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(54) Title: COMPOSITIONS AND METHODS FOR MODULATING UTRN EXPRESSION

(57) Abstract: Aspects of the invention provide single stranded oligonucleotides for activating or enhancing expression of UTRN. Further aspects provide compositions and kits comprising single stranded oligonucleotides for activating or enhancing expression of UTRN. Methods for modulating expression of UTRN using the single stranded oligonucleotides are also provided. Further aspects of the invention provide methods for selecting a candidate oligonucleotide for activating or enhancing expression of UTRN.

COMPOSITIONS AND METHODS FOR MODULATING UTRN EXPRESSION

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit under 35 U.S.C. §119(e) of U.S. Provisional Application No. 61/647,886, entitled "COMPOSITIONS AND METHODS FOR MODULATING UTRN EXPRESSION", filed May 16, 2012, which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

The invention relates to oligonucleotide based compositions, as well as methods of using oligonucleotide based compositions for treating disease.

BACKGROUND OF THE INVENTION

Muscular dystrophy (MD) is a group of inherited diseases characterized by damage to muscle fibers and includes Duchenne's muscular dystrophy, Becker's muscular dystrophy, and myotonic dystrophy. Duchenne's muscular dystrophy (DMD) is a recessive X-linked form of muscular dystrophy resulting from mutation in the dystrophin gene. Dystrophin is a structural component of muscle tissue that stabilized the dystroglycan complex and is important for connecting the cytoskeleton of muscle fibers to the basal lamina. When dystrophin is mutated, excess calcium penetrates the cell membrane of muscle cells, causing mitochondrial damage from an influx of water. This mitochondrial damage results in increased oxidative stress and cell death, leading to necrosis of muscle fibers. The destruction of muscle fibers causes the symptoms of DMD, including gradual muscular degeneration, gait ataxia, difficulty breathing, and eventually, death. Becker's Muscular dystrophy (BMD) is a less severe form of muscular dystrophy characterized by progressive muscle weakness in the legs and pelvis. BMD is also caused by a mutation in dystrophin, but unlike DMD, some functional dystrophin is present. Myotonic dystrophy is an autosomal dominant disease characterized by wasting of the muscles, cataracts, heart conduction defects, endocrine changes, and myotonia. Utrophin, encoded by the UTRN gene, is a component of the cytoskeleton located at the neuromuscular synapse and myotendinous junctions, and is involved in membrane maintenance and acetylchoine receptor clustering. Utrophin has homology with dystrophin, especially in the actin binding domain, and can

partially compensate for a lack of dystrophin in mice.

SUMMARY OF THE INVENTION

Aspects of the invention disclosed herein provide methods and compositions that are useful for overexpression of Utrophin (UTRN) for the treatment and/or prevention of diseases associated with reduced expression of UTRN, or for which enhanced expression of UTRN would be beneficial *(e.g.,* muscular dystrophies, including Duchenne muscular dystrophy (DMD), Becker Muscular Dystrophy (BMD), and myotonic dystrophy). In certain aspects, the invention provides methods and compositions that are useful for upregulating UTRN in a cell. In some embodiments, the methods and compositions are useful for the treatment and/or prevention *(e.g.,* reducing the risk or delaying the onset) of muscular dystrophies, including DMD, BMD, and myotonic dystrophy. In some embodiments, single stranded oligonucleotides are provided that target a PRC2-associated region of a UTRN gene (e.g., human UTRN) and thereby cause upregulation of the gene. In some embodiments, single stranded oligonucleotides are provided that target a PRC2-associated region of the gene encoding UTRN. In some embodiments, these single stranded oligonucleotides activate or enhance expression of UTRN by relieving or preventing PRC2 mediated repression of UTRN.

Further aspects of the invention provide methods for selecting oligonucleotides for activating or enhancing expression of UTRN. In some embodiments, methods are provided for selecting a set of oligonucleotides that is enriched in candidates *(e.g.,* compared with a random selection of oligonucleotides) for activating or enhancing expression of UTRN. Accordingly, the methods may be used to establish sets of clinical candidates that are enriched in oligonucleotides that activate or enhance expression of UTRN. Such libraries may be utilized, for example, to identify lead oligonucleotides for developing therapeutics to treat UTRN. Furthermore, in some embodiments, oligonucleotide chemistries are provided that are useful for controlling the pharmacokinetics, biodistribution, bioavailability and/or efficacy of the single stranded oligonucleotides for activating expression of UTRN.

According to some aspects of the invention single stranded oligonucleotides are provided that have a region of complementarity that is complementarty with *(e.g.,* at least 8 consecutive nucleotides of) a PRC2-associated region of a UTRN gene, e.g., a PRC2-

associated region of the nucleotide sequence set forth as SEQ ID NO: 1 or 2. In some embodiments, the oligonucleotide has at least one of the following features: a) a sequence that is 5'X-Y-Z, in which X is any nucleotide and in which X is at the 5' end of the oligonucleotide, Y is a nucleotide sequence of 6 nucleotides in length that is not a human seed sequence of a microRNA, and Z is a nucleotide sequence of 1 to 23 nucleotides in length; b) a sequence that does not comprise three or more consecutive guanosine nucleotides; c) a sequence that has less than a threshold level of sequence identity with every sequence of nucleotides, of equivalent length to the second nucleotide sequence, that are between 50 kilobases upstream of a 5'-end of an off-target gene and 50 kilobases downstream of a 3'-end of the off-target gene; d) a sequence that is complementary to a PRC2-associated region that encodes an RNA that forms a secondary structure comprising at least two single stranded loops; and e) a sequence that has greater than 60% G-C content. In some embodiments, the single stranded oligonucleotide has at least two of features a), b), c), d), and e), each independently selected. In some embodiments, the single stranded oligonucleotide has at least three of features a), b), c), d), and e), each independently selected. In some embodiments, the single stranded oligonucleotide has at least four of features a), b), c), d), and e), each independently selected. In some embodiments, the single stranded oligonucleotide has each of features a), b), c), d), and e). In certain embodiments, the oligonucleotide has the sequence 5'X-Y-Z, in which the oligonucleotide is 8-50 nucleotides in length.

According to some aspects of the invention, single stranded oligonucleotides are provided that have a sequence X-Y-Z, in which X is any nucleotide, Y is a nucleotide sequence of 6 nucleotides in length that is not a seed sequence of a human microRNA, and Z is a nucleotide sequence of 1 to 23 nucleotides in length, in which the single stranded oligonucleotide is complementary with a PRC2-associated region of a UTRN gene, e.g., a PRC2-associated region of the nucleotide sequence set forth as SEQ ID NO: 1 or 2. In some aspects of the invention, single stranded oligonucleotides are provided that have a sequence 5'-X-Y-Z, in which X is any nucleotide, Y is a nucleotide sequence of 6 nucleotides in length that is not a seed sequence of a human microRNA, and Z is a nucleotide sequence of 1 to 23 nucleotides in length, in which the single stranded oligonucleotide is complementary with at least 8 consecutive nucleotides of a PRC2-associated region of a UTRN gene, e.g., a PRC2-

associated region of the nucleotide sequence set forth as SEQ ID NO: 1 or 2. In some embodiments, Y is a sequence selected from Table 1. In some embodiments, the PRC2-associated region is a sequence listed in any one of SEQ ID NOS: 5 to 462.

