGCAGACCCACCTGCCACCA	28	1849
1339174	N/A	N/A	20792	20811	GCCAGAGGCTCTACTCCCGG	45	1850
1339218	N/A	N/A	70327	70346	CCAACCCACATCACAGTGTC	53	1851
1339248	N/A	N/A	85682	85701	CCGAAATTCCAAATCCTCCT	30	1852
1339260	N/A	N/A	21809	21828	CGGCCACTCCCTTCCCAGGT	33	1853
1339307	N/A	N/A	47184	47203	GCAGAAGAATCTACTTCCTG	24	1854
1339326	N/A	N/A	42671	42690	AGAACCTGCACCCGAAGCCG	39	1855
1339348	N/A	N/A	32414	32433	AATTTCCCATCTTCAAGGCC	54	1856
1339349	N/A	N/A	34341	34360	GTAGAAGCCTCAACTAGTTT	53	1857
1339379	N/A	N/A	59644	59663	TCACACCCTTCACTTTGTCC	28	1858
1339416	N/A	N/A	65508	65527	CCAACCCCTCCACTTCCGAT	10	1859
1339418	N/A	N/A	18825	18844	CTGTATACTTCATTTCCAAC	14	1860
1339439	N/A	N/A	63552	63571	GGATGAGTCCTCATTTGCAA	19	1861
1339475	N/A	N/A	24115	24134	ACGGACCCTCCTCCATGCCC	17	1862
1339528	N/A	N/A	83278	83297	ATCTGTCCCACATGGACCCC	26	1863
1339591	N/A	N/A	27994	28013	CGAGCCCCCACAGCCATGGC	23	1864
1339600	2643	2662	80470	80489	ACAGAGCCCTCCATGTAGTA	42	1865
1339625	N/A	N/A	39479	39498	GTCTGATTCATCCTCATTTC	22	1866
1339641	N/A	N/A	57684	57703	GTTTCCCTATTTACTGAGCC	15	1867
1339668	N/A	N/A	93391	93410	GCCTTCATCTACACCTGCAC	22	1868

Table 25. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	18	283
1337294	3274	3293	88219	88238	CCGTGTGTCCTCACAGTCCT	12	1869
1337303	N/A	N/A	93390	93409	CCTTCATCTACACCTGCACA	27	1870
1337343	N/A	N/A	31240	31259	GCCTCCAGTCACTTCACCTC	25	1871

1337350	N/A	N/A	18293	18312	TTTGATCAACCACAGCCACA	52	1872
1337357	4616	4635	94995	95014	CTGAGAAGATCCTCTCTCTC	21	1873
1337401	N/A	N/A	80378	80397	CCCACCCTGCTTCAAGGCCT	42	1874
1337416	N/A	N/A	55175	55194	TGGACATCCATCTATCATCC	18	1875
1337424	N/A	N/A	67277	67296	GCTGAGAGGACTCAGGGACT	36	1876
			67398	67417			
1337491	N/A	N/A	63399	63418	CCTCACTCCCGCCCTTGCCT	25	1877
1337496	N/A	N/A	37702	37721	GGATCTGTCTCTATTTCTTC	30	1878
1337527	N/A	N/A	83270	83289	CACATGGACCCCAGCACCAT	98	1879
1337552	N/A	N/A	26730	26749	CCCAATGAAATACATGACAC	59	1880
1337563	N/A	N/A	92953	92972	CAGCCCCCCCATCATCTCAC	33	1881
1337590	N/A	N/A	89933	89952	CAGTTGCTCCTTCCTTGCCA	20	1882
1337633	N/A	N/A	35153	35172	GCTGCACTAACCCAGGACAA	30	1883
1337691	N/A	N/A	18770	18789	TGCCCTGTACCCCATGGGCC	93	1884
1337717	N/A	N/A	45876	45895	AAAGGGCACACACATGTCTC	38	1885
1337734	N/A	N/A	68022	68041	TGACAGTTCACTCCAGATGA	49	1886
1337761	N/A	N/A	61134	61153	CCAGATGCTATCCTCATGGA	15	1887
1337826	N/A	N/A	19945	19964	ATCCTGATTTCCCTCATTGT	27	1888
1337863	N/A	N/A	37024	37043	GTGGAGTGCCCCAGAACGGC	31	1889
1337895	N/A	N/A	58494	58513	CCCACGGAACCCCTCTCAGC	53	1890
1337911	N/A	N/A	57683	57702	TTTCCCTATTTACTGAGCCT	22	1891
1337930	N/A	N/A	78860	78879	TGGCTGGAACATCTCCGGTT	42	1892
1338025	N/A	N/A	21808	21827	GGCCACTCCCTTCCCAGGTG	47	1893
1338070	N/A	N/A	32413	32432	ATTTCCCATCTTCAAGGCCC	41	1894
1338083	1868	1887	72881	72900	TCTTGTTGTCCTCCCGCTTC	31	1895
1338113	N/A	N/A	85672	85691	AAATCCTCCTGATAATCCTC	59	1896
1338117	N/A	N/A	24087	24106	AGGTGATGCCCCACAAGACA	38	1897
1338173	N/A	N/A	68537	68556	CCAGACGATCCACCCCAGAT	54	1898
1338260	N/A	N/A	17802	17821	AGAATATTCCATTCCCCGCA	23	1899
1338329	N/A	N/A	29910	29929	CCCACTGCAACATCTTTCCC	47	1900
1338344	N/A	N/A	30788	30807	GTGAATCACCATAACCAGAC	19	1901
1338361	N/A	N/A	41166	41185	GAGCTCCTCAGCATGGGCCC	66	1902
			50777	50796			
1338363	N/A	N/A	91738	91757	GACTCCTCCACCCAGACCCT	54	1903
1338416	N/A	N/A	47179	47198	AGAATCTACTTCCTGTGTCC	20	1904
1338458	3872	3891	94251	94270	GAGTGTGCCATCCCCAGGGT	12	1905
1338511	N/A	N/A	70316	70335	CACAGTGTCCCCCACGGGCA	28	1906
1338587	N/A	N/A	34077	34096	GTGAGCTGAAATATCATGCC	51	1907
1338590	N/A	N/A	56663	56682	CTATCTAACCCACAGCCCCC	52	1908
1338595	N/A	N/A	91139	91158	GACGCAGGCATCCCACTCAT	34	1909
1338644	N/A	N/A	55890	55909	CCCTGGCCCCTCTAGCACCA	24	1910
1338737	N/A	N/A	17140	17159	AGCTCCCTCATTGAATAATT	43	1911
1338754	N/A	N/A	62165	62184	CCGGCTGTCCACCTTGACCC	30	1912

1338767	N/A	N/A	24939	24958	TTCCCACGACATCTTTTGCA	43	1913
1338796	N/A	N/A	40925	40944	CCATTGGGCACTTTTACTCA	50	1914
1338801	N/A	N/A	48375	48394	GGCACCCCAGAAACAAGAGC	38	1915
1338809	N/A	N/A	69019	69038	GTGCACCGACACATTCTGGA	18	1916
1338837	4344	4363	94723	94742	TTCCCCGGGCCCTTTGCTGC	26	1917
1338848	N/A	N/A	82333	82352	GTGTCACAATCCTGCAGCCA	39	1918
1338857	N/A	N/A	49769	49788	GACAAGCCTCCCACAGACCA	50	1919
1338892	N/A	N/A	23044	23063	TCCCCGACTCCTCCTCGAAC	64	1920
1338929	N/A	N/A	77801	77820	CCTCGGCCCAATCTGAACTT	58	1921
1338932*	360	379	52129	52148	TTGAGCCGCTCCTTGAAGGT	3	1922
1338980	N/A	N/A	40380	40399	CCTGCCCTACTCATCTCAGC	33	1923
1339014	N/A	N/A	84626	84645	TCAGGACCTTCCAGAGATTT	48	1924
1339144	N/A	N/A	19317	19336	CCTGTCCCATCCTATAGACA	47	1925
1339219	N/A	N/A	74567	74586	AGGAGCTTCAATCTATGCCT	25	1926
1339220	N/A	N/A	22432	22451	AGGGATGATTCTAGAAGGCC	48	1927
1339243	N/A	N/A	59608	59627	CCATTTCATTTCCAGGCTTA	24	1928
1339272	N/A	N/A	39473	39492	TTCATCCTCATTTCCCCCGC	42	1929
1339290	N/A	N/A	42660	42679	CCGAAGCCGTCACCTCCCTC	39	1930
1339334	N/A	N/A	76820	76839	GGGCTCACCCCTCACCTGGT	46	1931
1339341	N/A	N/A	48938	48957	GGCCAACCATCCCCCACCAA	83	1932
1339353	N/A	N/A	86362	86381	TCCCCAAGCACCACATGACC	47	1933
1339362	N/A	N/A	27337	27356	AATGGCCTCACCTTGAGATC	25	1934
1339371	N/A	N/A	20738	20757	TGCTCGCTCACAGCCTGCCA	23	1935
1339391	N/A	N/A	27910	27929	CCAGGTGGTTCCTCCTGCCA	35	1936
1339408	N/A	N/A	87383	87402	AGGCTTCTCCATGTGAAGCT	39	1937
1339419	N/A	N/A	45275	45294	ATTTGACCTACATCTTAGCT	77	1938
1339424	N/A	N/A	75841	75860	GGCTCTTACCCACATACTTG	34	1939
1339486	N/A	N/A	65507	65526	CAACCCCTCCACTTCCGATT	32	1940
1339517	N/A	N/A	53757	53776	GACATGACTCAGGACAGGCC	8	1941
1339554	N/A	N/A	71468	71487	AGTTTGGACCCCCTAGGTCC	36	1942
1339598	N/A	N/A	33277	33296	CTGAGATTCTAACGCGAGCC	32	1943
1339632	N/A	N/A	31804	31823	CCTGAGGCCACACGCAGACA	51	1944
1339662	N/A	N/A	44003	44022	AAGGTGGTTGCAACCTGCAC	46	1945

Table 26. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	26	283
1337240	N/A	N/A	53715	53734	TGCTGATGTCCCCTGGGACC	29	1946

1337309	N/A	N/A	83188	83207	GTCCCTGTCACACAACTGCC	36	1947
1337312	N/A	N/A	27908	27927	AGGTGGTTCCTCCTGCCAGA	34	1948
1337336	N/A	N/A	57563	57582	GAGTTTGTCCCCAGTGCTCA	31	1949
1337374	N/A	N/A	55823	55842	GGGCCTCCTACTCACCCACC	24	1950
1337382	N/A	N/A	37628	37647	GCCTAGGACCCCCTGACAGC	68	1951
1337402	N/A	N/A	89929	89948	TGCTCCTTCCTTGCCAAGCT	31	1952
1337407	N/A	N/A	40378	40397	TGCCCTACTCATCTCAGCGC	41	1953
1337458	N/A	N/A	27328	27347	ACCTTGAGATCCTCAACTAA	51	1954
1337459	N/A	N/A	63383	63402	GCCTGGTTATGAAATGCGCA	19	1955
1337503	N/A	N/A	33276	33295	TGAGATTCTAACGCGAGCCG	60	1956
1337508	N/A	N/A	93368	93387	CCTGCAGATTCACCTCTGTA	43	1957
1337585	N/A	N/A	29904	29923	GCAACATCTTTCCCTCACTC	52	1958
1337601	N/A	N/A	45839	45858	TGTTTTGACACCCTTGGGCC	43	1959
1337609	N/A	N/A	48919	48938	ACCTCAGGCTCCTGTACCCT	39	1960
1337692	N/A	N/A	61133	61152	CAGATGCTATCCTCATGGAT	36	1961
1337774	N/A	N/A	18746	18765	CTGGAGAGGACCCACAGCCA	40	1962
1337832	N/A	N/A	24050	24069	GCCCTGGTCACCGACAGCCT	21	1963
1337834	N/A	N/A	82315	82334	CACGCAGGTCCCAGCAGCTC	45	1964
1337841	N/A	N/A	68018	68037	AGTTCACTCCAGATGATCCA	24	1965
1337869	N/A	N/A	41154	41173	ATGGGCCCCCTGCCCAGTGC	27	1966
			50765	50784			
1337885	N/A	N/A	33884	33903	ACGGAGTCCCAGGAAAACAA	52	1967
1337906	N/A	N/A	69018	69037	TGCACCGACACATTCTGGAA	38	1968
1337920	N/A	N/A	58493	58512	CCACGGAACCCCTCTCAGCA	48	1969
1337960	N/A	N/A	68532	68551	CGATCCACCCCAGATGGTCC	28	1970
1337973	N/A	N/A	17130	17149	TTGAATAATTAATCAAGGAC	61	1971
1338047	N/A	N/A	56621	56640	CCTCATCCATAAACAGGCAG	35	1972
1338096	N/A	N/A	36883	36902	TCACCGCGCCATGACTGCAC	13	1973
1338106	N/A	N/A	79652	79671	AAGGAGAGTCCCCCTTTTTA	100	1974
1338203	N/A	N/A	91136	91155	GCAGGCATCCCACTCATGAA	42	1975
1338219	N/A	N/A	92949	92968	CCCCCCATCATCTCACAGTC	55	1976
1338255	N/A	N/A	49707	49726	AGAGTGCCCCATCATGCCCT	32	1977
1338337	N/A	N/A	35150	35169	GCACTAACCCAGGACAACAA	25	1978
1338354	N/A	N/A	86360	86379	CCCAAGCACCACATGACCCA	64	1979
1338370	N/A	N/A	19942	19961	CTGATTTCCCTCATTGTTGC	39	1980
1338373	N/A	N/A	74566	74585	GGAGCTTCAATCTATGCCTC	30	1981
1338389	N/A	N/A	59489	59508	TTCCCGGTCCTCTACAGGTC	28	1982
1338408	N/A	N/A	30787	30806	TGAATCACCATAACCAGACC	29	1983
1338417	N/A	N/A	23043	23062	CCCCGACTCCTCCTCGAACC	39	1984
1338448	N/A	N/A	45274	45293	TTTGACCTACATCTTAGCTG	47	1985
1338534	N/A	N/A	91731	91750	CCACCCAGACCCTCCGACCT	57	1986
1338545	N/A	N/A	84618	84637	TTCCAGAGATTTCCTCCTGC	56	1987
1338558	N/A	N/A	42658	42677	GAAGCCGTCACCTCCCTCCC	46	1988

1338565	N/A	N/A	70315	70334	ACAGTGTCCCCCACGGGCAT	41	1989
1338614	N/A	N/A	22422	22441	CTAGAAGGCCCTCAGCACAC	45	1990
1338665	N/A	N/A	31794	31813	CACGCAGACACCAAGGGCAC	27	1991
1338778	N/A	N/A	62164	62183	CGGCTGTCCACCTTGACCCT	24	1992
1338783	N/A	N/A	19316	19335	CTGTCCCATCCTATAGACAC	34	1993
1338791	N/A	N/A	47167	47186	CTGTGTCCATTCTCATCCAC	67	1994
1338794	N/A	N/A	43884	43903	CCTTCACTGACTATGTGCCT	45	1995
1338807	N/A	N/A	18267	18286	ATCGAGTCATCTGGGAGCCC	26	1996
1338841	N/A	N/A	87216	87235	GCACGGAACATGCTTAGGGC	7	1997
1338842	N/A	N/A	67275	67294	TGAGAGGACTCAGGGACTTG	38	1998
			67396	67415			
1338859	N/A	N/A	48252	48271	CCCACCTGCACAGATGGCAC	53	1999
1338891	3870	3889	94249	94268	GTGTGCCATCCCCAGGGTCA	25	2000
1338902	N/A	N/A	65501	65520	CTCCACTTCCGATTCTGTCC	38	2001
1338904	4614	4633	94993	95012	GAGAAGATCCTCTCTCTCCA	23	2002
1338926	N/A	N/A	26729	26748	CCAATGAAATACATGACACA	62	2003
1338975	N/A	N/A	32404	32423	CTTCAAGGCCCTCCACTTAA	46	2004
1338979	N/A	N/A	72850	72869	GCACACGCCATACCTGGGCA	42	2005
1338981	N/A	N/A	76819	76838	GGCTCACCCCTCACCTGGTC	60	2006
1339101	N/A	N/A	71458	71477	CCCTAGGTCCCTTCTCGGAT	38	2007
1339153	N/A	N/A	31239	31258	CCTCCAGTCACTTCACCTCT	57	2008
1339231	N/A	N/A	40922	40941	TTGGGCACTTTTACTCAAAA	35	2009
1339238	N/A	N/A	39472	39491	TCATCCTCATTTCCCCCGCA	32	2010
1339287	N/A	N/A	52004	52023	CCTGACTGACTTCTTCCAAC	58	2011
1339310	N/A	N/A	75840	75859	GCTCTTACCCACATACTTGT	34	2012
1339316	N/A	N/A	24938	24957	TCCCACGACATCTTTTGCAG	37	2013
1339327	N/A	N/A	78802	78821	TCAGAAGCACCCAGAAGCCG	82	2014
1339382	N/A	N/A	17773	17792	GTTTTAAGACCCCCTTTTTA	70	2015
1339389	N/A	N/A	77775	77794	TGGATCAGACACCCATGCCG	77	2016
1339483	N/A	N/A	21698	21717	GGACGAAGCTTCCTCTTGCC	49	2017
1339513	N/A	N/A	55174	55193	GGACATCCATCTATCATCCA	23	2018
1339581	3271	3290	88216	88235	TGTGTCCTCACAGTCCTCCA	19	2019
1339596	N/A	N/A	85663	85682	TGATAATCCTCTCCTCCCCC	54	2020
1339646	4343	4362	94722	94741	TCCCCGGGCCCTTTGCTGCT	40	2021
1339650	N/A	N/A	20703	20722	ACCCGCTTCCCTCACAGAGC	55	2022

Table 27. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.