In some embodiments, the single stranded oligonucleotide comprises a nucleotide sequence as set forth in any one of SEQ ID NOS: 463 to 497728, or a fragment thereof that is at least 8 nucleotides. In some embodiments, the single stranded oligonucleotide comprises a nucleotide sequence as set forth in any one of SEQ ID NOS: 463 to 497728, in which the 5' end of the nucleotide sequence provided is the 5' end of the oligonucleotide. In some embodiments, the region of complementarity *(e.g.,* the at least 8 consecutive nucleotides) is also present within the nucleotide sequence set forth as SEQ ID NO: 3 or 4.

In some embodiments, the single stranded oligonucleotide comprises a nucleotide sequence as set forth in any one of SEQ ID NOS: 463 to 497728. In some embodiments, the single stranded oligonucleotide comprises a fragment of at least 8 nucleotides of a nucleotide sequence as set forth in any one of SEQ ID NOS: 463 to 497728.

In some embodiments, the PRC2-associated region is a sequence listed in any one of SEQ ID NOS: 5 to 328. In some embodiments, the single stranded oligonucleotide comprises a nucleotide sequence as set forth in any one of SEQ ID NOS: 463-307980 or a fragment thereof that is at least 8 nucleotides. In some embodiments, the single stranded oligonucleotide comprises a nucleotide sequence as set forth in any one of SEQ ID NOS: 463-307980, wherein the 5' end of the nucleotide sequence provided is the 5' end of the oligonucleotide. In some embodiments, the at least 8 consecutive nucleotides are also present within the nucleotide sequence set forth as SEQ ID NO: 3.

In some embodiments, the PRC2-associated region is a sequence listed in any one of SEQ ID NOS: 329 to 462. In some embodiments, the single stranded oligonucleotide comprises a nucleotide sequence as set forth in any one of SEQ ID NOS: 306018-497728 or a fragment thereof that is at least 8 nucleotides. In some embodiments, the single stranded oligonucleotide comprises a nucleotide sequence as set forth in any one of SEQ ID NOS: 306018-497728 wherein the 5' end of the nucleotide sequence provided is the 5' end of the oligonucleotide. In some embodiments, the at least 8 consecutive nucleotides are present within the nucleotide sequence set forth as SEQ ID NO: 4. In some embodiments, a single

stranded oligonucleotide comprises a nucleotide sequence as set forth in Table 4. In some embodiments, the single stranded oligonucleotide comprises a fragment of at least 8 nucleotides of a nucleotide sequence as set forth in Table 4. In some embodiments, a single stranded oligonucleotide consists of a nucleotide sequence as set forth in Table 4.

In some embodiments, the single stranded oligonucleotide does not comprise three or more consecutive guanosine nucleotides. In some embodiments, the single stranded oligonucleotide does not comprise four or more consecutive guanosine nucleotides.

In some embodiments, the single stranded oligonucleotide is 8 to 30 nucleotides in length. In some embodiments, the single stranded oligonucleotide is up to 50 nucleotides in length. In some embodiments, the single stranded oligonucleotide is 8 to 10 nucleotides in length and all but 1, 2, or 3 of the nucleotides of the complementary sequence of the PRC2-associated region are cytosine or guanosine nucleotides.

In some embodiments, the single stranded oligonucleotide is complementary with at least 8 consecutive nucleotides of a PRC2-associated region of a UTRN gene, e.g., a PRC2-associated region of a nucleotide sequence set forth as SEQ ID NO: 1 or 2, in which the nucleotide sequence of the single stranded oligonucleotide comprises one or more of a nucleotide sequence selected from the group consisting of

(a) (X)Xxxxxx, (X)xXxxxx, (X)xxXxxx, (X)xxxXxx, (X)xxxxXx and (X)xxxxxX,

(b) (X)XXxxxx, (X)XxXxxx, (X)XxxXxx, (X)XxxxXx, (X)XxxxxX, (X)xXXxxx, (X)xXxXxx, (X)xXxxXx, (X)xXxxxX, (X)xxXXxx, (X)xxXxXx, (X)xxXxxX, (X)xxxXXx, (X)xxxXxX and (X)xxxxXX,

(c) (X)XXXxxx, (X)xXXXxx, (X)xxXXXx, (X)xxxXXX, (X)XXxXxx, (X)XXxxXx, (X)XXxxxX, (X)xXXxXx, (X)xXXxxX, (X)xxXXxX, (X)XxXXxx, (X)XxxXXx (X)XxxxXX, (X)xXxXXx, (X)xXxxXX, (X)xxXxXX, (X)xXxXxX and (X)XxXxXx,

(d) (X)xxXXX, (X)xXxXXX, (X)xXXxXX, (X)xXXXxX, (X)xXXXXx, (X)XxxXXXX, (X)XxXxXX, (X)XxXXxX, (X)XxXXx, (X)XXxxXX, (X)XXxXxX, (X)XXxXXx, (X)XXXxxX, (X)XXXxXx, and (X)XXXXxx,

(e) (X)xXXXXX, (X)XxXXXX, (X)XXxXXX, (X)XXXxXX, (X)XXXXxX and (X)XXXXXx, and

(f) XXXXXX, XxXXXXX, XXxXXXX, XXXxXXX, XXXXxXX, XXXXXxX and XXXXXXx, wherein "X" denotes a nucleotide analogue, (X) denotes an optional nucleotide analogue, and "x" denotes a DNA or RNA nucleotide unit.

In some embodiments, at least one nucleotide of the oligonucleotide is a nucleotide analogue. In some embodiments, the at least one nucleotide analogue results in an increase in Tm of the oligonucleotide in a range of 1 to 5 °C compared with an oligonucleotide that does not have the at least one nucleotide analogue.

In some embodiments, at least one nucleotide of the oligonucleotide comprises a 2' O-methyl. In some embodiments, each nucleotide of the oligonucleotide comprises a 2' O-methyl. In some embodiments, the oligonucleotide comprises at least one ribonucleotide, at least one deoxyribonucleotide, or at least one bridged nucleotide. In some embodiments, the bridged nucleotide is a LNA nucleotide, a cEt nucleotide or a ENA modified nucleotide. In some embodiments, each nucleotide of the oligonucleotide is a LNA nucleotide.

In some embodiments, the nucleotides of the oligonucleotide comprise alternating deoxyribonucleotides and 2'-fluoro-deoxyribonucleotides. In some embodiments, the nucleotides of the oligonucleotide comprise alternating deoxyribonucleotides and 2'-0-methyl nucleotides. In some embodiments, the nucleotides of the oligonucleotide comprise alternating deoxyribonucleotides and ENA nucleotide analogues. In some embodiments, the nucleotides of the oligonucleotide comprise alternating deoxyribonucleotides and LNA nucleotides. In some embodiments, the 5' nucleotide of the oligonucleotide is a deoxyribonucleotide. In some embodiments, the nucleotides of the oligonucleotide comprise alternating LNA nucleotides and 2'-O-methyl nucleotides. In some embodiments, the 5' nucleotide of the oligonucleotide is a LNA nucleotide. In some embodiments, the nucleotides of the oligonucleotide comprise deoxyribonucleotides flanked by at least one LNA nucleotide on each of the 5' and 3' ends of the deoxyribonucleotides.

In some embodiments, the single stranded oligonucleotide comprises modified internucleotide linkages *(e.g.,* phosphorothioate internucleotide linkages or other linkages) between at least two, at least three, at least four, at least five or more nucleotides. In some embodiments, the single stranded oligonucleotide comprises modified internucleotide linkages *(e.g.,* phosphorothioate internucleotide linkages or other linkages) between between all nucleotides.

In some embodiments, the nucleotide at the 3' position of the oligonucleotide has a 3' hydroxyl group. In some embodiments, the nucleotide at the 3' position of the oligonucleotide has a 3' thiophosphate. In some embodiments, the single stranded oligonucleotide has a biotin moiety or other moiety conjugated to its 5' or 3' nucleotide. In some embodiments, the single stranded oligonucleotide has cholesterol, Vitamin A, folate, sigma receptor ligands, aptamers, peptides, such as CPP, hydrophobic molecules, such as lipids, ASGPR or dynamic polyconjugates and variants thereof at its 5' or 3' end.

According to some aspects of the invention compositions are provided that comprise any of the oligonucleotides disclosed herein, and a carrier. In some embodiments, compositions are provided that comprise any of the oligonucleotides in a buffered solution. In some embodiments, the oligonucleotide is conjugated to the carrier. In some embodiments, the carrier is a peptide. In some embodiments, the carrier is a steroid. According to some aspects of the invention pharmaceutical compositions are provided that comprise any of the oligonucleotides disclosed herein, and a pharmaceutically acceptable carrier.

According to other aspects of the invention, kits are provided that comprise a container housing any of the compositions disclosed herein.

According to some aspects of the invention, methods of increasing expression of UTRN in a cell are provided. In some embodiments, the methods involve delivering any one or more of the single stranded oligonucleotides disclosed herein into the cell. In some embodiments, delivery of the single stranded oligonucleotide into the cell results in a level of expression of UTRN that is greater *(e.g.,* at least 50% greater) than a level of expression of UTRN in a control cell that does not comprise the single stranded oligonucleotide.

According to some aspects of the invention, methods of increasing levels of UTRN in a subject are provided. According to some aspects of the invention, methods of treating a condition *(e.g.,* muscular dystrophies, including DMD, BMD, and myotonic dystrophy) associated with decreased levels of UTRN in a subject are provided. In some embodiments, the methods involve administering any one or more of the single stranded oligonucleotides disclosed herein to the subject.

BRIEF DESCRIPTION OF TABLES

Table 1: Hexamers that are not seed sequences of human miRNAs

Table 2: Oligonucleotide sequences made for testing. RQ (column 3) and RQ SE (column 4) shows the activity of the oligo relative to a control well (usually carrier alone) and the standard error or the triplicate replicates of the experiment. [oligo] is shown in nanomolar for in vitro experiments and in milligrams per kilogram of body weight for in vivo experiments. The Formatted Sequence column sequence of each oligonucleotide, including any modified nucleotides, is shown in Table 4.

Table 3: A listing of oligonucleotide modifications

Table 4: Formatted oligonucleotide sequences made for testing showing nucleotide modifications. The table shows the sequence of the modified nucleotides, where InaX represents an LNA nucleotide with 3' phosphorothioate linkage, omeX is a 2'**-0**-methyl nucleotide, dX is a deoxy nucleotide. An s at the end of a nucleotide code indicates that the nucleotide had a 3' phosphorothioate linkage. The "-Sup" at the end of the sequence marks the fact that the 3' end lacks either a phosphate or thiophosphate on the 3' linkage. The Formatted Sequence column shows the sequence of the oligonucleotide, including modified nucleotides, for the oligonucleotides tested in Table 2.

Table 5: Cell lines

DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS OF THE INVENTION

Aspects of the invention provided herein relate to the discovery of polycomb repressive complex 2 (PRC2)-interacting RNAs. Polycomb repressive complex 2 (PRC2) is a histone methyltransferase and a known epigenetic regulator involved in silencing of genomic regions through methylation of histone H3. Among other functions, PRC2 interacts with long noncoding RNAs (IncRNAs), such as RepA, Xist, and Tsix, to catalyze trimethylation of histone H3-lysine27. PRC2 contains four subunits, Eed, Suzl2, RbAp48, and Ezh2. Aspects of the invention relate to the recognition that single stranded oligonucleotides that bind to PRC2-associated regions of RNAs *(e.g.,* IncRNAs) that are expressed from within a genomic region that encompasses or that is in functional proximity to the UTRN gene can induce or enhance expression of UTRN. In some embodiments, this upregulation is believed to result from inhibition of PRC2 mediated repression of UTRN.

As used herein, the term "PRC2-associated region" refers to a region of a nucleic acid that comprises or encodes a sequence of nucleotides that interact directly or indirectly with a component of PRC2. A PRC2-associated region may be present in a RNA *(e.g.,* a long non-coding RNA (IncRNA)) that that interacts with a PRC2. A PRC2-associated region may be present in a DNA that encodes an RNA that interacts with PRC2. In some cases, the PRC2-associated region is equivalently referred to as a PRC2-interacting region.

In some embodiments, a PRC2-associated region is a region of an RNA that crosslinks to a component of PRC2 in response to *in situ* ultraviolet irradiation of a cell that expresses the RNA, or a region of genomic DNA that encodes that RNA region. In some embodiments, a PRC2-associated region is a region of an RNA that immunoprecipitates with an antibody that targets a component of PRC2, or a region of genomic DNA that encodes that RNA region. In some embodiments, a PRC2-associated region is a region of an RNA that immunoprecipitates with an antibody that binds specifically to SUZ12, EED, EZH2 or RBBP4 (which as noted above are components of PRC2), or a region of genomic DNA that encodes that RNA region.

In some embodiments, a PRC2-associated region is a region of an RNA that is protected from nucleases *(e.g.,* RNases) in an RNA-immunoprecipitation assay that employs an antibody that targets a component of PRC2, or a region of genomic DNA that encodes that protected RNA region. In some embodiments, a PRC2-associated region is a region of an RNA that is protected from nucleases *(e.g.,* RNases) in an RNA-immunoprecipitation assay that employs an antibody that targets SUZ12, EED, EZH2 or RBBP4, or a region of genomic DNA that encodes that protected RNA region.