1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	16	283
1337216	N/A	N/A	67267	67286	CTCAGGGACTTGCCAAGCAG	57	2023
			67388	67407			
1337218	N/A	N/A	18722	18741	CTAGCTAGCACACACAGCCA	61	2024
1337231	N/A	N/A	91728	91747	CCCAGACCCTCCGACCTTTA	50	2025
1337235	N/A	N/A	87155	87174	GGGCTGCCCGTATTCTTCCT	23	2026
1337236	N/A	N/A	27907	27926	GGTGGTTCCTCCTGCCAGAC	37	2027
1337238	N/A	N/A	67994	68013	GTATGGTCCACCTAAATGGT	40	2028
1337249	4581	4600	94960	94979	GGAGGCTGAATTGTGCTTCA	38	2029
1337308	N/A	N/A	35144	35163	ACCCAGGACAACAAACAAGC	41	2030
1337321	N/A	N/A	74565	74584	GAGCTTCAATCTATGCCTCA	54	2031
1337352	N/A	N/A	49632	49651	ACGCCTCTCCTCTGTGTGCC	45	2032
1337369	N/A	N/A	40377	40396	GCCCTACTCATCTCAGCGCG	43	2033
1337379	N/A	N/A	88001	88020	CCTCTGGAAAGAATGTGCCT	23	2034
1337490	N/A	N/A	78747	78766	GGTCCGAGCATCAGAATCAA	42	2035
1337566	N/A	N/A	61131	61150	GATGCTATCCTCATGGATGC	13	2036
1337579	N/A	N/A	22415	22434	GCCCTCAGCACACCGAGTCA	46	2037
1337666	N/A	N/A	89853	89872	GGCGGGATCATCCTCTGCCA	57	2038
1337716	N/A	N/A	53654	53673	AGAGTAGGTCCCAGCAGCCG	36	2039
1337755	N/A	N/A	47166	47185	TGTGTCCATTCTCATCCACT	37	2040
1337765	3857	3876	94236	94255	AGGGTCACGCTAGTGCCACC	27	2041
1337868	N/A	N/A	18251	18270	GCCCCAGGCACCATTAGGCG	34	2042
1337872	N/A	N/A	69017	69036	GCACCGACACATTCTGGAAA	34	2043
1337876	N/A	N/A	45273	45292	TTGACCTACATCTTAGCTGA	48	2044
1337912	N/A	N/A	48167	48186	GCCAGAGACATTAATGAAGC	38	2045
1337948	N/A	N/A	48887	48906	ACCAGAGCCATCAGCAGGTC	46	2046
1337949	4342	4361	94721	94740	CCCCGGGCCCTTTGCTGCTT	36	2047
1337983	N/A	N/A	33252	33271	GAAAGACCCATCCCCAGAGA	79	2048
1337995	N/A	N/A	43860	43879	TGGACCAGCTCCTCCTCAAA	43	2049
1338011	N/A	N/A	82160	82179	GTGCTGTCCCAGCTTGAGCA	56	2050
1338013	N/A	N/A	65493	65512	CCGATTCTGTCCTCCAGGGC	10	2051
1338052	N/A	N/A	16942	16961	TCTGGAAGACTCCGCAGCTC	27	2052
1338081	N/A	N/A	23040	23059	CGACTCCTCCTCGAACCTTC	31	2053
1338093	N/A	N/A	71422	71441	TCTGCCGTCCCCTCCAGCAC	27	2054
1338128	N/A	N/A	83187	83206	TCCCTGTCACACAACTGCCA	37	2055
1338170	N/A	N/A	19314	19333	GTCCCATCCTATAGACACCA	20	2056
1338184	N/A	N/A	24937	24956	CCCACGACATCTTTTGCAGC	21	2057
1338187	N/A	N/A	92948	92967	CCCCCATCATCTCACAGTCT	30	2058
1338191	N/A	N/A	40884	40903	CCTGACCCCACCACTGAAGC	61	2059
1338194	N/A	N/A	76797	76816	CCCAGGACCCCCCCATGGTC	65	2060
1338214	N/A	N/A	50742	50761	GCGAGGGCCACAACACAGTA	59	2061
1338216	N/A	N/A	45838	45857	GTTTTGACACCCTTGGGCCT	55	2062
1338244	N/A	N/A	57534	57553	GGTCCCCTACTTACTAAGCC	59	2063

1338277	N/A	N/A	33859	33878	AGGATGCATTCCATCCAGAT	33	2064
1338330	N/A	N/A	93366	93385	TGCAGATTCACCTCTGTATT	31	2065
1338406	N/A	N/A	24041	24060	ACCGACAGCCTCTGTGGCCC	34	2066
1338423	N/A	N/A	26721	26740	ATACATGACACACCTGGTGA	50	2067
1338469	N/A	N/A	17767	17786	AGACCCCCTTTTTACAAATC	58	2068
1338482	N/A	N/A	52001	52020	GACTGACTTCTTCCAACTTT	90	2069
1338484	N/A	N/A	91133	91152	GGCATCCCACTCATGAAGGC	21	2070
1338529	N/A	N/A	72827	72846	GCACCGGCAACTTCAGGTAC	73	2071
1338596	N/A	N/A	42630	42649	GTCTCAGCCCTGCTTAGGGC	26	2072
1338720	N/A	N/A	63303	63322	ACCCCACCCCACATGGTGGT	69	2073
1338768	N/A	N/A	37580	37599	CCCAAACTCACACCAGAAGC	64	2074
1338829	N/A	N/A	56516	56535	ACAGGTCTTAATCTCTGGAC	25	2075
1338880	N/A	N/A	32401	32420	CAAGGCCCTCCACTTAATCA	55	2076
1338930	N/A	N/A	77774	77793	GGATCAGACACCCATGCCGG	34	2077
1338933	N/A	N/A	75839	75858	CTCTTACCCACATACTTGTC	50	2078
1338991	N/A	N/A	36776	36795	GCGGCTCGCTCACATTCCCT	16	2079
1338995	N/A	N/A	21697	21716	GACGAAGCTTCCTCTTGCCT	29	2080
1339025	N/A	N/A	30782	30801	CACCATAACCAGACCCGGCA	28	2081
1339032	N/A	N/A	85537	85556	GCAATGGACCCACTGAGTTT	55	2082
1339116	N/A	N/A	68493	68512	GGATGGCCCACCCCAGACAA	28	2083
1339146	N/A	N/A	84616	84635	CCAGAGATTTCCTCCTGCTT	41	2084
1339254	N/A	N/A	59438	59457	GCACAGTGTCTTCCAGGGCC	19	2085
1339259	N/A	N/A	29902	29921	AACATCTTTCCCTCACTCGC	38	2086
1339276	N/A	N/A	31238	31257	CTCCAGTCACTTCACCTCTT	66	2087
1339313	N/A	N/A	31775	31794	CGTGCAACATTTTCAAGCCT	27	2088
1339315	N/A	N/A	55799	55818	GCTAACCCCCACATCAGAGC	13	2089
1339337	N/A	N/A	20702	20721	CCCGCTTCCCTCACAGAGCC	34	2090
1339384	N/A	N/A	79649	79668	GAGAGTCCCCCTTTTTAGGA	54	2091
1339435	N/A	N/A	86354	86373	CACCACATGACCCACAGGCA	35	2092
1339438	N/A	N/A	70303	70322	ACGGGCATCCTTGTGTGCCC	75	2093
1339441	N/A	N/A	58492	58511	CACGGAACCCCTCTCAGCAC	55	2094
1339442	N/A	N/A	27326	27345	CTTGAGATCCTCAACTAATC	65	2095
1339493	N/A	N/A	62162	62181	GCTGTCCACCTTGACCCTTC	17	2096
1339536	N/A	N/A	19931	19950	CATTGTTGCCCACCCATTCC	64	2097
1339539	N/A	N/A	54967	54986	ACCATCTGCTCATCATCCAT	37	2098
1339631	N/A	N/A	39470	39489	ATCCTCATTTCCCCCGCAGC	61	2099

Table 28. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	19	283
1337230	N/A	N/A	54962	54981	CTGCTCATCATCCATCCACT	20	2100
1337282	3855	3874	94234	94253	GGTCACGCTAGTGCCACCGT	16	2101
1337399	4575	4594	94954	94973	TGAATTGTGCTTCACAAGTC	16	2102
1337419	N/A	N/A	83141	83160	CCAGGACTGTTCACTGCTCT	53	2103
1337435	N/A	N/A	31774	31793	GTGCAACATTTTCAAGCCTC	31	2104
1337450	N/A	N/A	17765	17784	ACCCCCTTTTTACAAATCTT	67	2105
1337456	N/A	N/A	78743	78762	CGAGCATCAGAATCAATAAC	32	2106
1337477	N/A	N/A	23912	23931	CGGGAGCCACAGTCTCCACA	32	2107
1337498	N/A	N/A	48849	48868	GATGTTTCTTCCCTCTGACC	62	2108
1337525	N/A	N/A	58491	58510	ACGGAACCCCTCTCAGCACA	43	2109
1337532	N/A	N/A	79502	79521	AGGAGCCTCACTTGTTGTCC	48	2110
1337569	N/A	N/A	33858	33877	GGATGCATTCCATCCAGATA	55	2111
1337623	N/A	N/A	23035	23054	CCTCCTCGAACCTTCACGGC	35	2112
1337628	N/A	N/A	27855	27874	TTTTCCGGCATTTCTGCTTT	41	2113
1337637	N/A	N/A	86322	86341	GCCTTTTCTAAGAAAACTCC	13	2114
1337645	N/A	N/A	62155	62174	ACCTTGACCCTTCCCTGCAC	49	2115
1337656	N/A	N/A	27323	27342	GAGATCCTCAACTAATCACA	42	2116
1337660	N/A	N/A	18250	18269	CCCCAGGCACCATTAGGCGG	17	2117
1337672	N/A	N/A	75838	75857	TCTTACCCACATACTTGTCC	59	2118
1337675	N/A	N/A	21695	21714	CGAAGCTTCCTCTTGCCTGC	48	2119
1337736	N/A	N/A	91724	91743	GACCCTCCGACCTTTACTCC	38	2120
1337782	N/A	N/A	22319	22338	GCAGGGCTGTTCCTAGAGAC	49	2121
1337799	N/A	N/A	70294	70313	CTTGTGTGCCCTCCACCAGC	61	2122
1337810	N/A	N/A	35080	35099	GGCAGGTCAGCATCACAGAC	47	2123
1337822	N/A	N/A	32400	32419	AAGGCCCTCCACTTAATCAT	43	2124
1337828	N/A	N/A	84414	84433	GAGGAGAGATCACACAGGCT	19	2125
1337847	N/A	N/A	24885	24904	CTGAATTGCACCCCCAGATT	34	2126
1337870	N/A	N/A	63256	63275	GAGGCGAGCTTTACACTTTT	7	2127
1337883	N/A	N/A	61120	61139	CATGGATGCCCCAATCTGCC	21	2128
1337901	N/A	N/A	40883	40902	CTGACCCCACCACTGAAGCC	50	2129
1337926	N/A	N/A	89852	89871	GCGGGATCATCCTCTGCCAG	33	2130
1337939	N/A	N/A	42514	42533	GGGCCATCCCCACTTGACTT	49	2131
1337941	N/A	N/A	82116	82135	GTCAGCCAGATATCAAGGCA	35	2132
1337944	N/A	N/A	51997	52016	GACTTCTTCCAACTTTCCAA	38	2133
1337987	N/A	N/A	20637	20656	GCTGAGCCCCCACATTGCAC	47	2134
1338032	N/A	N/A	48166	48185	CCAGAGACATTAATGAAGCC	52	2135
1338126	N/A	N/A	71273	71292	CCAGACGCACCATCACCCAA	36	2136
1338166	4341	4360	94720	94739	CCCGGGCCCTTTGCTGCTTC	30	2137

1338174	N/A	N/A	26605	26624	TCTGACAGTCATATTTAACC	42	2138
1338227	N/A	N/A	40376	40395	CCCTACTCATCTCAGCGCGA	40	2139
1338247	N/A	N/A	29901	29920	ACATCTTTCCCTCACTCGCC	35	2140
1338262	N/A	N/A	53642	53661	AGCAGCCGCCACTTCTCGAA	35	2141
1338404	N/A	N/A	33203	33222	GAGTGTGGAAAATCTAGTTT	34	2142
1338405	N/A	N/A	76773	76792	CTCGGCATAACACATGGCCC	39	2143
1338441	N/A	N/A	74546	74565	AGTTTCCCCCTCCATACAAC	38	2144
1338457	N/A	N/A	49556	49575	CCGCCGTCTTTCTCTCTGAA	56	2145
1338509	N/A	N/A	50599	50618	TAAGCACCAGCCTAACCCCT	43	2146
1338531	N/A	N/A	19930	19949	ATTGTTGCCCACCCATTCCA	60	2147
1338594	N/A	N/A	91102	91121	GGTCCGAGCACCACAGTGCC	43	2148
1338598	N/A	N/A	36772	36791	CTCGCTCACATTCCCTGGGA	33	2149
1338600	N/A	N/A	92916	92935	CAGGGTAGCCCTGCCAAGCA	35	2150
1338605	N/A	N/A	16882	16901	AGATGCTTCCCCCTGCCCGC	31	2151
1338617	N/A	N/A	56498	56517	ACCAGGCACCCCAGTTGCCC	35	2152
1338630	N/A	N/A	65410	65429	GGATACTTCCAGGAGACCCA	9	2153
1338633	N/A	N/A	59373	59392	CCCCGGCTTACAATCATGTT	70	2154
1338785	N/A	N/A	55798	55817	CTAACCCCCACATCAGAGCT	19	2155
1338919	N/A	N/A	43834	43853	CAGAGGGACCTCTCTCTTTT	53	2156
1339000	N/A	N/A	68995	69014	TCCAGGTAATAATATACTCT	13	2157
1339041	N/A	N/A	87983	88002	CTGGTTTCCTCCTGAGCACA	11	2158
1339062	N/A	N/A	68444	68463	CCCTGATGATCTACCCCAGA	61	2159
1339064	N/A	N/A	31171	31190	AGACGCAGCCCACTCGGATA	48	2160
1339092	1126	1145	67047	67066	CTGCCGCTCCATCCAGAGGT	15	2161
1339123	N/A	N/A	30774	30793	CCAGACCCGGCAAAACACTC	32	2162
1339152	N/A	N/A	19239	19258	GAGCCAGGTCCCCTTCCCTC	8	2163
			19285	19304			
1339185	N/A	N/A	37579	37598	CCAAACTCACACCAGAAGCC	53	2164
1339247	N/A	N/A	67992	68011	ATGGTCCACCTAAATGGTCC	15	2165
1339261	N/A	N/A	72769	72788	TCCTGCAAATCACCAGAGTC	36	2166
1339286	N/A	N/A	39468	39487	CCTCATTTCCCCCGCAGCAT	18	2167
1339304	N/A	N/A	85511	85530	GCTCCCGTAACAAATGACCG	39	2168
1339344	N/A	N/A	45813	45832	GCCCCCCCATAGCTTGGCCA	53	2169
1339401	N/A	N/A	57485	57504	GGGTCCCTGTTTACTGATCC	8	2170
1339402	N/A	N/A	77771	77790	TCAGACACCCATGCCGGGCC	38	2171
1339409	N/A	N/A	87154	87173	GGCTGCCCGTATTCTTCCTG	9	2172
1339512	N/A	N/A	45197	45216	CCGAGAGCGCATCCCAGCTC	37	2173
1339514	N/A	N/A	93365	93384	GCAGATTCACCTCTGTATTC	20	2174
1339520	N/A	N/A	18696	18715	TCCAGCGGTCCACCTCCTAA	28	2175
1339532	N/A	N/A	47165	47184	GTGTCCATTCTCATCCACTC	14	2176