In some embodiments, a PRC2-associated region is a region of an RNA within which occur a relatively high frequency of sequence reads in a sequencing reaction of products of an RNA-immunoprecipitation assay that employs an antibody that targets a component of PRC2, or a region of genomic DNA that encodes that RNA region. In some embodiments, a PRC2-associated region is a region of an RNA within which occur a relatively high frequency of sequence reads in a sequencing reaction of products of an RNA-immunoprecipitation assay that employs an antibody that binds specifically to SUZ12, EED, EZH2 or RBBP4, or a region of genomic DNA that encodes that protected RNA region. In such embodiments, the PRC2-associated region may be referred to as a "peak."

In some embodiments, a PRC2-associated region comprises a sequence of 40 to 60 nucleotides that interact with PRC2 complex. In some embodiments, a PRC2-associated region comprises a sequence of 40 to 60 nucleotides that encode an RNA that interacts with PRC2. In some embodiments, a PRC2-associated region comprises a sequence of up to 5kb in length that comprises a sequence *(e.g.,* of 40 to 60 nucleotides) that interacts with PRC2. In some embodiments, a PRC2-associated region comprises a sequence of up to 5kb in length within which an RNA is encoded that has a sequence *(e.g.,* of 40 to 60 nucleotides) that is known to interact with PRC2. In some embodiments, a PRC2-associated region comprises a sequence of about 4kb in length that comprise a sequence *(e.g.,* of 40 to 60 nucleotides) that interacts with PRC2. In some embodiments, a PRC2-associated region comprises a sequence of about 4kb in length within which an RNA is encoded that includes a sequence *(e.g.,* of 40 to 60 nucleotides) that is known to interact with PRC2. In some embodiments, a PRC2-associated region has a sequence as set forth in any one of SEQ ID NOS: 5 to 462.

In some embodiments, single stranded oligonucleotides are provided that specifically bind to, or are complementary to, a PRC2-associated region in a genomic region that encompasses or that is in proximity to the UTRN gene. In some embodiments, single stranded oligonucleotides are provided that specifically bind to, or are complementary to, a PRC2-associated region that has a sequence as set forth in any one of SEQ ID NOS: 5 to 462. In some embodiments, single stranded oligonucleotides are provided that specifically bind to, or are complementary to, a PRC2-associated region that has a sequence as set forth in any one of SEQ ID NOS: 4 to 462 combined with up to 2kb, up to 5kb, or up to lOkb of flanking sequences from a corresponding genomic region to which these SEQ IDs map (e.g., in a human genome). In some embodiments, single stranded oligonucleotides have a sequence as set forth in any one of SEQ ID NOS: 463 to 497728. In some embodiments, single stranded oligonucleotides have a sequence as set forth in Table 4.

Without being bound by a theory of invention, these oligonucleotides are able to interfere with the binding of and function of PRC2, by preventing recruitment of PRC2 to a specific chromosomal locus. For example, a single administration of single stranded oligonucleotides designed to specifically bind a PRC2-associated region IncRNA can stably displace not only the IncRNA, but also the PRC2 that binds to the IncRNA, from binding

chromatin. After displacement, the full complement of PRC2 is not recovered for up to 24 hours. Further, IncRNA can recruit PRC2 in a cis fashion, repressing gene expression at or near the specific chromosomal locus from which the IncRNA was transcribed.

Methods of modulating gene expression are provided, in some embodiments, that may be carried out *in vitro, ex vivo,* or *in vivo.* It is understood that any reference to uses of compounds throughout the description contemplates use of the compound in preparation of a pharmaceutical composition or medicament for use in the treatment of muscular dystrophies, including DMD, BMD, and myotonic dystrophy. Thus, as one nonlimiting example, this aspect of the invention includes use of such single stranded oligonucleotides in the preparation of a medicament for use in the treatment of disease, wherein the treatment involves upregulating expression of UTRN.

In further aspects of the invention, methods are provided for selecting a candidate oligonucleotide for activating expression of UTRN. The methods generally involve selecting as a candidate oligonucleotide, a single stranded oligonucleotide comprising a nucleotide sequence that is complementary to a PRC2-associated region *(e.g.,* a nucleotide sequence as set forth in any one of SEQ ID NOS: 5 to 462). In some embodiments, sets of oligonucleotides may be selected that are enriched *(e.g.,* compared with a random selection of oligonucleotides) in oligonucleotides that activate expression of UTRN.

Single Stranded Oligonucleotides for Modulating Expression of UTRN

In one aspect of the invention, single stranded oligonucleotides complementary to the PRC2-associated regions are provided for modulating expression of UTRN in a cell. In some embodiments, expression of UTRN is upregulated or increased. In some embodiments, single stranded oligonucleotides complementary to these PRC2-associated regions inhibit the interaction of PRC2 with long RNA transcripts such that gene expression is upregulated or increased. In some embodiments, single stranded oligonucleotides complementary to these PRC2-associated regions inhibit the interaction of PRC2 with long RNA transcripts, resulting in reduced methylation of histone H3 and reduced gene inactivation, such that gene expression is upregulated or increased. In some embodiments, this interaction may be disrupted or inhibited due to a change in the structure of the long RNA that prevents or

reduces binding to PRC2. The oligonucleotide may be selected using any of the methods disclosed herein for selecting a candidate oligonucleotide for activating expression of UTRN.

The single stranded oligonucleotide may comprise a region of complementarity that is complementary with a PRC2-associated region of a nucleotide sequence set forth in any one of SEQ ID NOS: 1 to 4. The region of complementarity of the single stranded oligonucleotide may be complementary with at least 6, *e.g.,* at least 7, at least 8, at least 9, at least 10, at least 15 or more consecutive nucleotides of the PRC2-associated region.

The PRC2-associated region may map to a position in a chromosome between 50 kilobases upstream of a 5'-end of the UTRN gene and 50 kilobases downstream of a 3'-end of the UTRN gene. The PRC2-associated region may map to a position in a chromosome between 25 kilobases upstream of a 5'-end of the UTRN gene and 25 kilobases downstream of a 3'-end of the UTRN gene. The PRC2-associated region may map to a position in a chromosome between 12 kilobases upstream of a 5'-end of the UTRN gene and 12 kilobases downstream of a 3'-end of the UTRN gene. The PRC2-associated region may map to a position in a chromosome between 5 kilobases upstream of a 5'-end of the UTRN gene and 5 kilobases downstream of a 3'-end of the UTRN gene.

The genomic position of the selected PRC2-associated region relative to the UTRN gene may vary. For example, the PRC2-associated region may be upstream of the 5' end of the UTRN gene. The PRC2-associated region may be downstream of the 3' end of the UTRN gene. The PRC2-associated region may be within an intron of the UTRN gene. The PRC2-associated region may be within an exon of the UTRN gene. The PRC2-associated region may traverse an intron-exon junction, a 5'-UTR-exon junction or a 3'-UTR-exon junction of the UTRN gene.

The single stranded oligonucleotide may comprise a sequence having the formula X-Y-Z, in which X is any nucleotide, Y is a nucleotide sequence of 6 nucleotides in length that is not a human seed sequence of a microRNA, and Z is a nucleotide sequence of varying length. In some embodiments X is the 5' nucleotide of the oligonucleotide. In some embodiemnts, when X is anchored at the 5' end of the oligonucleotide, the oligonucleotide does not have any nucleotides or nucleotide analogs linked 5' to X. In some embodiments, other compounds such as peptides or sterols may be linked at the 5' end in this embodiment as long as they are not nucleotides or nucleotide analogs. In some embodiments, the single

stranded oligonucleotide has a sequence 5'X-Y-Z and is 8-50 nucleotides in length. Oligonucleotides that have these sequence characteristics are predicted to avoid the miRNA pathway. Therefore, in some embodiments, oligonucleotides having these sequence characteristics are unlikely to have an unintended consequence of functioning in a cell as a miRNA molecule. The Y sequence may be a nucleotide sequence of 6 nucleotides in length set forth in Table 1.

The single stranded oligonucleotide may have a sequence that does not contain guanosine nucleotide stretches *(e.g.,* 3 or more, 4 or more, 5 or more, 6 or more consecutive guanosine nucleotides). In some embodiments, oligonucleotides having guanosine nucleotide stretches have increased non-specific binding and/or off-target effects, compared with oligonucleotides that do not have guanosine nucleotide stretches.

The single stranded oligonucleotide may have a sequence that has less than a threshold level of sequence identity with every sequence of nucleotides, of equivalent length, that map to a genomic position encompassing or in proximity to an off-target gene. For example, an oligonucleotide may be designed to ensure that it does not have a sequence that maps to genomic positions encompassing or in proximity with all known genes *(e.g.,* all known protein coding genes) other than UTRN. In a similar embodiment, an oligonucleotide may be designed to ensure that it does not have a sequence that maps to any other known PRC2-associated region, particularly PRC2-associated regions that are functionally related to any other known gene *(e.g.,* any other known protein coding gene). In either case, the oligonucleotide is expected to have a reduced likelihood of having off-target effects. The threshold level of sequence identity may be 50%, 60%, 70%, 80%, 85%, 90%, 95%, 99% or 100% sequence identity.

The single stranded oligonucleotide may have a sequence that is complementary to a PRC2-associated region that encodes an RNA that forms a secondary structure comprising at least two single stranded loops. In has been discovered that, in some embodiments, oligonucleotides that are complementary to a PRC2-associated region that encodes an RNA that forms a secondary structure comprising one or more single stranded loops *(e.g.,* at least two single stranded loops) have a greater likelihood of being active *(e.g.,* of being capable of activating or enhancing expression of a target gene) than a randomly selected oligonucleotide. In some cases, the secondary structure may comprise a double stranded

stem between the at least two single stranded loops. Accordingly, the region of complementarity between the oligonucleotide and the PRC2-associated region may be at a location of the PRC2 associated region that encodes at least a portion of at least one of the loops. In some cases, the region of complementarity between the oligonucleotide and the PRC2-associated region may be at a location of the PRC2-associated region that encodes at least a portion of at least two of the loops. In some cases, the region of complementarity between the oligonucleotide and the PRC2-associated region may be at a location of the PRC2 associated region that encodes at least a portion of the double stranded stem. In some embodiments, a PRC2-associated region *(e.g.,* of an IncRNA) is identified *(e.g.,* using RIP-Seq methodology or information derived therefrom). In some embodiments, the predicted secondary structure RNA *(e.g.,* IncRNA) containing the PRC2-associated region is determined using RNA secondary structure prediction algorithms, *e.g.,* RNAfold, mfold. In some embodiments, oligonucleotides are designed to target a region of the RNA that forms a secondary structure comprising one or more single stranded loop *(e.g.,* at least two single stranded loops) structures which may comprise a double stranded stem between the at least two single stranded loops.

The single stranded oligonucleotide may have a sequence that is has greater than 30% G-C content, greater than 40% G-C content, greater than 50% G-C content, greater than 60% G-C content, greater than 70% G-C content, or greater than 80% G-C content. The single stranded oligonucleotide may have a sequence that has up to 100% G-C content, up to 95% G-C content, up to 90% G-C content, or up to 80% G-C content. In some embodiments in which the oligonucleotide is 8 to 10 nucleotides in length, all but 1, 2, 3, 4, or 5 of the nucleotides of the complementary sequence of the PRC2-associated region are cytosine or guanosine nucleotides. In some embodiments, the sequence of the PRC2-associated region to which the single stranded oligonucleotide is complementary comprises no more than 3 nucleotides selected from adenine and uracil.

The single stranded oligonucleotide may be complementary to a chromosome of a different species *(e.g.,* a mouse, rat, rabbit, goat, monkey, *etc.)* at a position that encompasses or that is in proximity to that species' homolog of UTRN. The single stranded oligonucleotide may be complementary to a human genomic region encompassing or in proximity to the UTRN gene and also be complementary to a mouse genomic region

encompassing or in proximity to the mouse homolog of UTRN. For example, the single stranded oligonucleotide may be complementary to a sequence as set forth in SEQ ID NO: 1 or 2, which is a human genomic region encompassing or in proximity to the UTRN gene, and also be complementary to a sequence as set forth in SEQ ID NO: 3 or 4, which is a mouse genomic region encompassing or in proximity to the mouse homolog of the UTRN gene. Oligonucleotides having these characteristics may be tested *in vivo* or *in vitro* for efficacy in multiple species *(e.g.,* human and mouse). This approach also facilitates development of clinical candidates for treating human disease by selecting a species in which an appropriate animal exists for the disease.

In some embodiments, the region of complementarity of the single stranded oligonucleotide is complementary with at least 8 to 15, 8 to 30, 8 to 40, or 10 to 50, or 5 to 50, or 5 to 40 bases, *e.g.,* 5, 6, 7, 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, or 50 consecutive nucleotides of a PRC2-associated region. In some embodiments, the region of complementarity is complementary with at least 8 consecutive nucleotides of a PRC2-associated region. In some embodiments the sequence of the single stranded oligonucleotide is based on an RNA sequence that binds to PRC2, or a portion thereof, said portion having a length of from 5 to 40 contiguous base pairs, or about 8 to 40 bases, or about 5 to 15, or about 5 to 30, or about 5 to 40 bases, or about 5 to 50 bases.

Complementary, as the term is used in the art, refers to the capacity for precise pairing between two nucleotides. For example, if a nucleotide at a certain position of an oligonucleotide is capable of hydrogen bonding with a nucleotide at the same position of PRC2-associated region, then the single stranded nucleotide and PRC2-associated region are considered to be complementary to each other at that position. The single stranded nucleotide and PRC2-associated region are complementary to each other when a sufficient number of corresponding positions in each molecule are occupied by nucleotides that can hydrogen bond with each other through their bases. Thus, "complementary" is a term which is used to indicate a sufficient degree of complementarity or precise pairing such that stable and specific binding occurs between the single stranded nucleotide and PRC2-associated region. For example, if a base at one position of a single stranded nucleotide is capable of hydrogen bonding with a base at the corresponding position of a PRC2-associated region,

then the bases are considered to be complementary to each other at that position. 100% complementarity is not required.