Table 29. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	21	283
1081135	N/A	N/A	87153	87172	GCTGCCCGTATTCTTCCTGA	11	174
1337221	N/A	N/A	74540	74559	CCCCTCCATACAACAGGGAC	20	2177
1337286	N/A	N/A	43832	43851	GAGGGACCTCTCTCTTTTAA	31	2178
1337375	N/A	N/A	26604	26623	CTGACAGTCATATTTAACCA	18	2179
1337380	N/A	N/A	49350	49369	GCTTAGGAACCCACCCTCCC	42	2180
1337432	N/A	N/A	82115	82134	TCAGCCAGATATCAAGGCAA	22	2181
1337433	N/A	N/A	50597	50616	AGCACCAGCCTAACCCCTGT	33	2182
1337481	N/A	N/A	87975	87994	CTCCTGAGCACAGATCGCCG	18	2183
1337541	N/A	N/A	84309	84328	GGAGAGACTCCTCTCACACA	29	2184
1337599	N/A	N/A	45703	45722	ACGGCGGCACACACTATAGC	57	2185
1337664	N/A	N/A	40882	40901	TGACCCCACCACTGAAGCCA	40	2186
1337706	N/A	N/A	27835	27854	CCAGCATATATTCAATCAAC	15	2187
1337715	N/A	N/A	27322	27341	AGATCCTCAACTAATCACAT	14	2188
1337721	N/A	N/A	48848	48867	ATGTTTCTTCCCTCTGACCT	39	2189
1337783	N/A	N/A	47164	47183	TGTCCATTCTCATCCACTCA	10	2190
1337802	N/A	N/A	76772	76791	TCGGCATAACACATGGCCCC	43	2191
1337892	N/A	N/A	37541	37560	TGTTCCCCCACCCTGAATCC	52	2192
1337918	N/A	N/A	91723	91742	ACCCTCCGACCTTTACTCCA	28	2193
1337940	3851	3870	94230	94249	ACGCTAGTGCCACCGTGTCC	8	2194
1337954	N/A	N/A	17764	17783	CCCCCTTTTTACAAATCTTC	20	2195
1337968	N/A	N/A	75837	75856	CTTACCCACATACTTGTCCA	59	2196
1337972	N/A	N/A	68982	69001	ATACTCTTGTTACCTTGTCA	9	2197
1338045	N/A	N/A	36771	36790	TCGCTCACATTCCCTGGGAA	8	2198
1338058	N/A	N/A	42499	42518	GACTTGTGCCCATAAGGAGC	38	2199
1338111	N/A	N/A	33073	33092	GACAATGATTCAAACATGGC	20	2200
1338157	N/A	N/A	57435	57454	GGTCAGTAAATGCTGGGTTT	46	2201
			57977	57996			
1338190	N/A	N/A	63255	63274	AGGCGAGCTTTACACTTTTA	5	2202
1338234	N/A	N/A	18233	18252	CGGATGGACACCACTTCCTG	34	2203
1338286	N/A	N/A	70290	70309	TGTGCCCTCCACCAGCAGGC	19	2204
1338306	N/A	N/A	72768	72787	CCTGCAAATCACCAGAGTCC	16	2205
1338309	N/A	N/A	22308	22327	CCTAGAGACATCCCCACCGC	41	2206
1338345	N/A	N/A	71272	71291	CAGACGCACCATCACCCAAC	25	2207
1338346	N/A	N/A	21649	21668	CTTCCTGGCACCTCTCATGT	58	2208
1338385	N/A	N/A	78741	78760	AGCATCAGAATCAATAACGA	29	2209
1338386	N/A	N/A	45196	45215	CGAGAGCGCATCCCAGCTCC	28	2210
1338510	N/A	N/A	53583	53602	AGCAAGTTCCCACCCACCCT	11	2211

1338526	N/A	N/A	86315	86334	CTAAGAAAACTCCCTTGCCA	41	2212
1338570	N/A	N/A	19226	19245	TTCCCTCTCATCCTATAGAC	27	2213
			19272	19291			
1338597	N/A	N/A	66872	66891	GGGCCTTTCCCACATGGAAA	20	2214
1338620	N/A	N/A	19929	19948	TTGTTGCCCACCCATTCCAG	26	2215
1338652	N/A	N/A	55797	55816	TAACCCCCACATCAGAGCTC	12	2216
1338669	4574	4593	94953	94972	GAATTGTGCTTCACAAGTCA	17	2217
1338693	4334	4353	94713	94732	CCTTTGCTGCTTCTAACTTC	12	2218
1338715	N/A	N/A	93364	93383	CAGATTCACCTCTGTATTCC	16	2219
1338770	N/A	N/A	39360	39379	TGCTGTGTCCCACCCTGAGC	23	2220
1338821	N/A	N/A	51951	51970	AGCAGGACCACTCCCTCCAC	49	2221
1338850	N/A	N/A	89851	89870	CGGGATCATCCTCTGCCAGC	12	2222
1338875	N/A	N/A	92886	92905	GAGGCCACCATCCCAGCAGT	46	2223
1338925	N/A	N/A	58477	58496	AGCACAGGCATCTACTGACC	11	2224
1338947	N/A	N/A	33857	33876	GATGCATTCCATCCAGATAT	23	2225
1338994	N/A	N/A	54492	54511	GGGATGTGAAACCAGAAGCC	5	2226
1339068	N/A	N/A	62100	62119	ACTGGAGACCCACCATCTCC	14	2227
1339071	N/A	N/A	35078	35097	CAGGTCAGCATCACAGACCT	47	2228
1339122	N/A	N/A	20636	20655	CTGAGCCCCCACATTGCACC	42	2229
1339132	N/A	N/A	65402	65421	CCAGGAGACCCAGCCGGCGC	29	2230
1339176	N/A	N/A	30772	30791	AGACCCGGCAAAACACTCCT	27	2231
1339183	N/A	N/A	91101	91120	GTCCGAGCACCACAGTGCCC	24	2232
1339188	246	265	16638	16657	AAGGGCAGCACCTCGGAGTC	9	2233
1339255	N/A	N/A	61118	61137	TGGATGCCCCAATCTGCCCA	10	2234
1339279	N/A	N/A	68440	68459	GATGATCTACCCCAGAGGAC	35	2235
1339293	N/A	N/A	56480	56499	CCCGCAGTCACCTCCCACTG	21	2236
1339333	N/A	N/A	67983	68002	CTAAATGGTCCATCCCAGAA	49	2237
			68122	68141			
1339359	N/A	N/A	77748	77767	GTCCCTGTCCTAATGAGCTG	15	2238
1339428	N/A	N/A	18695	18714	CCAGCGGTCCACCTCCTAAT	20	2239
1339433	N/A	N/A	23034	23053	CTCCTCGAACCTTCACGGCC	18	2240
1339462	N/A	N/A	85508	85527	CCCGTAACAAATGACCGCAA	18	2241
1339534	N/A	N/A	29900	29919	CATCTTTCCCTCACTCGCCT	21	2242
1339542	N/A	N/A	31764	31783	TTCAAGCCTCGATCAAGTAA	39	2243
1339547	N/A	N/A	48121	48140	CTGTGGCCGCCCACTTCTCC	20	2244
1339561	N/A	N/A	24881	24900	ATTGCACCCCCAGATTCCCT	26	2245
1339584	N/A	N/A	31170	31189	GACGCAGCCCACTCGGATAA	43	2246
1339590	N/A	N/A	59372	59391	CCCGGCTTACAATCATGTTT	49	2247
1339612	2552	2571	79466	79485	GGTTCAGCTCCTTGCGGGAT	5	2248
1339637	N/A	N/A	82970	82989	GCTTGCTGACCCAAACTTCA	26	2249
1339640	N/A	N/A	32399	32418	AGGCCCTCCACTTAATCATA	43	2250
1339651	N/A	N/A	40308	40327	GGCAGCAGCTCCATTACCTC	36	2251
1339657	N/A	N/A	23907	23926	GCCACAGTCTCCACAGCAGA	50	2252

Table 30. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	22	283
1337225	N/A	N/A	23025	23044	CCTTCACGGCCCCTAAACCA	71	2253
1337252	N/A	N/A	91074	91093	CGAGGGTCTTCCATGAGCGC	21	2254
1337257	N/A	N/A	29891	29910	CTCACTCGCCTTTTTAGAGC	56	2255
1337260	N/A	N/A	22307	22326	CTAGAGACATCCCCACCGCA	80	2256
1337265	2551	2570	79465	79484	GTTCAGCTCCTTGCGGGATC	18	2257
1337296	N/A	N/A	37528	37547	TGAATCCCCCCACCCTTGGC	70	2258
1337389	N/A	N/A	45047	45066	GCTGCGGACCACCCACCTCT	81	2259
1337415	N/A	N/A	27295	27314	GACCGTGTTTCTACATAAGC	40	2260
1337497	N/A	N/A	74473	74492	CCAGTGCCCCATCGGTGCCA	43	2261
1337572	N/A	N/A	57286	57305	TTCTTAGCATTTACTGAGAC	52	2262
1337613	N/A	N/A	48115	48134	CCGCCCACTTCTCCGAGCAC	54	2263
1337627	3849	3868	94228	94247	GCTAGTGCCACCGTGTCCTC	17	2264
1337650	N/A	N/A	54491	54510	GGATGTGAAACCAGAAGCCC	31	2265
1337830	N/A	N/A	20635	20654	TGAGCCCCCACATTGCACCT	27	2266
1337858	N/A	N/A	75833	75852	CCCACATACTTGTCCAGCCA	37	2267
1337861	N/A	N/A	61117	61136	GGATGCCCCAATCTGCCCAC	28	2268
1337867	762	781	59310	59329	ATGAACAGGTTCCGCAGCGG	18	2269
1337889	N/A	N/A	32397	32416	GCCCTCCACTTAATCATATC	59	2270
1337891	N/A	N/A	14709	14728	CTGTTGTGTTGGCTGAGGGC	91	2271
			14747	14766			
1337904	N/A	N/A	27834	27853	CAGCATATATTCAATCAACT	39	2272
1337963	N/A	N/A	62099	62118	CTGGAGACCCACCATCTCCC	37	2273
1337970	N/A	N/A	63252	63271	CGAGCTTTACACTTTTAGAA	12	2274
1338001	N/A	N/A	24860	24879	GTTGAAGCCCCCACCGCTGA	79	2275
1338006	N/A	N/A	86311	86330	GAAAACTCCCTTGCCAGGCA	38	2276
1338016	N/A	N/A	40866	40885	GCCACGCTGTCTAATCAGCT	25	2277
1338034	N/A	N/A	77665	77684	GTGGCTCCAACCTGTTCTCA	41	2278
1338102	N/A	N/A	55796	55815	AACCCCCACATCAGAGCTCT	40	2279
1338156	N/A	N/A	67982	68001	TAAATGGTCCATCCCAGAAG	79	2280
			68121	68140			
1338186	N/A	N/A	76764	76783	ACACATGGCCCCATACAGGC	51	2281
1338258	N/A	N/A	51950	51969	GCAGGACCACTCCCTCCACC	62	2282
1338273	N/A	N/A	72767	72786	CTGCAAATCACCAGAGTCCC	51	2283
1338319	4333	4352	94712	94731	CTTTGCTGCTTCTAACTTCC	16	2284

1338394	N/A	N/A	17763	17782	CCCCTTTTTACAAATCTTCA	23	2285
1338436	N/A	N/A	18694	18713	CAGCGGTCCACCTCCTAATA	65	2286
1338494	N/A	N/A	19225	19244	TCCCTCTCATCCTATAGACA	42	2287
			19271	19290			
1338501	N/A	N/A	82966	82985	GCTGACCCAAACTTCAAGCC	35	2288
1338524	N/A	N/A	33854	33873	GCATTCCATCCAGATATGGC	17	2289
1338532	N/A	N/A	92794	92813	CTGGATTCCTGTTCCAGGAC	74	2290
1338547	N/A	N/A	30767	30786	CGGCAAAACACTCCTGGATT	70	2291
1338569	N/A	N/A	18230	18249	ATGGACACCACTTCCTGCCC	50	2292
1338585	N/A	N/A	39359	39378	GCTGTGTCCCACCCTGAGCT	41	2293
1338602	N/A	N/A	43830	43849	GGGACCTCTCTCTTTTAATC	58	2294
1338628	N/A	N/A	21648	21667	TTCCTGGCACCTCTCATGTC	89	2295
1338661	N/A	N/A	84308	84327	GAGAGACTCCTCTCACACAC	41	2296
1338712	N/A	N/A	42485	42504	AGGAGCAGTCTCAGCTGCCA	76	2297
1338738	N/A	N/A	23768	23787	GGCAACACAGGCAAACCGAC	37	2298
1338782	N/A	N/A	26547	26566	CAGCAGACACTCAACTTGAC	66	2299
1338820	N/A	N/A	36770	36789	CGCTCACATTCCCTGGGAAC	41	2300
1338888	4553	4572	94932	94951	GGGTTTAGAAAATGAGGCTT	24	2301
1338894	N/A	N/A	87152	87171	CTGCCCGTATTCTTCCTGAA	19	2302
1338921	N/A	N/A	40307	40326	GCAGCAGCTCCATTACCTCT	51	2303
1338928	N/A	N/A	82102	82121	AAGGCAACAGCAACAGTGCC	41	2304
1338958	N/A	N/A	31747	31766	TAAGCTCTGTCCAGCAGGCC	27	2305
1338962	N/A	N/A	19927	19946	GTTGCCCACCCATTCCAGCA	27	2306
1338974	N/A	N/A	65338	65357	ATCACTCTGCTTCAAGGGCT	23	2307
1338985	N/A	N/A	58476	58495	GCACAGGCATCTACTGACCC	26	2308
1339002	N/A	N/A	93354	93373	TCTGTATTCCACACACATTT	29	2309
1339020	N/A	N/A	91722	91741	CCCTCCGACCTTTACTCCAG	30	2310
1339113	N/A	N/A	48805	48824	CTGGCCACTCCTCCTAGGCG	46	2311
1339140	N/A	N/A	70224	70243	CCCGCAGGCATCCTGGGCCT	55	2312
1339148	N/A	N/A	50595	50614	CACCAGCCTAACCCCTGTTC	65	2313
1339154	N/A	N/A	49317	49336	CTGTCCCGCCCTCCATGGCA	41	2314
1339175	N/A	N/A	71271	71290	AGACGCACCATCACCCAACA	48	2315
1339195	N/A	N/A	68966	68985	GTCACTCTGTCAATTTGTCT	5	2316
1339241	N/A	N/A	89763	89782	CGTGAAGTCCCTCCCGGGAC	25	2317
1339256	N/A	N/A	33038	33057	TGCTGTGGTTACAAATGACC	61	2318
1339282	N/A	N/A	53582	53601	GCAAGTTCCCACCCACCCTC	32	2319
1339299	N/A	N/A	56479	56498	CCGCAGTCACCTCCCACTGC	32	2320
1339302	N/A	N/A	68439	68458	ATGATCTACCCCAGAGGACC	51	2321
1339303	N/A	N/A	85496	85515	GACCGCAAACTTAGCAGCTA	55	2322
1339335	N/A	N/A	87908	87927	GAGGGCAGCTCCCTTCGCCT	16	2323
1339350	N/A	N/A	35077	35096	AGGTCAGCATCACAGACCTC	70	2324
1339550	N/A	N/A	45702	45721	CGGCGGCACACACTATAGCC	60	2325
1339570	N/A	N/A	78737	78756	TCAGAATCAATAACGATCTG	43	2326

1339643	N/A	N/A	66663	66682	CTTCCAGGCACTCGCAGGCC	6	2327
1339654	N/A	N/A	47163	47182	GTCCATTCTCATCCACTCAT	48	2328
1339667	N/A	N/A	31156	31175	GGATAATCGCCCTTTGATTA	40	2329

Table 31. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080740	760	779	59308	59327	GAACAGGTTCCGCAGCGGCG	16	108
1080818	2550	2569	79464	79483	TTCAGCTCCTTGCGGGATCT	15	199
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	24	283
1337292	N/A	N/A	27293	27312	CCGTGTTTCTACATAAGCCA	30	2330
1337355	N/A	N/A	85488	85507	ACTTAGCAGCTAAAACGACA	39	2331
1337395	N/A	N/A	18228	18247	GGACACCACTTCCTGCCCAA	24	2332
1337396	N/A	N/A	22306	22325	TAGAGACATCCCCACCGCAA	72	2333
1337405	N/A	N/A	55795	55814	ACCCCCACATCAGAGCTCTA	30	2334
1337448	N/A	N/A	77630	77649	CAGGTGCCTCTAACATAGAC	66	2335
1337460	N/A	N/A	87862	87881	GGCCTGGGACCCATCTGGAC	17	2336
1337471	N/A	N/A	27833	27852	AGCATATATTCAATCAACTT	71	2337
1337475	N/A	N/A	35075	35094	GTCAGCATCACAGACCTCCT	59	2338
1337514	N/A	N/A	67981	68000	AAATGGTCCATCCCAGAAGG	41	2339
			68120	68139			
1337518	N/A	N/A	57207	57226	CCTCAGTGCTTACTGAGCAC	17	2340
1337571	N/A	N/A	92789	92808	TTCCTGTTCCAGGACTCCAA	30	2341
1337657	4540	4559	94919	94938	GAGGCTTTGCTTTAAAAGGT	16	2342
1337769	N/A	N/A	40865	40884	CCACGCTGTCTAATCAGCTC	36	2343
1337773	N/A	N/A	43829	43848	GGACCTCTCTCTTTTAATCC	55	2344
1337792	N/A	N/A	29888	29907	ACTCGCCTTTTTAGAGCCCT	19	2345
1337835	N/A	N/A	42403	42422	GTGGAGTGTCCCTCTGCACC	36	2346
1337879	N/A	N/A	66524	66543	CAGATCCAAAACAGAGGCCA	48	2347
1337887	N/A	N/A	90968	90987	GGCATTGTGGCAAACAGGTC	21	2348
1337894	N/A	N/A	31729	31748	CCTGCAGACCCAACTTCCAC	43	2349
1337938	N/A	N/A	53575	53594	CCCACCCACCCTCATCGCGG	46	2350
1337982	N/A	N/A	65337	65356	TCACTCTGCTTCAAGGGCTT	15	2351
1338074	N/A	N/A	84307	84326	AGAGACTCCTCTCACACACC	38	2352
1338080	N/A	N/A	82964	82983	TGACCCAAACTTCAAGCCAC	61	2353
1338112	N/A	N/A	23024	23043	CTTCACGGCCCCTAAACCAC	73	2354
1338114	N/A	N/A	68946	68965	TTAAAAGGAACTCTACCTTC	64	2355
1338127	N/A	N/A	26546	26565	AGCAGACACTCAACTTGACC	47	2356
1338140	N/A	N/A	76763	76782	CACATGGCCCCATACAGGCA	42	2357