The single stranded oligonucleotide may be at least 80% complementary to (optionally one of at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% complementary to) the consecutive nucleotides of a PRC2-associated region. In some embodiments the single stranded oligonucleotide may contain 1, 2 or 3 base mismatches compared to the portion of the consecutive nucleotides of a PRC2-associated region. In some embodiments the single stranded oligonucleotide may have up to 3 mismatches over 15 bases, or up to 2 mismatches over 10 bases.

It is understood in the art that a complementary nucleotide sequence need not be 100% complementary to that of its target to be specifically hybridizable. In some embodiments, a complementary nucleic acid sequence for purposes of the present disclosure is specifically hybridizable when binding of the sequence to the target molecule *(e.g.,* IncRNA) interferes with the normal function of the target *(e.g.,* IncRNA) to cause a loss of activity *(e.g.,* inhibiting PRC2-associated repression with consequent up-regulation of gene expression) and there is a sufficient degree of complementarity to avoid non-specific binding of the sequence to non-target sequences under conditions in which avoidance of non-specific binding is desired, *e.g.,* under physiological conditions in the case of *in vivo* assays or therapeutic treatment, and in the case of *in vitro* assays, under conditions in which the assays are performed under suitable conditions of stringency.

In some embodiments, the single stranded oligonucleotide is 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50 or more nucleotides in length. In a preferred embodiment, the oligonucleotide is 8 to 30 nucleotides in length.

In some embodiments, the PRC2-associated region occurs on the same DNA strand as a gene sequence (sense). In some embodiments, the PRC2-associated region occurs on the opposite DNA strand as a gene sequence (anti-sense). Oligonucleotides complementary to a PRC2-associated region can bind either sense or anti-sense sequences. Base pairings may include both canonical Watson-Crick base pairing and non-Watson-Crick base pairing *(e.g.,* Wobble base pairing and Hoogsteen base pairing). It is understood that for complementary base pairings, adenosine-type bases (A) are complementary to thymidine-type bases (T) or

uracil-type bases (U), that cytosine-type bases (C) are complementary to guanosine-type bases (G), and that universal bases such as 3-nitropyrrole or 5-nitroindole can hybridize to and are considered complementary to any A, C, U, or T. Inosine (I) has also been considered in the art to be a universal base and is considered complementary to any A, C, U or T.

In some embodiments, any one or more thymidine (T) nucleotides (or modified nucleotide thereof) or uridine (U) nucleotides (or a modified nucleotide thereof) in a sequence provided herein, including a sequence provided in the sequence listing, may be replaced with any other nucleotide suitable for base pairing (e.g., via a Watson-Crick base pair) with an adenosine nucleotide. In some embodiments, any one or more thymidine (T) nucleotides (or modified nucleotide thereof) or uridine (U) nucleotides (or a modified nucleotide thereof) in a sequence provided herein, including a sequence provided in the sequence listing, may be suitably replaced with a different pyrimidine nucleotide or vice versa. In some embodiments, any one or more thymidine (T) nucleotides (or modified nucleotide thereof) in a sequence provided herein, including a sequence provided in the sequence listing, may be suitably replaced with a uridine (U) nucleotide (or a modified nucleotide thereof) or vice versa.

In some embodiments, GC content of the single stranded oligonucleotide is preferably between about 30-60 %. Contiguous runs of three or more Gs or Cs may not be preferable in some embodiments. Accordingly, in some embodiments, the oligonucleotide does not comprise a stretch of three or more guanosine nucleotides.

In some embodiments, the single stranded oligonucleotide specifically binds to, or is complementary to an RNA that is encoded in a genome (e.g., a human genome) as a single contiguous transcript (e.g., as a non-spliced RNA). In some embodiments, the single stranded oligonucleotide specifically binds to, or is complementary to an RNA that is encoded in a genome (e.g., a human genome), in which the distance in the genome between the 5'end of the coding region of the RNA and the 3' end of the coding region of the RNA is less than 1 kb, less than 2 kb, less than 3 kb, less than 4 kb, less than 5 kb, less than 7 kb, less than 8 kb, less than 9 kb, less than 10 kb, or less than 20 kb.

It is to be understood that any oligonucleotide provided herein can be excluded. In some embodiments, a single stranded oligonucleotide is not complementary to SEQ ID NO: 497807.

In some embodiments, a single-stranded oligonucleotide is complementary to a sequence within nucleotides 1 to 2897 or 2931 to 4046 of SEQ ID NO: 272. In some embodiments, a single-stranded oligonucleotide is complementary to a sequence within nucleotides 1 to 2737 or 3137 to 4024 of SEQ ID NO: 399.

In some embodiments, it has been found that single stranded oligonucleotides disclosed herein may increase expression of mRNA corresponding to the gene by at least about 50% (i.e. 150% of normal or 1.5 fold), or by about 2 fold to about 5 fold. In some embodiments, expression may be increased by at least about 15 fold, 20 fold, 30 fold, 40 fold, 50 fold or 100 fold, or any range between any of the foregoing numbers. It has also been found that increased mRNA expression has been shown to correlate to increased protein expression.

In some or any of the embodiments of the oligonucleotides described herein, or processes for designing or synthesizing them, the oligonucleotides will upregulate gene expression and may specifically bind or specifically hybridize or be complementary to the PRC2 binding RNA that is transcribed from the same strand as a protein coding reference gene. The oligonucleotide may bind to a region of the PRC2 binding RNA that originates within or overlaps an intron, exon, intron exon junction, 5' UTR, 3' UTR, a translation initiation region, or a translation termination region of a protein coding sense strand of a reference gene (refGene).

In some or any of the embodiments of oligonucleotides described herein, or processes for designing or synthesizing them, the oligonucleotides will upregulate gene expression and may specifically bind or specifically hybridize or be complementary to a PRC2 binding RNA that transcribed from the opposite strand (the antisense strand) of a protein coding reference gene. The oligonucleotide may bind to a region of the PRC2 binding RNA that originates within or overlaps an intron, exon, intron exon junction, 5' UTR, 3' UTR, a translation initiation region, or a translation termination region of a protein coding antisense strand of a reference gene

The oligonucleotides described herein may be modified, *e.g.,* comprise a modified sugar moiety, a modified internucleoside linkage, a modified nucleotide and/or combinations thereof. In addition, the oligonucleotides can exhibit one or more of the following properties: do not induce substantial cleavage or degradation of the target RNA; do not cause

substantially complete cleavage or degradation of the target RNA; do not activate the RNAse H pathway; do not activate RISC; do not recruit any Argonaute family protein; are not cleaved by Dicer; do not mediate alternative splicing; are not immune stimulatory; are nuclease resistant; have improved cell uptake compared to unmodified oligonucleotides; are not toxic to cells or mammals; may have improved endosomal exit; do interfere with interaction of IncRNA with PRC2, preferably the Ezh2 subunit but optionally the Suzl2, Eed, RbAp46/48 subunits or accessory factors such as Jarid2; do decrease histone H3 lysine27 methylation and/or do upregulate gene expression.

Oligonucleotides that are designed to interact with RNA to modulate gene expression are a distinct subset of base sequences from those that are designed to bind a DNA target *(e.g.,* are complementary to the underlying genomic DNA sequence from which the RNA is transcribed).

Any of the oligonucleotides disclosed herein may be linked to one or more other oligonucleotides disclosed herein by a linker, *e.g.,* a cleavable linker.

Method for Selecting Candidate Oligonucleotides for Activating Expression of UTRN

Methods are provided herein for selecting a candidate oligonucleotide for activating or enhancing expression of UTRN. The target selection methods may generally involve steps for selecting single stranded oligonucleotides having any of the structural and functional characteristics disclosed herein. Typically, the methods involve one or more steps aimed at identifying oligonucleotides that target a PRC2-associated region that is functionally related to UTRN, for example a PRC2-associated region of a IncRNA that regulates expression of UTRN by facilitating *(e.g.,* in a *cis*-regulatory manner) the recruitment of PRC2 to the UTRN gene. Such oligonucleotides are expected to be candidates for activating expression of UTRN because of their ability to hybridize with the PRC2-associated region of a nucleic acid *(e.g.,* a IncRNA). In some embodiments, this hybridization event is understood to disrupt interaction of PRC2 with the nucleic acid *(e.g.,* a IncRNA) and as a result disrupt recruitment of PRC2 and its associated co-repressors *(e.g.,* chromatin remodeling factors) to the UTRN gene locus.

Methods of selecting a candidate oligonucleotide may involve selecting a PRC2-associated region *(e.g.,* a nucleotide sequence as set forth in any one of SEQ ID NOS: 5 to

462) that maps to a chromosomal position encompassing or in proximity to the UTRN gene *(e.g.,* a chromosomal position having a sequence as set forth in any one of SEQ ID NOS: 1 to 4). The PRC2-associated region may map to the strand of the chromosome comprising the sense strand of the UTRN gene, in which case the candidate oligonucleotide is complementary to the sense strand of the UTRN gene *(i.e.,* is antisense to the UTRN gene). Alternatively, the PRC2-associated region may map to the strand of the first chromosome comprising the antisense strand of the UTRN gene, in which case the oligonucleotide is complementary to the antisense strand (the template strand) of the UTRN gene *(i.e.,* is sense to the UTRN gene).

Methods for selecting a set of candidate oligonucleotides that is enriched in oligonucleotides that activate expression of UTRN may involve selecting one or more PRC2-associated regions that map to a chromosomal position that encompasses or that is in proximity to the UTRN gene and selecting a set of oligonucleotides, in which each oligonucleotide in the set comprises a nucleotide sequence that is complementary with the one or more PRC2-associated regions. As used herein, the phrase, "a set of oligonucleotides that is enriched in oligonucleotides that activate expression of refers to a set of oligonucleotides that has a greater number of oligonucleotides that activate expression of a target gene *(e.g.,* UTRN) compared with a random selection of oligonucleotides of the same physicochemical properties *(e.g.,* the same GC content, T_m, length *etc.)* as the enriched set.

Where the design and/or synthesis of a single stranded oligonucleotide involves design and/or synthesis of a sequence that is complementary to a nucleic acid or PRC2-associated region described by such sequence information, the skilled person is readily able to determine the complementary sequence, *e.g.,* through understanding of Watson Crick base pairing rules which form part of the common general knowledge in the field.

In some embodiments design and/or synthesis of a single stranded oligonucleotide involves manufacture of an oligonucleotide from starting materials by techniques known to those of skill in the art, where the synthesis may be based on a sequence of a PRC2-associated region, or portion thereof.

Methods of design and/or synthesis of a single stranded oligonucleotide may involve one or more of the steps of:

Identifying and/or selecting PRC2-associated region;

Designing a nucleic acid sequence having a desired degree of sequence identity or complementarity to a PRC2-associated region or a portion thereof;

Synthesizing a single stranded oligonucleotide to the designed sequence;

Purifying the synthesized single stranded oligonucleotide; and

Optionally mixing the synthesized single stranded oligonucleotide with at least one pharmaceutically acceptable diluent, carrier or excipient to form a pharmaceutical composition or medicament.

Single stranded oligonucleotides so designed and/or synthesized may be useful in method of modulating gene expression as described herein.

Preferably, single stranded oligonucleotides of the invention are synthesized chemically. Oligonucleotides used to practice this invention can be synthesized *in vitro* by well-known chemical synthesis techniques.

Oligonucleotides of the invention can be stabilized against nucleolytic degradation such as by the incorporation of a modification, *e.g.*, a nucleotide modification. For example, nucleic acid sequences of the invention include a phosphorothioate at least the first, second, or third internucleotide linkage at the 5' or 3' end of the nucleotide sequence. As another example, the nucleic acid sequence can include a 2'-modified nucleotide, *e.g.*, a 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-0-methyl, 2'-0-methoxyethyl (2'-0-MOE), 2'-0-aminopropyl (2'-0-AP), 2'-0-dimethylaminoethyl (2'-0-DMAOE), 2'-0-dimethylaminopropyl (2'-0-DMAP), 2'-0-dimethylaminoethyloxyethyl (2'-0-DMAEOE), or 2'-0-N-methylacetamido (2'-0-NMA). As another example, the nucleic acid sequence can include at least one 2'-0-methyl-modified nucleotide, and in some embodiments, all of the nucleotides include a 2'-0-methyl modification. In some embodiments, the nucleic acids are "locked," i.e., comprise nucleic acid analogues in which the ribose ring is "locked" by a methylene bridge connecting the 2'-O atom and the 4'-C atom.

It is understood that any of the modified chemistries or formats of single stranded oligonucleotides described herein can be combined with each other, and that one, two, three, four, five, or more different types of modifications can be included within the same molecule.

In some embodiments, the method may further comprise the steps of amplifying the synthesized single stranded oligonucleotide, and/or purifying the single stranded

oligonucleotide (or amplified single stranded oligonucleotide), and/or sequencing the single stranded oligonucleotide so obtained.

As such, the process of preparing a single stranded oligonucleotide may be a process that is for use in the manufacture of a pharmaceutical composition or medicament for use in the treatment of disease, optionally wherein the treatment involves modulating expression of a gene associated with a PRC2-associated region.

In the methods described above a PRC2-associated region may be, or have been, identified, or obtained, by a method that involves identifying RNA that binds to PRC2.