1338155	N/A	N/A	72765	72784	GCAAATCACCAGAGTCCCCA	37	2358
1338217	N/A	N/A	58468	58487	ATCTACTGACCCCTCTGGAA	73	2359
1338241	N/A	N/A	18693	18712	AGCGGTCCACCTCCTAATAC	28	2360
1338297	N/A	N/A	56478	56497	CGCAGTCACCTCCCACTGCC	69	2361
1338302	N/A	N/A	93327	93346	TGCACAGATCTTCATAGCAA	23	2362
1338338	N/A	N/A	49280	49299	GGTCTGCTCACCTCACTTGC	32	2363
1338360	N/A	N/A	68424	68443	GGACCAACCCCAGATGGTCC	82	2364
1338366	N/A	N/A	40305	40324	AGCAGCTCCATTACCTCTGC	20	2365
1338368	N/A	N/A	17758	17777	TTTTACAAATCTTCATGGTC	36	2366
1338410	N/A	N/A	30710	30729	GGGAGATGTCTCTCCAAGCT	53	2367
1338419	N/A	N/A	74436	74455	GGCCTCAGCACCAGATGCCT	66	2368
1338444	N/A	N/A	48804	48823	TGGCCACTCCTCCTAGGCGG	59	2369
1338496	N/A	N/A	51910	51929	GGGTCCGTCACACCCAGCAG	29	2370
1338527	N/A	N/A	19223	19242	CCTCTCATCCTATAGACACC	44	2371
			19269	19288			
1338610	N/A	N/A	21647	21666	TCCTGGCACCTCTCATGTCC	38	2372
1338692	N/A	N/A	63249	63268	GCTTTACACTTTTAGAAGAA	18	2373
1338740	3843	3862	94222	94241	GCCACCGTGTCCTCACACGC	18	2374
1338805	N/A	N/A	36757	36776	TGGGAACGAACCCACAGCCC	66	2375
1338851	N/A	N/A	82076	82095	CCTGGGTTCCACACCTGACC	33	2376
1338858	N/A	N/A	39315	39334	GCGCTGCTCCACCTGCCCAA	30	2377
1338873	N/A	N/A	48113	48132	GCCCACTTCTCCGAGCACCA	38	2378
1338883	N/A	N/A	23720	23739	ATGACATGCATTTCACTCAC	33	2379
1338890	N/A	N/A	78706	78725	GCTACTGCAATGACCGGCCA	30	2380
1338978	N/A	N/A	31138	31157	TAATTCAAATTCAACTGCTC	59	2381
1339012	N/A	N/A	89662	89681	GGAAAGGTCTTCACAGGCCA	22	2382
1339098	N/A	N/A	47161	47180	CCATTCTCATCCACTCATCA	41	2383
1339114	N/A	N/A	50594	50613	ACCAGCCTAACCCCTGTTCC	68	2384
1339141	N/A	N/A	87150	87169	GCCCGTATTCTTCCTGAAGA	27	2385
1339147	N/A	N/A	32396	32415	CCCTCCACTTAATCATATCT	43	2386
1339199	N/A	N/A	19890	19909	GCCATGCCAGACTCACCCAA	36	2387
1339236	N/A	N/A	54409	54428	GCCCAGTTCTCCTTCTCAAA	22	2388
1339284	N/A	N/A	8844	8863	TCATGCTCAGAAAATGACCA	34	2389
			37288	37307			
1339345	N/A	N/A	33853	33872	CATTCCATCCAGATATGGCT	44	2390
1339352	N/A	N/A	71268	71287	CGCACCATCACCCAACAGCA	37	2391
1339354	N/A	N/A	70215	70234	ATCCTGGGCCTCTCCAGACT	74	2392
1339364	N/A	N/A	20603	20622	TGGTTGGGTCTCCCTGCCCC	30	2393
1339374	N/A	N/A	75812	75831	GCTGTTGTCCCCAGCAGGCC	41	2394
1339440	4330	4349	94709	94728	TGCTGCTTCTAACTTCCAGA	24	2395
1339460	N/A	N/A	45026	45045	GGGAGCCCATTTCCCAAGTT	43	2396
1339494	N/A	N/A	86301	86320	TTGCCAGGCACCCATAGGTC	26	2397
1339497	N/A	N/A	60946	60965	AGAGCAGCAACATGGAGCCC	40	2398

1339499	N/A	N/A	62098	62117	TGGAGACCCACCATCTCCCC	46	2399
1339522	N/A	N/A	33022	33041	GACCACAAATTCAATTGCTA	43	2400
1339551	N/A	N/A	37527	37546	GAATCCCCCCACCCTTGGCT	75	2401
1339572	N/A	N/A	91721	91740	CCTCCGACCTTTACTCCAGG	17	2402
1339604	N/A	N/A	45701	45720	GGCGGCACACACTATAGCCT	43	2403
1339610	N/A	N/A	24678	24697	GAGATGCTCTCACCAGGAGC	33	2404

Table 32. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	31	283
1337251	N/A	N/A	20547	20566	GCACTTCCACCTTACCCAGA	72	2405
1337284	N/A	N/A	31720	31739	CCAACTTCCACTTTGCAAAA	63	2406
1337289	N/A	N/A	8834	8853	AAAATGACCAACTCACTGGC	66	2407
			37278	37297			
1337328	N/A	N/A	36573	36592	ACAAGAGAACATCTGTGCCG	94	2408
1337330	N/A	N/A	89589	89608	AGCCCAGTCACCCGTGAGCA	28	2409
1337335	N/A	N/A	65183	65202	CATCACTGTCCCAATCACCC	96	2410
1337341	N/A	N/A	27810	27829	ACACGCCCAGGCAAACCGCC	60	2411
1337476	N/A	N/A	37491	37510	CACTAGGCCTCCATGCACCC	66	2412
1337531	N/A	N/A	91717	91736	CGACCTTTACTCCAGGCCTC	35	2413
1337550	N/A	N/A	45675	45694	CAGACGCATCCATTTCCTCC	48	2414
1337562	N/A	N/A	58399	58418	TGGGACCCAGTCATGAACTA	59	2415
1337635	N/A	N/A	54379	54398	GGGTTCTGCCCTCTTCTGAC	18	2416
1337643	N/A	N/A	42263	42282	CCCACACGCAACAAAGGCAC	70	2417
1337718	N/A	N/A	86290	86309	CCATAGGTCAAAAAGGGCCC	38	2418
1337735	N/A	N/A	40233	40252	AGCGAGGCCACCCATGTGAA	89	2419
1337821	N/A	N/A	93320	93339	ATCTTCATAGCAACCCATGC	49	2420
1337875	N/A	N/A	32682	32701	CACAAGTGTTTTAAGCACAC	42	2421
1337929	N/A	N/A	73956	73975	TGCACTGAACCACCTGGTGC	80	2422
1337932	N/A	N/A	67949	67968	GGTCCACCCCAGACGATCCA	21	2423
			68545	68564			
1337961	N/A	N/A	90921	90940	CAGGAGGCCCTTCAAGCTCC	36	2424
1337962	N/A	N/A	32357	32376	TGTGGTCCCCCTCGCCACGC	33	2425
1337980	N/A	N/A	68900	68919	GCAGCTGACTCTCCCGCCCC	79	2426
1338245	N/A	N/A	27211	27230	CTGGAGTACTCTCCACAGAC	69	2427
1338251	N/A	N/A	82003	82022	CCACTTGCTCCACTGTGCGA	58	2428
1338252	N/A	N/A	24541	24560	GAGGCATAAACACACTTACA	36	2429
1338279	N/A	N/A	92435	92454	TCCTGTGTCCACACCTGCGG	41	2430

1338347	N/A	N/A	62062	62081	CTCACGGGACTCCATCATTA	41	2431
1338379	N/A	N/A	19882	19901	AGACTCACCCAACCCTACCA	77	2432
1338384	N/A	N/A	25808	25827	GCCGGACACCAGGCCTGCAA	49	2433
1338395	N/A	N/A	23663	23682	TTTGGACACCATCCCGGGCC	54	2434
1338407	N/A	N/A	22295	22314	CCACCGCAACCCCTTCTGCT	84	2435
1338428	569	588	57124	57143	TCTCCACCCACAGAATAGGA	24	2436
1338452	N/A	N/A	71121	71140	GCCCTGCCCCAGACGCACCG	30	2437
			71161	71180			
1338466	N/A	N/A	47079	47098	ACATCGCCATTCCCAGAGTC	55	2438
1338490	N/A	N/A	78689	78708	CCACAGATTATAACCCACAG	49	2439
1338505	N/A	N/A	87843	87862	CCCCAGCACATCCTGGCCTT	43	2440
1338541	N/A	N/A	49202	49221	GACCAGACCCCAGAATCTCC	75	2441
1338551	N/A	N/A	48079	48098	TGAAAACGATCCATTTTCCC	79	2442
1338554	N/A	N/A	69862	69881	CCATGGTGCTTCCTAGGGCA	29	2443
1338567	N/A	N/A	85146	85165	AGGCGGTACATCCACGGGCT	48	2444
1338599	N/A	N/A	17735	17754	ATGGATACAGTCCCTAGGAC	19	2445
1338654	N/A	N/A	51867	51886	TCTGAAGATTCCTCCCCGCA	80	2446
1338655	N/A	N/A	48763	48782	CCATCGCCCCACACTCCACT	76	2447
1338670	N/A	N/A	77545	77564	GTGGCTCTCCCTTGCAGAAT	37	2448
1338678	3838	3857	94217	94236	CGTGTCCTCACACGCTCCTC	40	2449
1338685	N/A	N/A	62940	62959	CGGGAAAGCCACACACAACT	70	2450
1338689	N/A	N/A	50512	50531	GCTGTGAGCCTCACCTCCCC	65	2451
1338704	N/A	N/A	55657	55676	GGTACATCCCACATCTGCGG	26	2452
1338718	N/A	N/A	72558	72577	CCTGATGCCCTCCCCCGAGC	74	2453
1338734	N/A	N/A	21424	21443	TCCCCCGACATACACAGCAT	44	2454
1338743	N/A	N/A	18668	18687	GCACACAACCCATGTGCCCA	55	2455
1338780	N/A	N/A	43240	43259	CATCTCCCGATATAGCCCTA	74	2456
1338788	N/A	N/A	29733	29752	CTGTCCGGAGAATCCAGGCC	41	2457
1338836	N/A	N/A	23014	23033	CCTAAACCACCACTGCCCCT	103	2458
1338838	N/A	N/A	82825	82844	CGGAGAGTCCTCCCAGCCCT	47	2459
1338893	N/A	N/A	66014	66033	CTGCCTTGCCACACAAAACA	53	2460
1338898	N/A	N/A	76608	76627	TCGACACACAACATACACAA	135	2461
1338927	N/A	N/A	79252	79271	CCCAGACCCCTCACCAAACA	92	2462
1338968	N/A	N/A	39252	39271	ACCAGACACCAGCCCAAGCA	77	2463
1339022	N/A	N/A	18188	18207	GCTGCCGTTTTCAAGAATTA	45	2464
1339091	4266	4285	94645	94664	CCAGAGTGCAGAACAGCAGC	65	2465
1339145	N/A	N/A	34966	34985	GAATCCTCACCCTTAGCCCT	67	2466
1339159	N/A	N/A	60802	60821	CCAAGAGACCCCACCTGGCC	76	2467
1339178	N/A	N/A	33778	33797	AACCAGTGAGTCACTACGAA	37	2468
1339207	N/A	N/A	44865	44884	AACAAGGGCTCTCACACCTC	103	2469
1339232	N/A	N/A	30493	30512	GCCTCCTGAAATCTGGGCTT	80	2470
1339281	N/A	N/A	84242	84261	TGTCACCCCACCAGCAGCAT	82	2471
1339291	N/A	N/A	56449	56468	CAGGTGCCTTCCTTTGCCGT	23	2472

1339295	N/A	N/A	53292	53311	TCCGTGGACCTTCTGGGTCC	31	2473
1339311	N/A	N/A	31120	31139	TCAGCGAACTTAATTATATC	54	2474
1339361	N/A	N/A	75709	75728	GTTGACCCCACCCCAGAGGC	56	2475
1339376	N/A	N/A	19222	19241	CTCTCATCCTATAGACACCA	23	2476
			19268	19287			
1339504	4524	4543	94903	94922	AGGTAAGTGTAAAATGGTCC	24	2477
1339506	711	730	59192	59211	GTGTTGATCATCTCCAGGAC	33	2478
1339543	N/A	N/A	40856	40875	CTAATCAGCTCCCAATCCCT	72	2479
1339613	N/A	N/A	87046	87065	GGAGCTGCCAGCAATAGCAA	31	2480
1339656	N/A	N/A	68289	68308	CAGATGGTCCACCCTGGACA	48	2481

Table 33. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
855082	N/A	N/A	90144	90163	CCTTGCAAATATCCCAGGTT	19	2482
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	30	283
1337283	N/A	N/A	50286	50305	GTAGAGTCCCAGCACCTGCC	62	2483
1337340	N/A	N/A	58657	58676	AGTCTTGAAACCATGGTCCT	31	2484
1337345	N/A	N/A	93464	93483	CACCAGCGCACACCTGCCAC	56	2485
1337390	N/A	N/A	32087	32106	TGCACAGCTCCCATGGATGA	35	2486
1337423	N/A	N/A	62367	62386	GGCCCAAGCACTTCACACCC	28	2487
1337426	N/A	N/A	57691	57710	GGGCCTGGTTTCCCTATTTA	24	2488
1337431	N/A	N/A	83348	83367	GTCCACGGCACCCTCTCCTC	54	2489
1337464	N/A	N/A	25093	25112	GGCCTCAGCCTTCACTCACA	38	2490
1337529	N/A	N/A	17851	17870	CCACTCCTGACTCTTGGTTC	30	2491
1337544	N/A	N/A	39661	39680	CCCTGATGAAACTTCAGCCC	57	2492
1337596	N/A	N/A	91525	91544	GTGCCTCCCCCCACGGCAGC	17	2493
1337612	N/A	N/A	74945	74964	CAAGGCAGCACTCACTCTAC	56	2494
1337630	N/A	N/A	29978	29997	CCATTTTAACCCTCTTTGCC	46	2495
1337659	N/A	N/A	35707	35726	ATCTGAAGCCCCAAACTAGC	99	2496
1337764	N/A	N/A	76997	77016	AGGTGCCGAACCTTAAGGAC	39	2497
1337766	N/A	N/A	69099	69118	ACACTATGCCACTAAGGACA	47	2498
1337800	N/A	N/A	42693	42712	GGCTCGCTGTCAACACACGA	46	2499
1337807	N/A	N/A	28486	28505	CCAAGGGACCCACTGAGGCT	52	2500
1337809	N/A	N/A	32441	32460	TCTTGGCTCACCCAGATCAT	48	2501
1337820	N/A	N/A	45449	45468	CCCTGGATGCTCAACAGCCG	42	2502
1337829	N/A	N/A	82463	82482	CGGAACACACTTTCACTCTC	25	2503
1337848*	N/A	N/A	52249	52268	TCACAGCCCCAGCCTTCGCC	28	2504
1337922	N/A	N/A	84923	84942	CCCTTACTCATCAGTGGCCG	64	2505

1337933	N/A	N/A	85800	85819	TCCCAGACACACTCAGGGCC	44	2506
1337936	N/A	N/A	22750	22769	CACGCAGAAACTCTGGGCTC	30	2507
1338065	N/A	N/A	18312	18331	CAGGAATACAGCATTACAAT	41	2508
1338067	N/A	N/A	33379	33398	CAGGTAAGCATTTAAACCTT	43	2509
1338133	N/A	N/A	53949	53968	ACTGGAGACACCATCTTCGG	25	2510
1338149	N/A	N/A	73377	73396	GAGAGACTCCACCTGTCCAA	40	2511
1338249	N/A	N/A	19540	19559	AAGTTGCCCACTCCTGTACT	49	2512
1338261	N/A	N/A	17278	17297	GAATTATTCCCATGGGCTCA	28	2513
1338285	N/A	N/A	31390	31409	CTGCGGAATCCCCTCCTGCA	27	2514
1338293	N/A	N/A	48489	48508	CACTGGCTTCCGGACAGCCA	66	2515
1338381	N/A	N/A	40418	40437	TCCAGAAGAACAAACCTACC	62	2516
1338390	N/A	N/A	37960	37979	TGGGCCCGCACATCTCACAT	65	2517
1338421	N/A	N/A	68591	68610	GGATGATCCACCCCAGACGG	45	2518
1338486	N/A	N/A	93131	93150	GTGCTCAGCCCTTTGCTTCA	28	2519
1338493	N/A	N/A	47513	47532	CTGCTCAAACCATCAGGACC	36	2520
1338552	N/A	N/A	78953	78972	TCTTGGTTTCCAATCATCAT	26	2521
1338568	N/A	N/A	64020	64039	CTGCACATCCCGATTTGGCC	30	2522
1338580	N/A	N/A	20942	20961	CTGTCCACTTCCTCCACCGG	47	2523
1338586	N/A	N/A	41277	41296	ACCACGCTAGACCTCAGGCT	16	2524
1338591	N/A	N/A	70371	70390	ACAGTGCCCCCTCAGTGGGC	62	2525
1338613	N/A	N/A	30923	30942	GGACACAGTTCAATCCCGAA	33	2526
1338646	N/A	N/A	71737	71756	GTGGACCTTCCATCGCTCCT	13	2527
1338647	N/A	N/A	48965	48984	CAGAATTCTCCATTCCTGAT	61	2528
1338653	N/A	N/A	18846	18865	TCTCCCTCCAATAGAACCTC	49	2529
1338666	N/A	N/A	34506	34525	TTATGACTCAATGAGCCCAA	44	2530
1338691	N/A	N/A	56048	56067	GGAGACTCATCCCACCCCAC	15	2531
			56112	56131			
1338695	N/A	N/A	21900	21919	AGGAGCTAATGAAACAGCCT	29	2532
1338696	N/A	N/A	77997	78016	CACCACCAAGAAACATCGCA	51	2533
1338697	N/A	N/A	68150	68169	CTAGACAATCCACCCTGGAT	57	2534
1338717	N/A	N/A	26887	26906	TCAGGGTCATCCTCGAAGCC	38	2535
1338728	N/A	N/A	51101	51120	GAGGAAAACTCCAATGCTGC	46	2536
1338853	N/A	N/A	55300	55319	AAGGAGACCTCACTGCTCAC	25	2537
1338856	4696	4715	95075	95094	GTACAAACCAGTAAGGAACC	30	2538
1338874	N/A	N/A	75902	75921	CCGCCATGCCTCCCTGACAT	70	2539
1338922	N/A	N/A	24240	24259	GGATTCGCCCTCTCAGGGTC	20	2540
1338931	N/A	N/A	27520	27539	TGGCAGGTCCACCCTCCCCC	23	2541
1338940	N/A	N/A	23103	23122	GCCACCCTTCCCAAACTCAG	73	2542
1338945	N/A	N/A	61550	61569	GTGCATCACCAGGCGAGCCC	17	2543
1338953	N/A	N/A	20130	20149	TGGGATGGCTTCTAATGGCA	11	2544
1338954	4364	4383	94743	94762	ACCCCTCTCACATGCCCGGC	41	2545
1339097	N/A	N/A	67530	67549	TGTTTGTGCCCACCACCTCT	51	2546
1339104	3939	3958	94318	94337	TGAGCTGGCCCTCCCCCCGC	51	2547

1339142	N/A	N/A	46151	46170	CGGGAAGCTCCACACCAGCT	71	2548
1339210	N/A	N/A	59818	59837	ACTGCTGCCATTCACATGAC	31	2549
1339224	N/A	N/A	88951	88970	GGCTGGCCCAACTCTAGCTG	42	2550
1339252	N/A	N/A	44273	44292	GTGAGCTCCACCTCATGCCG	33	2551
1339319	N/A	N/A	37049	37068	GATGGAAGCCCCCTTCAACC	68	2552
1339369	N/A	N/A	92124	92143	CAGCTCATTTCACTCCGGCA	13	2553
1339370	N/A	N/A	65554	65573	GGCATGGGACAATCTCCCCC	8	2554
1339411	N/A	N/A	86432	86451	ACACAGGTCCATACCCCACC	82	2555
1339449	N/A	N/A	56671	56690	AGGTCGGGCTATCTAACCCA	38	2556
1339519	N/A	N/A	87545	87564	CAGGCTACTCCCCCCAGGCC	41	2557
1339652	N/A	N/A	81593	81612	CCACGCCATCTCCTGAGTTC	88	2558

Table 34. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	74	283
1081145	N/A	N/A	91719	91738	TCCGACCTTTACTCCAGGCC	29	487
1337232	N/A	N/A	19885	19904	GCCAGACTCACCCAACCCTA	66	2559
1337354	N/A	N/A	74252	74271	GGGTTGTGGACCTCTAGGTA	48	2560
1337377	N/A	N/A	29759	29778	CCTTTGCTCCCCTGTGGGCC	54	2561
1337391	N/A	N/A	30627	30646	GCGGCCCTCACTCTCCGGCC	72	2562
1337406	N/A	N/A	55750	55769	CCCCTCCCCACCTACTGCGG	39	2563
1337429	N/A	N/A	58432	58451	GTGAAAGACCCTCTCTGGTC	54	2564
1337444	N/A	N/A	68924	68943	CCCGTTCTCCCACCTTGACT	115	2565
1337467	N/A	N/A	43243	43262	CTGCATCTCCCGATATAGCC	39	2566
1337499	N/A	N/A	18675	18694	ACCATCGGCACACAACCCAT	69	2567
1337504	N/A	N/A	87148	87167	CCGTATTCTTCCTGAAGACT	18	2568
1337561	4306	4325	94685	94704	GCTTGGGACAGCAAACAGCC	39	2569
1337629	N/A	N/A	82864	82883	ATCCCTGTCCACACAGGGTC	110	2570
1337663	N/A	N/A	51903	51922	TCACACCCAGCAGACAGCCG	100	2571
1337710	N/A	N/A	56475	56494	AGTCACCTCCCACTGCCTGC	47	2572
1337731	N/A	N/A	69899	69918	CTGACAGCTTCTCCTGGCCA	51	2573
1337739	N/A	N/A	27829	27848	TATATTCAATCAACTTAGGA	57	2574
1337780	N/A	N/A	90945	90964	CCCGAGCTAACACCCGTCCT	35	2575
1337897	N/A	N/A	87845	87864	GACCCCAGCACATCCTGGCC	27	2576
1337923	N/A	N/A	53304	53323	TGCTCCAGCCTTTCCGTGGA	39	2577
1337928	N/A	N/A	93325	93344	CACAGATCTTCATAGCAACC	52	2578
1337996	N/A	N/A	85469	85488	ACCTGTCTCCTCTCTCCCGT	44	2579
1338014	N/A	N/A	48101	48120	GAGCACCACCACAAAAAGGA	61	2580

1338024	N/A	N/A	20550	20569	GCGGCACTTCCACCTTACCC	57	2581
1338120	N/A	N/A	18220	18239	CTTCCTGCCCAATATCGGAA	80	2582
1338164	N/A	N/A	84246	84265	TGCATGTCACCCCACCAGCA	69	2583
1338177	N/A	N/A	60854	60873	CCCCCACCTTTACCCTGGCT	53	2584
1338246	N/A	N/A	27291	27310	GTGTTTCTACATAAGCCACA	25	2585
1338248	N/A	N/A	47129	47148	GTTTATCTGGCAAACAGCAA	56	2586
1338257	N/A	N/A	37501	37520	TTTCTGACCTCACTAGGCCT	76	2587
1338280	N/A	N/A	65245	65264	AGGCTCAGTCTTTCCAGTCA	63	2588
1338342	N/A	N/A	79263	79282	ACTGGAGCCCTCCCAGACCC	92	2589
1338364	N/A	N/A	23016	23035	CCCCTAAACCACCACTGCCC	91	2590
1338409	N/A	N/A	31723	31742	GACCCAACTTCCACTTTGCA	88	2591
1338414	N/A	N/A	19227	19246	CTTCCCTCTCATCCTATAGA	91	2592
			19273	19292			
1338455	N/A	N/A	77627	77646	GTGCCTCTAACATAGACACT	50	2593
1338465	N/A	N/A	23713	23732	GCATTTCACTCACTCAGGAC	34	2594
1338503	758	777	59306	59325	ACAGGTTCCGCAGCGGCGGC	35	2595
1338522	N/A	N/A	45024	45043	GAGCCCATTTCCCAAGTTCA	50	2596
1338542	N/A	N/A	54395	54414	CTCAAACTCTCCTAGTGGGT	35	2597
1338616	N/A	N/A	75801	75820	CAGCAGGCCACCACCCCGTC	80	2598
1338664	N/A	N/A	21434	21453	AAAGCATGCATCCCCCGACA	51	2599
1338667	N/A	N/A	48765	48784	GACCATCGCCCCACACTCCA	59	2600
1338703	N/A	N/A	22304	22323	GAGACATCCCCACCGCAACC	105	2601
1338713	N/A	N/A	92580	92599	TTGGAGTTCCCACAGTGTGA	43	2602
1338749	N/A	N/A	40863	40882	ACGCTGTCTAATCAGCTCCC	44	2603
1338765	3841	3860	94220	94239	CACCGTGTCCTCACACGCTC	44	2604
1338772	N/A	N/A	40303	40322	CAGCTCCATTACCTCTGCTC	67	2605
1338777	N/A	N/A	68397	68416	ATGGTCCACCTTGAATGGTC	36	2606
1338804	N/A	N/A	32378	32397	CTGCTAATCCCCCTCACCAC	61	2607
1338885	N/A	N/A	39300	39319	CCCAACCATCCCCAGAGGAC	99	2608
1338901	N/A	N/A	31122	31141	GCTCAGCGAACTTAATTATA	61	2609
1338916	N/A	N/A	89652	89671	TCACAGGCCACCTGTTCCCC	81	2610
1338951	N/A	N/A	49228	49247	GGGAGCCTCACCATGCCCTT	82	2611
1338963	N/A	N/A	71266	71285	CACCATCACCCAACAGCATG	70	2612
1338965	N/A	N/A	17748	17767	CTTCATGGTCCTCATGGATA	22	2613
1339061	N/A	N/A	36681	36700	CGGCTGCTCCATGATGCAGT	78	2614
1339084	N/A	N/A	8837	8856	CAGAAAATGACCAACTCACT	52	2615
			37281	37300			
1339094	N/A	N/A	63151	63170	GATTGGTGAATCAAAGCCAA	47	2616
1339103	N/A	N/A	72697	72716	TGGCTGAGCCCTCCCGTCCC	120	2617
1339105	N/A	N/A	45677	45696	TGCAGACGCATCCATTTCCT	63	2618
1339171	N/A	N/A	33842	33861	GATATGGCTCCTACTCCACC	70	2619
1339186	N/A	N/A	26466	26485	GCCACGCCCCTCGCCGACCA	31	2620
1339214	N/A	N/A	76739	76758	GAAATGGACACACCCGGACA	120	2621

1339234	N/A	N/A	66023	66042	GAGGCTCCACTGCCTTGCCA	49	2622
1339264	4538	4557	94917	94936	GGCTTTGCTTTAAAAGGTAA	87	2623
1339269	N/A	N/A	50557	50576	TGTCACTGTCCACCAGGGCA	45	2624
1339274	N/A	N/A	67952	67971	AATGGTCCACCCCAGACGAT	54	2625
1339429	N/A	N/A	42388	42407	GCACCCCACAACCCCAAGTC	73	2626
1339446	N/A	N/A	62095	62114	AGACCCACCATCTCCCCAGA	100	2627
1339464	N/A	N/A	33011	33030	CAATTGCTAAACCACACTTT	63	2628
1339474	N/A	N/A	78691	78710	GGCCACAGATTATAACCCAC	73	2629
1339490	N/A	N/A	57163	57182	GTAGGGCACTCACCTGGATC	93	2630
1339515	N/A	N/A	34973	34992	AGTGCCGGAATCCTCACCCT	37	2631
1339546	N/A	N/A	24575	24594	GGTGCTTTTCCATAGCAGCT	31	2632
1339620	N/A	N/A	86299	86318	GCCAGGCACCCATAGGTCAA	30	2633
1339666	N/A	N/A	82025	82044	CAGAAAGCCAATTCCAGCTC	67	2634

Table 35. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	20	283
1080889	4699	4718	95078	95097	ACCGTACAAACCAGTAAGGA	21	133
1337293	N/A	N/A	48995	49014	CTGGCATCCACCGGCTCCCC	32	2635
1337302	N/A	N/A	83422	83441	CTGGTGCCTTCTACAGGCTC	50	2636
1337333	N/A	N/A	90157	90176	CAGGGCAGAATTACCTTGCA	28	2637
1337360	N/A	N/A	20273	20292	CGTCCTCCCACCTCACACGG	39	2638
1337411	N/A	N/A	17299	17318	CTGCCAGCCCCCTCAGCGGA	33	2639
1337501	N/A	N/A	54076	54095	CTGAGCACTCTTACGCATAA	22	2640
1337549	N/A	N/A	93600	93619	GTCCCATCTCCACACAGGGC	34	2641
1337567	N/A	N/A	71769	71788	GGACCTCAACCCCCTACTTG	44	2642
1337576	N/A	N/A	75974	75993	GGTCTTTCTCCTCCCACCAC	46	2643
1337606	N/A	N/A	38100	38119	CACCCCCCAATTCCTACCTC	81	2644
1337608	N/A	N/A	58710	58729	GTCTTAGCCACCAAGGCCTT	47	2645
1337614	N/A	N/A	79138	79157	CAGCTGTACCCACAGGCGGC	64	2646
1337616	N/A	N/A	62591	62610	CAGAGGCTCCCTAGGAGCAC	81	2647
1337711	N/A	N/A	67861	67880	CTATAATGCTCTCATGGCTC	49	2648
1337763	N/A	N/A	40427	40446	GATCCACACTCCAGAAGAAC	39	2649
1337805	N/A	N/A	87555	87574	TCCAAACTCACAGGCTACTC	18	2650
1337817	N/A	N/A	93151	93170	ACAGGCCATTCCCACTCGCT	26	2651
1337840	N/A	N/A	31008	31027	CTTAATTACCTCTAAAGAAC	64	2652
1337862	N/A	N/A	56769	56788	ACGACAGGCAACAGCAGCCT	23	2653

1337884	N/A	N/A	51263	51282	ACCGTGGCCACCTGCATGAC	61	2654
1337915	N/A	N/A	46179	46198	GCAGGTAGTCATACACAGAT	48	2655
1337947	N/A	N/A	17963	17982	TGGGCTCATTATTAGAGCAC	40	2656
1337964	N/A	N/A	73399	73418	GACAGATTCAAAAACAGGCC	18	2657
1337966	1414	1433	70612	70631	GCAGGCCTCCCCATTGTCCA	28	2658
1337969	N/A	N/A	85810	85829	AGCTCTATCTTCCCAGACAC	50	2659
1337993	N/A	N/A	35834	35853	CTGGACATTCTCAAAGTGCC	53	2660
1338000	N/A	N/A	61853	61872	CCAGAGGACCCACCTGCAGT	83	2661
1338012	N/A	N/A	82499	82518	TCCAGGATCCCTATGGGCTC	38	2662
1338038	N/A	N/A	81677	81696	CAGTGCCTCACACGCGGTCA	46	2663
1338040	N/A	N/A	27581	27600	GCCCAAAACTACAGCGGTCT	26	2664
1338043	N/A	N/A	64148	64167	TGGCCTTGTCTTACTTCTTA	36	2665
1338061	N/A	N/A	86661	86680	GCCCATCCACCCACTTGGAC	77	2666
1338144	N/A	N/A	39870	39889	CAGGTGCTTGACCTTAGCCT	42	2667
1338159	N/A	N/A	21946	21965	TGCTCAACTCCAGAGAACCA	47	2668
1338180	N/A	N/A	42852	42871	CAGCATCCAAACCCACGGTG	33	2669
1338198	N/A	N/A	18867	18886	GAAGCTCTAATCCCTGGCCA	29	2670
1338201	N/A	N/A	75153	75172	TCAGTGACACTCAAAAGTGC	57	2671
1338218	N/A	N/A	32485	32504	GCGACTCTGAACCTCTGCCT	24	2672
1338282	N/A	N/A	25303	25322	CAGCTGGAACTCCTGACACC	45	2673
1338300	N/A	N/A	48515	48534	TGCAACCCTGCCCATTGCCA	37	2674
1338365	N/A	N/A	69372	69391	AGGGAACCCCACCACATCAC	37	2675
1338391	4367	4386	94746	94765	CGCACCCCTCTCACATGCCC	38	2676
1338429	N/A	N/A	31446	31465	GCTGGGCCCGCATCTGGAGC	72	2677
1338445	N/A	N/A	26983	27002	CCAAGATTACCCTCAGGATC	29	2678
1338447	N/A	N/A	77135	77154	CCCTTAACCACCTGTGCATC	73	2679
1338478	N/A	N/A	41675	41694	TGACGGGACCATACTCAGGA	50	2680
1338498	N/A	N/A	22835	22854	GCGCAGCCCAGCCCTAGCTT	27	2681
1338571	N/A	N/A	68088	68107	GGTCCACCCCAGACAGTCCA	14	2682
			68615	68634			
1338611	N/A	N/A	59992	60011	ACGGGTCCCCATCTTGCCTA	42	2683
1338671	N/A	N/A	91603	91622	CGCCTGAATCCCCCACGCCA	33	2684
1338707	N/A	N/A	50381	50400	CCAAAGCTCACAACACTCAG	50	2685
1338879	N/A	N/A	24380	24399	TCTGTTTTACACTAATGCGG	24	2686
1338884	N/A	N/A	68191	68210	TGGATGGTCCCCCCTGGACA	72	2687
1338889	N/A	N/A	89080	89099	CCAAAGTCTCCCCCCTACCC	59	2688
1338906	N/A	N/A	78023	78042	GCTGGCCCCACATGCAGGCA	39	2689
1338937	3974	3993	94353	94372	AAAACTCTCCTCACTAGCCT	32	2690
1338957	N/A	N/A	34522	34541	CCCACACGCCATACAGTTAT	51	2691
1339011*	N/A	N/A	52596	52615	CAAGTCCTCACCTGCAATCC	45	2692
1339086	N/A	N/A	28503	28522	CCAACAGGTTCTACCTACCA	53	2693
1339090	N/A	N/A	19574	19593	AAGCCCCCAACTCACTTGCC	48	2694
1339126	N/A	N/A	45576	45595	CACCCGTCACCCTCTGCACC	41	2695

1339136	N/A	N/A	44337	44356	CCCTGCTCAGCACGAAGCCA	56	2696
1339196	N/A	N/A	20955	20974	TGAGCTCCCAACTCTGTCCA	27	2697
1339230	N/A	N/A	29995	30014	GCATAACACAAATATTGCCA	16	2698
1339258	N/A	N/A	57906	57925	GTCCTTGGCATTCACTGAGC	20	2699
1339301	N/A	N/A	56215	56234	AGGCTGGGCATTATCCCTCA	18	2700
1339321	N/A	N/A	23380	23399	GACTGGGATCCCACCTGGCC	75	2701
1339363	N/A	N/A	47598	47617	TCCCAGGCTTCTCTTGGGAC	80	2702
1339398	N/A	N/A	84932	84951	CCGGGTTCGCCCTTACTCAT	56	2703
1339415	N/A	N/A	32173	32192	CTGCAATTCAACACTGCCTT	30	2704
1339421	N/A	N/A	55333	55352	CCCAGACCATCATCGATGCC	18	2705
1339422	N/A	N/A	18334	18353	CTGCTGTCCACTCCTGAACA	70	2706
1339466	N/A	N/A	33510	33529	AAGCTGCTAAAAGAAATGCC	38	2707
1339484	N/A	N/A	37163	37182	GCATGTCGCCCTGGCTGCCT	15	2708
1339629	N/A	N/A	65742	65761	GATCTGATTGGAAATAGGTC	10	2709
1339645	N/A	N/A	92127	92146	CACCAGCTCATTTCACTCCG	24	2710

Table 36. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	31	283
1337223	N/A	N/A	56050	56069	GTGGAGACTCATCCCACCCC	13	2711
			56114	56133			
1337322	N/A	N/A	17280	17299	ATGAATTATTCCCATGGGCT	26	2712
1337364	N/A	N/A	39845	39864	GCCTCTTCTGCAAATGGGAC	35	2713
1337371	N/A	N/A	41284	41303	GAACTGGACCACGCTAGACC	51	2714
1337376	N/A	N/A	23302	23321	ATATAACCACCCCCTACCCC	97	2715
1337422	N/A	N/A	93147	93166	GCCATTCCCACTCGCTGTGC	41	2716
1337441	N/A	N/A	50377	50396	AGCTCACAACACTCAGGGTA	50	2717
1337446	N/A	N/A	77078	77097	TCATAGGGCCTGCCTAGCCT	37	2718
1337449	N/A	N/A	29979	29998	GCCATTTTAACCCTCTTTGC	13	2719
1337451	N/A	N/A	75041	75060	GAAGCTGCAATTCAGAGCAT	52	2720
1337461	N/A	N/A	48501	48520	TTGCCAGGACCTCACTGGCT	69	2721
1337509	N/A	N/A	92125	92144	CCAGCTCATTTCACTCCGGC	19	2722
1337519	N/A	N/A	17895	17914	CGCTCACTCCCTGATTCTGA	26	2723
1337535	N/A	N/A	68593	68612	CTGGATGATCCACCCCAGAC	59	2724
1337631	4365	4384	94744	94763	CACCCCTCTCACATGCCCGG	30	2725
1337679	N/A	N/A	91527	91546	TAGTGCCTCCCCCCACGGCA	56	2726
1337786	3941	3960	94320	94339	GGTGAGCTGGCCCTCCCCCC	22	2727
1337873	N/A	N/A	64025	64044	GCCTGCTGCACATCCCGATT	46	2728

1337893	N/A	N/A	45489	45508	TTTGGGATAATAATAGGTCC	59	2729
1337898	N/A	N/A	61584	61603	CCCACGGGACCCTCACTGCC	58	2730
1337927	N/A	N/A	42768	42787	CTGCCAGCCCTAACTTAGCT	37	2731
1337945	N/A	N/A	70397	70416	CCCCTACTCTCTGCTGGTCA	42	2732
1337953*	N/A	N/A	52279	52298	TGGCTCCCACCCCATGGACT	59	2733
1337974	N/A	N/A	88953	88972	CTGGCTGGCCCAACTCTAGC	45	2734
1338017	N/A	N/A	22781	22800	CCCTAGGTCCTGCCCAGGCC	37	2735
1338057	N/A	N/A	58658	58677	GAGTCTTGAAACCATGGTCC	36	2736
1338090	N/A	N/A	85806	85825	CTATCTTCCCAGACACACTC	63	2737
1338095	N/A	N/A	82466	82485	GGCCGGAACACACTTTCACT	44	2738
1338207	N/A	N/A	81634	81653	CTGGTTCCACCATCAAGAGC	34	2739
1338240	N/A	N/A	78003	78022	GAGTCCCACCACCAAGAAAC	75	2740
1338278	N/A	N/A	56694	56713	CATGAATGTCCCTAAGAGCA	56	2741
1338349	N/A	N/A	34508	34527	AGTTATGACTCAATGAGCCC	84	2742
1338377	N/A	N/A	18850	18869	CCACTCTCCCTCCAATAGAA	36	2743
1338431	N/A	N/A	75920	75939	CCACAGGGCTCTGCCCGCCC	27	2744
1338473	N/A	N/A	59959	59978	GAGGCTTAAGTCTCAGGTCA	14	2745
1338550	N/A	N/A	27521	27540	TTGGCAGGTCCACCCTCCCC	55	2746
1338601	N/A	N/A	24347	24366	TTGTGTCACACACATGAGTC	32	2747
1338606	N/A	N/A	78954	78973	GTCTTGGTTTCCAATCATCA	29	2748
1338618	N/A	N/A	26888	26907	TTCAGGGTCATCCTCGAAGC	45	2749
1338642	N/A	N/A	71740	71759	TCGGTGGACCTTCCATCGCT	33	2750
1338659	N/A	N/A	38011	38030	CACAGATCCCACCTGTGTGT	58	2751
1338662	N/A	N/A	83387	83406	GGCGGATCCCAGCCTCTGCA	44	2752
1338673	N/A	N/A	47519	47538	ACCCGTCTGCTCAAACCATC	50	2753
1338682	N/A	N/A	57749	57768	TGCTCACTGACCCTGAGTCA	22	2754
1338688	N/A	N/A	62436	62455	CATCTCCCCAATAGCAGGGT	23	2755
1338729	N/A	N/A	51123	51142	CCAGGGTTTAATGATCCCCT	77	2756
1338733	N/A	N/A	21901	21920	GAGGAGCTAATGAAACAGCC	72	2757
1338741	N/A	N/A	18326	18345	CACTCCTGAACACTCAGGAA	58	2758
1338763	N/A	N/A	32443	32462	GATCTTGGCTCACCCAGATC	64	2759
1338935	N/A	N/A	90145	90164	ACCTTGCAAATATCCCAGGT	24	2760
1338946	N/A	N/A	55301	55320	CAAGGAGACCTCACTGCTCA	18	2761
1338986	N/A	N/A	28498	28517	AGGTTCTACCTACCAAGGGA	39	2762
1339001	4697	4716	95076	95095	CGTACAAACCAGTAAGGAAC	19	2763
1339017	N/A	N/A	20943	20962	TCTGTCCACTTCCTCCACCG	43	2764
1339035	N/A	N/A	31403	31422	TCATTCCCGCCATCTGCGGA	54	2765
1339047	N/A	N/A	86433	86452	GACACAGGTCCATACCCCAC	66	2766
1339054	N/A	N/A	73378	73397	AGAGAGACTCCACCTGTCCA	59	2767
1339056	N/A	N/A	46152	46171	CCGGGAAGCTCCACACCAGC	88	2768
1339106	N/A	N/A	67589	67608	AGGGTCAGACCCTCTGAGCC	136	2769
1339119	N/A	N/A	65618	65637	GAGGTTTCTACAGCCACCGT	38	2770
1339253	N/A	N/A	54032	54051	CTACGGGTATGAAAAAGTCA	43	2771

1339294	N/A	N/A	30945	30964	GCTTTGATATATAAATCTTG	31	2772
1339306	N/A	N/A	25240	25259	GTCACGGGACAGCTCACCCA	40	2773
1339324	N/A	N/A	32165	32184	CAACACTGCCTTACTGTGAA	46	2774
1339383	N/A	N/A	48966	48985	GCAGAATTCTCCATTCCTGA	30	2775
1339390	N/A	N/A	20207	20226	AGGCAGACGACCCCTGGTCT	44	2776
1339394	N/A	N/A	19541	19560	AAAGTTGCCCACTCCTGTAC	126	2777
1339407	N/A	N/A	35743	35762	TCTGAGACCCATCTGGGTCT	102	2778
1339458	N/A	N/A	68151	68170	CCTAGACAATCCACCCTGGA	78	2779
1339505	N/A	N/A	33412	33431	CGTTAGAGAATTACACAAAA	35	2780
1339524	N/A	N/A	93465	93484	ACACCAGCGCACACCTGCCA	38	2781
1339545	N/A	N/A	87546	87565	ACAGGCTACTCCCCCCAGGC	49	2782
1339563	N/A	N/A	84924	84943	GCCCTTACTCATCAGTGGCC	57	2783
1339568	N/A	N/A	44274	44293	GGTGAGCTCCACCTCATGCC	47	2784
1339587	N/A	N/A	37093	37112	CACGAGTACCCTCTGCCAGC	38	2785
1339592	N/A	N/A	40421	40440	CACTCCAGAAGAACAAACCT	83	2786
1339599	N/A	N/A	69368	69387	AACCCCACCACATCACTGGC	64	2787

Table 37. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080852	3842	3861	94221	94240	CCACCGTGTCCTCACACGCT	18	49
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	19	283
1337273	N/A	N/A	72758	72777	ACCAGAGTCCCCACCGGAGC	45	2788
1337300	N/A	N/A	42401	42420	GGAGTGTCCCTCTGCACCCC	43	2789
1337306	759	778	59307	59326	AACAGGTTCCGCAGCGGCGG	18	2790
1337311	N/A	N/A	56477	56496	GCAGTCACCTCCCACTGCCT	58	2791
1337394	N/A	N/A	40304	40323	GCAGCTCCATTACCTCTGCT	35	2792
1337412	N/A	N/A	27292	27311	CGTGTTTCTACATAAGCCAC	28	2793
1337414	N/A	N/A	20553	20572	CAAGCGGCACTTCCACCTTA	62	2794
1337453	N/A	N/A	53574	53593	CCACCCACCCTCATCGCGGC	50	2795
1337480	N/A	N/A	21634	21653	CATGTCCTGCTTAATGCCTG	33	2796
1337486	N/A	N/A	23714	23733	TGCATTTCACTCACTCAGGA	27	2797
1337502	N/A	N/A	62097	62116	GGAGACCCACCATCTCCCCA	54	2798
1337556	N/A	N/A	34992	35011	CTTCTGAGTCCAAACTGGGA	66	2799
1337559	N/A	N/A	26544	26563	CAGACACTCAACTTGACCTC	48	2800
1337605	N/A	N/A	48770	48789	GCCCTGACCATCGCCCCACA	259	2801
1337689	N/A	N/A	43462	43481	GGCTCAGCTTCCCTCTCGCT	61	2802
1337699	N/A	N/A	77629	77648	AGGTGCCTCTAACATAGACA	46	2803
1337733	N/A	N/A	85486	85505	TTAGCAGCTAAAACGACACC	85	2804

1337744	N/A	N/A	93326	93345	GCACAGATCTTCATAGCAAC	25	2805
1337749	N/A	N/A	33852	33871	ATTCCATCCAGATATGGCTC	49	2806
1337767	N/A	N/A	18692	18711	GCGGTCCACCTCCTAATACC	37	2807
1337785	N/A	N/A	57198	57217	TTACTGAGCACCACTGCAGT	71	2808
1337839	N/A	N/A	36753	36772	AACGAACCCACAGCCCACCG	48	2809
1337914	N/A	N/A	40864	40883	CACGCTGTCTAATCAGCTCC	44	2810
1337979	N/A	N/A	33014	33033	ATTCAATTGCTAAACCACAC	71	2811
1338023	N/A	N/A	47136	47155	CTCATTTGTTTATCTGGCAA	29	2812
1338097	N/A	N/A	58467	58486	TCTACTGACCCCTCTGGAAC	71	2813
1338125	N/A	N/A	45025	45044	GGAGCCCATTTCCCAAGTTC	50	2814
1338224	N/A	N/A	63220	63239	CCAGGTTTATGATCGAGGGA	18	2815
1338263	N/A	N/A	89659	89678	AAGGTCTTCACAGGCCACCT	29	2816
1338305	N/A	N/A	19228	19247	CCTTCCCTCTCATCCTATAG	77	2817
			19274	19293			
1338320	N/A	N/A	32379	32398	TCTGCTAATCCCCCTCACCA	54	2818
1338362	N/A	N/A	17757	17776	TTTACAAATCTTCATGGTCC	37	2819
1338588	4539	4558	94918	94937	AGGCTTTGCTTTAAAAGGTA	18	2820
1338612	2540	2559	79454	79473	TGCGGGATCTGTAGTAGGCC	51	2821
1338623	N/A	N/A	74292	74311	AGACTCTGCCACTCCTGCAC	52	2822
1338640	N/A	N/A	31727	31746	TGCAGACCCAACTTCCACTT	36	2823
1338736	N/A	N/A	66027	66046	TGACGAGGCTCCACTGCCTT	51	2824
1338745	N/A	N/A	71267	71286	GCACCATCACCCAACAGCAT	47	2825
1338787	N/A	N/A	78692	78711	CGGCCACAGATTATAACCCA	46	2826
1338808	N/A	N/A	67953	67972	GAATGGTCCACCCCAGACGA	26	2827
1338832	N/A	N/A	84247	84266	ATGCATGTCACCCCACCAGC	47	2828
1338870	N/A	N/A	31129	31148	TTCAACTGCTCAGCGAACTT	45	2829
1338878	N/A	N/A	22305	22324	AGAGACATCCCCACCGCAAC	64	2830
1338910	N/A	N/A	76762	76781	ACATGGCCCCATACAGGCAC	56	2831
1338976	N/A	N/A	23017	23036	GCCCCTAAACCACCACTGCC	41	2832
1339009	N/A	N/A	90957	90976	AAACAGGTCCCTCCCGAGCT	39	2833
1339026	N/A	N/A	18222	18241	CACTTCCTGCCCAATATCGG	42	2834
1339034	N/A	N/A	45700	45719	GCGGCACACACTATAGCCTC	46	2835
1339075	N/A	N/A	69900	69919	GCTGACAGCTTCTCCTGGCC	39	2836
1339078	N/A	N/A	29823	29842	AGGATGGTCATCCTTCGGCT	24	2837
1339079	N/A	N/A	82053	82072	GGTGGTGCCCTTCATGGAGC	40	2838
1339089	N/A	N/A	49279	49298	GTCTGCTCACCTCACTTGCT	47	2839
1339139	N/A	N/A	48106	48125	TCTCCGAGCACCACCACAAA	69	2840
1339164	N/A	N/A	55785	55804	CAGAGCTCTAACACCTGGGA	11	2841
1339193	4329	4348	94708	94727	GCTGCTTCTAACTTCCAGAA	26	2842
1339197	N/A	N/A	50558	50577	TTGTCACTGTCCACCAGGGC	31	2843
1339203	N/A	N/A	51907	51926	TCCGTCACACCCAGCAGACA	48	2844
1339204	N/A	N/A	19887	19906	ATGCCAGACTCACCCAACCC	50	2845
1339233	N/A	N/A	39301	39320	GCCCAACCATCCCCAGAGGA	63	2846

1339237	N/A	N/A	60880	60899	GCTGGAGGCCCTCGCAGCTC	39	2847
1339240	N/A	N/A	8840	8859	GCTCAGAAAATGACCAACTC	40	2848
			37284	37303			
1339245	N/A	N/A	87149	87168	CCCGTATTCTTCCTGAAGAC	28	2849
1339257	N/A	N/A	75811	75830	CTGTTGTCCCCAGCAGGCCA	179	2850
1339273	N/A	N/A	68939	68958	GAACTCTACCTTCAGCCCGT	48	2851
1339317	N/A	N/A	92695	92714	TCTGCCCGTCCTCTCCCCTT	40	2852
1339366	N/A	N/A	24676	24695	GATGCTCTCACCAGGAGCCT	45	2853
1339387	N/A	N/A	30630	30649	GCTGCGGCCCTCACTCTCCG	51	2854
1339400	N/A	N/A	91720	91739	CTCCGACCTTTACTCCAGGC	24	2855
1339452	N/A	N/A	82963	82982	GACCCAAACTTCAAGCCACC	61	2856
1339485	N/A	N/A	54406	54425	CAGTTCTCCTTCTCAAACTC	21	2857
1339495	N/A	N/A	87859	87878	CTGGGACCCATCTGGACCCC	32	2858
1339510	N/A	N/A	86300	86319	TGCCAGGCACCCATAGGTCA	21	2859
1339540	N/A	N/A	68401	68420	CTAGATGGTCCACCTTGAAT	75	2860
1339555	N/A	N/A	65327	65346	TCAAGGGCTTTTACTGGTGC	22	2861
1339562	N/A	N/A	27832	27851	GCATATATTCAATCAACTTA	38	2862
1339627	N/A	N/A	37502	37521	GTTTCTGACCTCACTAGGCC	30	2863

Table 38. Reduction of KCNT1 RNA by 4,000 nM 5-10-5 MOE gapmers with a mixed backbone measured with human KCNT1 primer probe set RTS39496

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	KCNT1 (% UTC)	SEQ ID No.
1080855	3854	3873	94233	94252	GTCACGCTAGTGCCACCGTG	20	283
1081057	N/A	N/A	67950	67969	TGGTCCACCCCAGACGATCC	13	161
			68546	68565			
1337381	N/A	N/A	17747	17766	TTCATGGTCCTCATGGATAC	24	2864
1337408	N/A	N/A	18201	18220	AGGATCTCCCAGGGCTGCCG	20	2865
1337413	4525	4544	94904	94923	AAGGTAAGTGTAAAATGGTC	51	2866
1337438	N/A	N/A	39255	39274	AGCACCAGACACCAGCCCAA	51	2867
1337440	N/A	N/A	8835	8854	GAAAATGACCAACTCACTGG	81	2868
			37279	37298			
1337455	N/A	N/A	27237	27256	GGCCCTGTTCAAACACTATA	54	2869
1337524	N/A	N/A	90922	90941	TCAGGAGGCCCTTCAAGCTC	42	2870
1337553	N/A	N/A	47080	47099	AACATCGCCATTCCCAGAGT	101	2871
1337564	3839	3858	94218	94237	CCGTGTCCTCACACGCTCCT	15	2872
1337634	N/A	N/A	85147	85166	GAGGCGGTACATCCACGGGC	50	2873
1337642	N/A	N/A	45676	45695	GCAGACGCATCCATTTCCTC	47	2874
1337651	4299	4318	94678	94697	ACAGCAAACAGCCCAGGGTC	46	2875
1337652	N/A	N/A	57161	57180	AGGGCACTCACCTGGATCGC	92	2876

1337994	N/A	N/A	31721	31740	CCCAACTTCCACTTTGCAAA	69	2877
1337999	N/A	N/A	32359	32378	CGTGTGGTCCCCCTCGCCAC	52	2878
1338069	N/A	N/A	82863	82882	TCCCTGTCCACACAGGGTCA	80	2879
1338086	N/A	N/A	33841	33860	ATATGGCTCCTACTCCACCT	47	2880
1338092	N/A	N/A	86291	86310	CCCATAGGTCAAAAAGGGCC	39	2881
1338100	N/A	N/A	24542	24561	CGAGGCATAAACACACTTAC	31	2882
1338179	N/A	N/A	60826	60845	ACCCTGCTTTCAGCTGGGCC	57	2883
1338182	N/A	N/A	37492	37511	TCACTAGGCCTCCATGCACC	60	2884
1338208	N/A	N/A	23015	23034	CCCTAAACCACCACTGCCCC	85	2885
1338264	N/A	N/A	26411	26430	TCTCTGGCCACCACAAGGCT	66	2886
1338288	N/A	N/A	78690	78709	GCCACAGATTATAACCCACA	66	2887
1338321	N/A	N/A	36574	36593	GACAAGAGAACATCTGTGCC	38	2888
1338335	N/A	N/A	31121	31140	CTCAGCGAACTTAATTATAT	39	2889
1338336	N/A	N/A	55749	55768	CCCTCCCCACCTACTGCGGA	44	2890
1338400	N/A	N/A	54394	54413	TCAAACTCTCCTAGTGGGTT	21	2891
1338403	N/A	N/A	93323	93342	CAGATCTTCATAGCAACCCA	35	2892
1338425	N/A	N/A	20548	20567	GGCACTTCCACCTTACCCAG	24	2893
1338434	N/A	N/A	18669	18688	GGCACACAACCCATGTGCCC	83	2894
1338438	N/A	N/A	42376	42395	CCCAAGTCCCATAAGATGCT	41	2895
1338471	N/A	N/A	34971	34990	TGCCGGAATCCTCACCCTTA	40	2896
1338476	N/A	N/A	51894	51913	GCAGACAGCCGACCCAGCCT	50	2897
1338515	N/A	N/A	75728	75747	TGGGCTGTCATTACAGTGTG	36	2898
1338517	N/A	N/A	50534	50553	GGCTGTGACACCCAGTGGGT	45	2899
1338518	N/A	N/A	44948	44967	CCCAGAGGCACCAGCGGGTA	75	2900
1338576	N/A	N/A	76709	76728	ACATGCGCACAGAAATGAAC	80	2901
1338636	N/A	N/A	74163	74182	GGCAGAGTGCCTACTGCGCA	41	2902
1338657	N/A	N/A	66019	66038	CTCCACTGCCTTGCCACACA	24	2903
1338694	N/A	N/A	63147	63166	GGTGAATCAAAGCCAAGCCG	14	2904
1338818	N/A	N/A	82024	82043	AGAAAGCCAATTCCAGCTCA	66	2905
1338824	N/A	N/A	71123	71142	GCGCCCTGCCCCAGACGCAC	16	2906
			71163	71182			
			71283	71302			
1338826	N/A	N/A	89623	89642	CCTCTGAGTCTCCTTCGGGC	38	2907
1338886	N/A	N/A	59222	59241	GGCTCACCCACCGTGATGAT	65	2908
1338967	N/A	N/A	19884	19903	CCAGACTCACCCAACCCTAC	52	2909
1338999	N/A	N/A	77546	77565	TGTGGCTCTCCCTTGCAGAA	49	2910
1339081	N/A	N/A	62094	62113	GACCCACCATCTCCCCAGAA	61	2911
1339102	N/A	N/A	43242	43261	TGCATCTCCCGATATAGCCC	32	2912
1339117	N/A	N/A	65191	65210	GTCAGCGGCATCACTGTCCC	61	2913
1339184	N/A	N/A	56450	56469	GCAGGTGCCTTCCTTTGCCG	9	2914
1339192	N/A	N/A	91718	91737	CCGACCTTTACTCCAGGCCT	12	2915
1339201	N/A	N/A	68299	68318	CAGCCCACCCCAGATGGTCC	42	2916
1339229	N/A	N/A	29746	29765	GTGGGCCCCACCTCTGTCCG	41	2917

1339242	N/A	N/A	21430	21449	CATGCATCCCCCGACATACA	52	2918
1339270	N/A	N/A	87844	87863	ACCCCAGCACATCCTGGCCT	41	2919
1339296	N/A	N/A	79253	79272	TCCCAGACCCCTCACCAAAC	103	2920
1339314	N/A	N/A	48099	48118	GCACCACCACAAAAAGGAGA	64	2921
1339328	N/A	N/A	30557	30576	GGGAGATGCCTCCCACTTCC	69	2922
1339386	N/A	N/A	69863	69882	CCCATGGTGCTTCCTAGGGC	16	2923
1339412	N/A	N/A	92479	92498	GCTTCAGGCCTTTCGCACAC	17	2924
1339425	N/A	N/A	68901	68920	AGCAGCTGACTCTCCCGCCC	37	2925
1339459	N/A	N/A	33010	33029	AATTGCTAAACCACACTTTT	43	2926
1339473	N/A	N/A	48764	48783	ACCATCGCCCCACACTCCAC	69	2927
1339503	N/A	N/A	19224	19243	CCCTCTCATCCTATAGACAC	54	2928
			19270	19289			
1339548	N/A	N/A	40302	40321	AGCTCCATTACCTCTGCTCT	29	2929
1339556	N/A	N/A	49203	49222	TGACCAGACCCCAGAATCTC	66	2930
1339559	N/A	N/A	22303	22322	AGACATCCCCACCGCAACCC	69	2931
1339608	N/A	N/A	53303	53322	GCTCCAGCCTTTCCGTGGAC	9	2932
1339611	N/A	N/A	40862	40881	CGCTGTCTAATCAGCTCCCA	40	2933
1339623	N/A	N/A	27828	27847	ATATTCAATCAACTTAGGAC	61	2934
1339633	N/A	N/A	58431	58450	TGAAAGACCCTCTCTGGTCT	80	2935
1339634	N/A	N/A	84245	84264	GCATGTCACCCCACCAGCAG	61	2936
1339636	N/A	N/A	23675	23694	CCTGCCAGAACTTTTGGACA	41	2937
1339638	N/A	N/A	72652	72671	GGGTCAGCCCACAAGCCTCA	48	2938
1339661	N/A	N/A	87135	87154	GAAGACTCCCCTGAGCCTCT	12	2939

Example 2: Effect of modified oligonucleotides on human KCNT1 RNA *in vitro*, multiple doses

Modified oligonucleotides selected from the example above were tested at various doses in SH-SY5Y cells. Cultured SH-SY5Y cells at a density of 20,000 cells per well were treated with modified oligonucleotide at various doses by electroporation, as specified in the tables below. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and KCNT1 RNA levels were measured by quantitative real-time RTPCR. Human KCNT1 primer probe set RTS39508 (forward sequence GTCAACGTGCAGACCATGT, designated herein as SEQ ID NO: 11; reverse sequence TCGCTCCCTCTTTTCTAGTTTG, designated herein as SEQ ID NO: 12; probe sequence AGCTCACCCACCCTTCCAACATG, designated herein as SEQ ID NO: 13) was used to measure RNA levels presented in Tables 39-42 and human KCNT1 primer probe set RTS39496 (forward sequence CAGGTGGAGTTCTACGTCAA, designated herein as SEQ ID NO: 14; reverse sequence GAGAAGTTGAACAGCCGGAT, designated herein as SEQ ID NO: 15; probe sequence TGATGAAGAACAGCTTGAGCCGCT, designated herein as SEQ ID NO: 16) was used to measure RNA levels presented in Tables 43-60. Each table represents results from an individual assay plate. KCNT1 RNA levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented in the tables below as percent reduction of the amount of KCNT1 RNA, relative to untreated

control. The half maximal inhibitory concentration (IC_{50}) of each modified oligonucleotide is also presented. IC_{50} was calculated using a linear regression on a log/linear plot of the data in Excel. In some cases, when the IC_{50} could not be reliably calculated, it is indicated as N.C. (Not Calculated).

Table 39. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39508

Compound No.	%UTC				IC50 (μM)
	94 nM	375 nM	1500 nM	6000 nM	
1080715	88	79	46	25	1.4
1080740	76	54	46	14	0.6
1080846	98	106	32	17	1.3
1080847	84	63	36	23	0.8
1080852	76	62	33	17	0.6
1080858	101	83	57	25	1.8
1080859	79	51	30	19	0.5
1080865	117	85	50	24	1.7
1080888	65	53	26	15	0.3
1080889	72	46	23	16	0.3
1080894	80	74	36	16	0.8
1080895	85	74	39	15	0.9
1080978	85	67	49	26	1.2
1080996	91	85	72	17	2.0
1081080	96	92	43	21	1.4
1081092	66	56	54	15	0.6
1081093	104	55	20	12	0.7
1081135	83	57	28	13	0.6
1081148	97	73	42	32	1.5

Table 40. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39508

Compound No.	%UTC				IC50 (μM)
	94 nM	375 nM	1500 nM	6000 nM	
1080722	106	109	48	36	2.6
1080723	90	54	28	13	0.6
1080741	98	111	61	35	3.5
1080753	135	108	62	26	2.6
1080818	76	53	41	19	0.6
1080854	100	74	44	16	1.1
1080878	71	53	31	15	0.4
1080890	86	77	44	25	1.3
1080896	83	88	49	22	1.4

1080902	112	92	46	18	1.5
1080992	75	84	72	42	N.C.
1081040	88	88	40	14	1.1
1081052	76	68	32	20	0.7
1081057	72	61	24	16	0.5
1081076	76	77	55	26	1.5
1081100	81	75	31	12	0.7
1081136	94	72	46	16	1.1
1081147	79	74	34	13	0.8
1081148	105	89	56	25	2.0

Table 41. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39508

Compound No.	%UTC				IC50 (μM)
	94 nM	375 nM	1500 nM	6000 nM	
1080706	97	59	58	29	1.5
1080806	131	138	126	71	N.C.
1080819	69	67	59	29	1.5
1080831	115	71	37	37	1.6
1080855	53	39	33	16	0.1
1080862	77	41	15	9	0.3
1080891	76	52	29	16	0.5
1080892	140	66	33	9	1.1
1080903	97	55	31	19	0.8
1080944	120	123	103	85	N.C.
1080952	132	76	53	23	1.7
1080962	80	122	76	43	N.C.
1081016	98	95	77	59	N.C.
1081023	80	91	38	31	1.5
1081028	104	112	72	29	3.4
1081064	107	97	55	33	2.5
1081089	88	66	28	15	0.7
1081107	84	82	52	36	2.2
1081148	88	79	66	23	1.9

Table 42. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39508

Compound No.	%UTC				IC50 (μM)
	94 nM	375 nM	1500 nM	6000 nM	
1080707	101	96	74	29	3.2
1080720	99	57	26	15	0.7
1080779	74	87	46	21	1.2

1080821	92	91	63	18	1.8
1080844	107	111	47	40	2.9
1080851	95	50	23	9	0.6
1080856	103	52	40	24	1.0
1080857	97	61	32	16	0.8
1080863	99	56	33	16	0.8
1080958	96	95	62	41	3.8
1080976	91	100	66	33	3.3
1080977	163	92	60	18	2.0
1081043	81	67	41	16	0.8
1081048	124	120	67	33	3.4
1081072	105	89	69	47	5.4
1081084	111	75	28	21	1.1
1081085	67	56	29	8	0.4
1081145	77	44	24	11	0.4
1081148	114	89	50	34	2.2

Table 43. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	110	52	35	36	1.0
1337226	65	49	35	23	0.3
1337327	58	38	19	23	0.1
1337329	62	47	25	15	0.2
1337332	75	36	24	7	0.3
1337575	84	65	30	13	0.6
1338042	99	56	28	6	0.6
1338312	90	62	22	11	0.5
1338475	78	37	31	9	0.3
1338533	44	48	37	16	< 0.1
1338584	109	58	29	24	0.8
1339151	97	88	47	26	1.4
1339156	93	70	19	24	0.7
1339160	89	87	39	26	1.1
1339168	91	83	47	33	1.5
1339194	89	59	28	16	0.6
1339451	95	77	41	21	1.0
1339481	77	47	16	8	0.3
1339491	85	60	48	14	0.7

Table 44. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	312 nM	1250 nM	5000 nM	
1080855	82	49	22	19	0.4
1337259	76	67	41	12	0.6
1337266	88	63	34	14	0.6
1337483	67	56	36	26	0.4
1337702	78	65	36	22	0.6
1337728	69	63	29	16	0.4
1337794	84	32	12	3	0.2
1337803	81	46	23	7	0.3
1338185	66	60	34	22	0.4
1338229	64	44	20	13	0.2
1338679	103	90	52	36	2.0
1338911	87	68	35	17	0.7
1338969	78	50	32	10	0.4
1339055	92	58	29	16	0.6
1339128	95	88	56	26	1.6
1339372	86	50	23	9	0.4
1339479	83	56	27	22	0.5
1339525	65	46	14	14	0.2
1339573	91	72	35	29	1.0

Table 45. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	312 nM	1250 nM	5000 nM	
1080855	110	49	22	23	0.7
1080862	73	42	23	17	0.3
1080878	84	68	36	22	0.7
1337279	98	81	52	20	1.2
1337488	83	82	35	15	0.8
1337603	98	73	24	15	0.7
1337640	102	77	48	25	1.2
1337648	59	32	25	14	0.1
1337681	73	69	43	10	0.6
1337837	77	81	35	14	0.7
1337916	91	72	46	17	0.9
1338005	94	70	30	21	0.8
1338107	97	71	35	21	0.9
1338237	84	65	33	18	0.6
1338313	79	52	32	12	0.4
1338333	81	62	33	16	0.6
1338427	100	85	31	19	0.9

1338577	111	52	31	25	0.8
1339030	105	75	32	23	1.0

Table 46. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	85	48	22	14	0.4
1081085	73	31	13	7	0.2
1337229	112	91	64	28	2.1
1337304	72	38	15	6	0.2
1337393	125	72	20	11	0.8
1337500	96	49	28	16	0.5
1337618	57	35	10	9	0.1
1337714	106	63	39	14	0.8
1338087	83	71	32	11	0.6
1338188	84	75	50	30	1.3
1338537	77	46	36	20	0.4
1338574	75	56	43	15	0.5
1338660	88	70	24	6	0.5
1338686	87	57	26	8	0.5
1338800	60	35	10	4	0.1
1338887	107	86	54	27	1.6
1338990	97	72	39	27	1.0
1339227	76	42	22	7	0.3
1339431	101	40	18	12	0.4

Table 47. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	73	46	19	21	0.3
1337542	51	40	17	7	0.1
1337683	75	42	14	5	0.2
1337722	78	49	27	11	0.4
1337814	52	37	26	12	0.1
1337976	105	57	25	18	0.7
1338215	76	48	29	13	0.4
1338315	71	46	26	7	0.3
1338356	78	50	23	11	0.4
1338442	64	49	18	12	0.2
1338453	69	73	24	8	0.4
1338784	76	54	24	17	0.4

1338789	90	64	25	10	0.5
1338823	87	70	37	29	0.9
1338830	101	76	42	28	1.2
1339073	78	38	18	15	0.3
1339312	73	50	22	17	0.3
1339437	60	41	26	19	0.2
1339529	61	53	20	14	0.2

Table 48. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	106	58	64	39	2.1
1337285	79	70	39	32	0.9
1337334	98	80	59	40	2.5
1337447	103	99	65	32	2.5
1337827	91	86	49	20	1.2
1337899	77	57	18	15	0.4
1337919	92	83	64	35	2.5
1338010	79	57	35	37	0.7
1338094	93	85	68	26	1.9
1338199	93	65	48	18	0.9
1338226	113	94	73	33	2.8
1338504	76	54	28	9	0.4
1339039	99	107	62	38	3.1
1339072	87	77	53	33	1.6
1339318	78	50	50	20	0.6
1339436	88	82	48	37	1.7
1339456	106	88	51	31	1.7
1339609	123	113	59	38	2.8
1339639	93	72	45	29	1.2

Table 49. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	102	51	33	15	0.6
1080889	65	48	28	8	0.3
1337223	93	49	23	6	0.4
1337278	91	92	59	33	2.2
1337320	78	40	21	3	0.3
1337449	140	63	29	26	1.1

1337501	83	47	19	8	0.3
1337724	89	69	41	15	0.8
1338119	90	86	64	25	1.8
1338307	105	97	45	18	1.3
1338473	94	50	31	11	0.5
1338485	80	60	24	15	0.5
1338564	113	96	45	14	1.2
1338719	71	42	21	7	0.2
1338862	95	62	25	11	0.6
1338924	80	49	19	17	0.4
1339021	84	52	19	13	0.4
1339258	94	59	11	6	0.4
1339432	79	35	15	11	0.2

Table 50. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
855082	79	51	30	15	0.4
1080855	109	74	30	23	1.0
1337509	60	37	19	15	0.1
1337596	96	53	36	14	0.6
1337786	76	62	32	22	0.5
1338586	97	80	44	18	1.0
1338646	71	62	31	18	0.5
1338682	95	83	33	14	0.8
1338688	97	73	25	12	0.7
1338691	76	56	21	16	0.4
1338922	113	77	46	17	1.1
1338931	118	76	34	30	1.2
1338935	83	60	25	14	0.5
1338945	78	43	27	10	0.3
1338946	86	76	32	11	0.7
1338953	88	62	21	8	0.5
1339001	67	40	25	17	0.2
1339369	59	42	18	9	0.1
1339370	83	50	18	6	0.4

Table 51. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	

1080855	103	51	38	14	0.7
1337426	84	64	38	14	0.6
1337591	109	57	28	16	0.7
1337697	47	29	19	11	< 0.1
1337777	63	44	27	18	0.2
1337784	83	63	41	25	0.8
1337997	102	81	53	37	1.9
1338036	77	40	22	10	0.3
1338147	95	69	30	17	0.7
1338351	85	51	39	26	0.6
1338690	78	49	28	18	0.4
1338751	65	47	27	17	0.2
1338795	65	35	16	26	0.1
1338843	75	64	35	12	0.5
1338895	85	75	47	22	1.0
1338936	60	39	17	15	0.1
1339278	81	51	30	9	0.4
1339351	77	59	33	12	0.5
1339496	79	50	30	4	0.4

Table 52. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	99	44	27	14	0.5
1337314	107	75	26	7	0.7
1337421	108	75	54	22	1.3
1337445	87	48	19	10	0.4
1337482	111	52	31	17	0.7
1337757	121	76	29	12	0.9
1337812	107	97	37	16	1.1
1337825	75	50	29	6	0.3
1338068	119	95	64	30	2.2
1338116	88	78	35	8	0.7
1338378	87	72	32	9	0.6
1338491	78	28	12	2	0.2
1338650	84	51	26	8	0.4
1338742	112	66	25	10	0.7
1339058	95	61	36	18	0.7
1339191	113	90	62	28	1.9
1339308	87	45	19	7	0.4
1339329	84	51	27	13	0.4
1339531	96	69	32	13	0.7

Table 53. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	101	57	32	21	0.7
1080859	91	62	39	25	0.8
1337299	113	75	29	16	0.9
1337356	101	104	73	34	3.3
1337442	86	53	31	17	0.5
1337505	78	54	23	7	0.4
1338008	99	79	60	27	1.6
1338151	67	54	22	16	0.3
1338382	120	70	52	26	1.4
1338437	89	72	59	33	1.7
1338454	97	53	41	18	0.7
1338624	97	87	60	28	1.8
1338681	92	63	37	9	0.6
1338912	112	72	38	37	1.4
1339049	85	52	27	15	0.5
1339110	91	65	43	13	0.7
1339112	113	71	29	14	0.8
1339360	86	72	33	14	0.7
1339416	94	93	53	27	1.6

Table 54. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	113	59	29	20	0.8
1337294	77	55	24	22	0.4
1337416	75	50	22	8	0.3
1337459	55	32	17	13	0.1
1337761	90	73	35	16	0.8
1337832	91	63	18	21	0.6
1338096	91	53	30	12	0.5
1338233	**76**	**57**	**23**	21	0.4
1338344	88	78	44	16	0.9
1338416	82	67	38	15	0.6
1338458	86	47	31	17	0.5
1338778	82	47	27	17	0.4
1338809	78	63	41	17	0.6
1338841	35	23	12	7	< 0.1

1338904	105	80	42	18	1.1
1339418	75	88	53	25	1.4
1339513	74	46	17	16	0.3
1339517	50	30	17	7	< 0.1
1339581	86	49	24	21	0.5

Table 55. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	84	49	35	14	0.5
1337235	70	44	30	22	0.3
1337374	103	81	44	23	1.2
1337379	83	63	46	25	0.9
1337566	54	46	19	11	0.1
1337841	77	66	44	19	0.7
1337870	73	47	23	6	0.3
1338013	62	33	14	6	0.1
1338170	77	66	32	18	0.6
1338184	104	98	52	26	1.7
1338337	89	88	73	37	3.6
1338484	84	77	50	24	1.1
1338891	67	45	25	14	0.2
1338991	82	73	47	24	1.0
1339152	83	44	27	20	0.4
1339254	68	55	27	15	0.3
1339315	71	52	23	11	0.3
1339401	88	42	36	16	0.5
1339493	72	62	33	10	0.4

Table 56. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	117	37	14	10	0.5
1337282	80	64	28	14	0.5
1337399	47	54	29	10	0.1
1337637	88	52	34	14	0.5
1337940	64	36	20	13	0.2
1337972	96	49	21	7	0.5
1338045	85	56	42	14	0.6
1338190	78	54	23	6	0.4

1338630	78	50	12	4	0.3
1338994	73	64	24	12	0.4
1339000	67	37	17	4	0.2
1339041	63	39	11	7	0.2
1339092	85	56	24	5	0.4
1339188	145	99	43	12	1.3
1339247	81	58	17	10	0.4
1339255	83	51	17	8	0.4
1339409	72	40	21	9	0.2
1339532	66	65	17	3	0.3
1339612	50	25	19	7	< 0.1

Table 57. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	77	42	29	19	0.3
1081135	93	38	35	11	0.5
1337627	69	39	25	11	0.2
1337706	77	102	39	20	1.1
1337715	72	74	48	27	1.0
1337783	98	71	41	18	0.9
1337867	80	70	43	22	0.8
1337970	86	41	6	9	0.3
1338319	69	47	33	17	0.3
1338510	103	82	56	24	1.5
1338524	90	73	43	27	1.0
1338652	72	64	36	10	0.5
1338693	74	65	36	21	0.6
1338850	96	76	30	24	0.9
1338925	100	98	60	14	1.5
1339068	94	86	49	25	1.4
1339195	88	52	22	12	0.4
1339335	69	42	18	11	0.2
1339643	72	47	25	16	0.3

Table 58. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080740	120	67	34	13	0.9
1080818	104	76	31	14	0.8

1080855	66	58	25	29	0.4
1337252	90	75	52	20	1.1
1337265	72	62	33	28	0.6
1337460	99	90	64	49	4.7
1337518	96	62	56	15	0.9
1337657	76	56	21	23	0.4
1337792	112	91	44	51	2.7
1337887	73	53	33	12	0.4
1337982	101	90	36	16	1.0
1338366	94	112	51	23	1.7
1338394	117	104	85	46	> 5.0
1338692	83	59	27	19	0.5
1338740	90	64	45	23	0.9
1338894	81	67	51	23	0.9
1339012	116	73	28	20	0.9
1339236	105	43	21	8	0.5
1339572	105	71	35	43	1.4

Table 59. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080852	117	69	40	55	2.3
1080855	109	69	45	31	1.3
1081145	84	63	48	19	0.8
1337306	99	80	44	26	1.2
1337504	82	52	41	13	0.5
1337897	115	84	53	29	1.6
1338224	95	64	34	20	0.7
1338246	95	95	63	38	2.9
1338588	69	58	36	23	0.5
1338965	95	97	43	19	1.2
1339078	81	56	50	28	0.9
1339164	78	40	21	12	0.3
1339184	79	53	22	22	0.4
1339400	89	69	33	23	0.8
1339485	113	70	31	14	0.8
1339510	121	79	51	28	1.5
1339555	139	87	37	23	1.3
1339608	92	38	17	12	0.4
1339620	115	72	52	22	1.3

Table 60. Dose-dependent percent reduction of human KCNT1 RNA by modified oligonucleotides measured with human KCNT1 primer probe set RTS39496

Compound Number	KCNT1 (% UTC)				IC_{50} µM
	78 nM	313 nM	1250 nM	5000 nM	
1080855	165	60	35	16	1.1
1081057	69	49	20	14	0.3
1337330	106	78	33	24	1.0
1337408	86	55	20	18	0.5
1337564	61	48	32	18	0.2
1337635	51	28	7	13	< 0.1
1337932	53	40	23	11	0.1
1338428	110	83	51	39	2.0
1338599	92	73	35	22	0.8
1338694	85	51	26	20	0.5
1338704	103	53	25	8	0.5
1338824	94	47	24	9	0.4
1339192	69	51	58	19	0.6
1339291	69	43	24	25	0.3
1339376	86	90	51	21	1.3
1339386	96	43	25	7	0.4
1339412	80	50	35	13	0.4
1339504	79	66	57	25	1.1
1339661	63	22	26	29	< 0.1

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CLAIMS

1. A modified oligonucleotide consisting of 20 linked nucleosides, wherein the modified oligonucleotide has the nucleobase sequence of 5'-GGTCCACCCCAGACGATCCA– 3' (SEQ ID NO: 2423), wherein the modified oligonucleotide has a sugar motif of 5' – eeeeeddddddddddeeeee – 3', wherein
e is a 2'-$O(CH_2)_2OCH_3$ ribosyl sugar moiety; and
d is a 2'-β-D-deoxyribosyl sugar moiety; and
wherein the modified oligonucleotide has an internucleoside linkage motif of 5' – soooosssssssssooss – 3', wherein
s is a phosphorothioate internucleoside linkage; and
o is a phosphodiester internucleoside linkage; and
wherein each C is a 5-methylcytosine nucleobase.

2. A modified oligonucleotide consisting of 20 linked nucleosides, wherein the modified oligonucleotide has the nucleobase sequence of 5'-GCATCCATTTAATAGAAGTT- 3' (SEQ ID NO: 1188), wherein the modified oligonucleotide has a sugar motif of 5' – eeeeeddddddddddeeeee – 3', wherein
e is a 2'-$O(CH_2)_2OCH_3$ ribosyl sugar moiety; and
d is a 2'-β-D-deoxyribosyl sugar moiety; and
wherein the modified oligonucleotide has an internucleoside linkage motif of 5' – soooosssssssssooss – 3', wherein
s is a phosphorothioate internucleoside linkage; and
o is a phosphodiester internucleoside linkage; and
wherein each C is a 5-methylcytosine nucleobase.

3. A modified oligonucleotide consisting of 20 linked nucleosides, wherein the modified oligonucleotide has the nucleobase sequence of 5'-CACAATTCTCAAACTGCTCC- 3' (SEQ ID NO: 1330), wherein the modified oligonucleotide has a sugar motif of 5' – eeeeeddddddddddeeeee – 3', wherein
e is a 2'-$O(CH_2)_2OCH_3$ ribosyl sugar moiety; and
d is a 2'-β-D-deoxyribosyl sugar moiety; and
wherein the modified oligonucleotide has an internucleoside linkage motif of 5' – soooosssssssssooss – 3', wherein
s is a phosphorothioate internucleoside linkage; and

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o is a phosphodiester internucleoside linkage; and
wherein each C is a 5-methylcytosine nucleobase.

4. A modified oligonucleotide consisting of 20 linked nucleosides,
wherein the modified oligonucleotide has the nucleobase sequence of 5'-TCACCTGTTTTACTGAGCCT- 3' (SEQ ID NO: 1387), wherein the modified oligonucleotide has a sugar motif of 5' – eeeeeddddddddddeeeee – 3', wherein
e is a 2'-$O(CH_2)_2OCH_3$ ribosyl sugar moiety; and
d is a 2'-β-D-deoxyribosyl sugar moiety; and
wherein the modified oligonucleotide has an internucleoside linkage motif of 5' – soooosssssssssooss – 3', wherein
s is a phosphorothioate internucleoside linkage; and
o is a phosphodiester internucleoside linkage; and
wherein each C is a 5-methylcytosine nucleobase.

5. A modified oligonucleotide consisting of 20 linked nucleosides,
wherein the modified oligonucleotide has the nucleobase sequence of 5'-GCTCCGCTTGAATCTAAACA- 3' (SEQ ID NO: 1522), wherein the modified oligonucleotide has a sugar motif of 5' – eeeeeddddddddddeeeee – 3', wherein
e is a 2'-$O(CH_2)_2OCH_3$ ribosyl sugar moiety; and
d is a 2'-β-D-deoxyribosyl sugar moiety; and
wherein the modified oligonucleotide has an internucleoside linkage motif of 5' – soooosssssssssooss – 3', wherein
s is a phosphorothioate internucleoside linkage; and
o is a phosphodiester internucleoside linkage; and
wherein each C is a 5-methylcytosine nucleobase.

6. The modified oligonucleotide of any one of claims 1-5, which is a salt.

7. The modified oligonucleotide of claim 6, which is a sodium salt, a potassium salt, or a combination thereof.

8. An oligomeric compound comprising the modified oligonucleotide of any one of claims 1-7 and a conjugate group.

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9. A population of modified oligonucleotides of any one of claims 1-7, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

10. A population of oligomeric compounds of claim 8, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

11. A pharmaceutical composition comprising a modified oligonucleotide of any one of claims 1-7, an oligomeric compound of claim 8, a population of modified oligonucleotides of claim 9, or a population of oligomeric compounds of claim 10, and a pharmaceutically acceptable diluent.

12. The pharmaceutical composition of claim 11, wherein the pharmaceutically acceptable diluent is an artificial cerebrospinal fluid or phosphate-buffered saline (PBS).

13. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and the artificial cerebrospinal fluid.

14. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and PBS.

15. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition consists essentially of the oligomeric compound and the artificial cerebrospinal fluid.

16. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition consists essentially of the oligomeric compound and PBS.

17. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition consists essentially of the population of modified oligonucleotides and the artificial cerebrospinal fluid.

18. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition consists essentially of the population of modified oligonucleotides and PBS.

19. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition consists essentially of the population of oligomeric compounds and the artificial cerebrospinal fluid.

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20. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition consists essentially of the population of oligomeric compounds and PBS.

SEQUENCE LISTING

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<120> COMPOUNDS AND METHODS FOR REDUCING KCNT1 EXPRESSION

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