Such methods may involve the following steps: providing a sample containing nuclear ribonucleic acids, contacting the sample with an agent that binds specifically to PRC2 or a subunit thereof, allowing complexes to form between the agent and protein in the sample, partitioning the complexes, synthesizing nucleic acid that is complementary to nucleic acid present in the complexes.

Where the single stranded oligonucleotide is based on a PRC2-associated region, or a portion of such a sequence, it may be based on information about that sequence, *e.g.*, sequence information available in written or electronic form, which may include sequence information contained in publicly available scientific publications or sequence databases.

Nucleotide Analogues

In some embodiments, the oligonucleotide may comprise at least one ribonucleotide, at least one deoxyribonucleotide, and/or at least one bridged nucleotide. In some embodiments, the oligonucleotide may comprise a bridged nucleotide, such as a locked nucleic acid (LNA) nucleotide, a constrained ethyl (cEt) nucleotide, or an ethylene bridged nucleic acid (ENA) nucleotide. Examples of such nucleotides are disclosed herein and known in the art. In some embodiments, the oligonucleotide comprises a nucleotide analog disclosed in one of the following United States Patent or Patent Application Publications: US 7,399,845, US 7,741,457, US 8,022,193, US 7,569,686, US 7,335,765, US 7,314,923, US 7,335,765, and US 7,816,333, US 20110009471, the entire contents of each of which are incorporated herein by reference for all purposes. The oligonucleotide may have one or more 2' O-methyl nucleotides. The oligonucleotide may consist entirely of 2' O-methyl nucleotides.

Often the single stranded oligonucleotide has one or more nucleotide analogues. For example, the single stranded oligonucleotide may have at least one nucleotide analogue that results in an increase in T_m of the oligonucleotide in a range of 1°C, 2 °C, 3°C, 4 °C, or 5°C compared with an oligonucleotide that does not have the at least one nucleotide analogue. The single stranded oligonucleotide may have a plurality of nucleotide analogues that results in a total increase in T_m of the oligonucleotide in a range of 2 °C, 3 °C, 4 °C, 5 °C, 6 °C, 7 °C, 8 °C, 9 °C, 10 °C, 15 °C, 20 °C, 25 °C, 30 °C, 35 °C, 40 °C, 45 °C or more compared with an oligonucleotide that does not have the nucleotide analogue.

The oligonucleotide may be of up to 50 nucleotides in length in which 2 to 10, 2 to 15, 2 to 16, 2 to 17, 2 to 18, 2 to 19, 2 to 20, 2 to 25, 2 to 30, 2 to 40, 2 to 45, or more nucleotides of the oligonucleotide are nucleotide analogues. The oligonucleotide may be of 8 to 30 nucleotides in length in which 2 to 10, 2 to 15, 2 to 16, 2 to 17, 2 to 18, 2 to 19, 2 to 20, 2 to 25, 2 to 30 nucleotides of the oligonucleotide are nucleotide analogues.

The oligonucleotide may be of 8 to 15 nucleotides in length in which 2 to 4, 2 to 5, 2 to 6, 2 to 7, 2 to 8, 2 to 9, 2 to 10, 2 to 11, 2 to 12, 2 to 13, 2 to 14 nucleotides of the oligonucleotide are nucleotide analogues. Optionally, the oligonucleotides may have every nucleotide except 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides modified.

The oligonucleotide may consist entirely of bridged nucleotides *(e.g.,* LNA nucleotides, cEt nucleotides, ENA nucleotides). The oligonucleotide may comprise alternating deoxyribonucleotides and 2'-fluoro-deoxyribonucleotides. The oligonucleotide may comprise alternating deoxyribonucleotides and 2'-0-methyl nucleotides. The oligonucleotide may comprise alternating deoxyribonucleotides and ENA nucleotide analogues. The oligonucleotide may comprise alternating deoxyribonucleotides and LNA nucleotides. The oligonucleotide may comprise alternating LNA nucleotides and 2'-0-methyl nucleotides. The oligonucleotide may have a 5' nucleotide that is a bridged nucleotide *(e.g.,* a LNA nucleotide, cEt nucleotide, ENA nucleotide). The oligonucleotide may have a 5' nucleotide that is a deoxyribonucleotide.

The oligonucleotide may comprise deoxyribonucleotides flanked by at least one bridged nucleotide *(e.g.,* a LNA nucleotide, cEt nucleotide, ENA nucleotide) on each of the 5' and 3' ends of the deoxyribonucleotides. The oligonucleotide may comprise deoxyribonucleotides flanked by 1, 2, 3, 4, 5, 6, 7, 8 or more bridged nucleotides *(e.g.,* LNA

nucleotides, cEt nucleotides, ENA nucleotides) on each of the 5' and 3' ends of the deoxyribonucleotides. The 3' position of the oligonucleotide may have a 3' hydroxyl group. The 3' position of the oligonucleotide may have a 3' thiophosphate.

The oligonucleotide may be conjugated with a label. For example, the oligonucleotide may be conjugated with a biotin moiety, cholesterol, Vitamin A, folate, sigma receptor ligands, aptamers, peptides, such as CPP, hydrophobic molecules, such as lipids, ASGPR or dynamic polyconjugates and variants thereof at its 5' or 3' end.

Preferably the single stranded oligonucleotide comprises one or more modifications comprising: a modified sugar moiety, and/or a modified internucleoside linkage, and/or a modified nucleotide and/or combinations thereof. It is not necessary for all positions in a given oligonucleotide to be uniformly modified, and in fact more than one of the modifications described herein may be incorporated in a single oligonucleotide or even at within a single nucleoside within an oligonucleotide.

In some embodiments, the single stranded oligonucleotides are chimeric oligonucleotides that contain two or more chemically distinct regions, each made up of at least one nucleotide. These oligonucleotides typically contain at least one region of modified nucleotides that confers one or more beneficial properties (such as, for example, increased nuclease resistance, increased uptake into cells, increased binding affinity for the target) and a region that is a substrate for enzymes capable of cleaving RNA:DNA or RNA:RNA hybrids. Chimeric single stranded oligonucleotides of the invention may be formed as composite structures of two or more oligonucleotides, modified oligonucleotides, oligonucleosides and/or oligonucleotide mimetics as described above. Such compounds have also been referred to in the art as hybrids or gapmers. Representative United States patents that teach the preparation of such hybrid structures comprise, but are not limited to, US patent nos. 5,013,830; 5,149,797; 5, 220,007; 5,256,775; 5,366,878; 5,403,711; 5,491,133; 5,565,350; 5,623,065; 5,652,355; 5,652,356; and 5,700,922, each of which is herein incorporated by reference.

In some embodiments, the single stranded oligonucleotide comprises at least one nucleotide modified at the 2' position of the sugar, most preferably a 2'-0-alkyl, 2'-0-alkyl-0-alkyl or 2'-fluoro-modified nucleotide. In other preferred embodiments, RNA modifications include 2'-fluoro, 2'-amino and 2' O-methyl modifications on the ribose of pyrimidines,

abasic residues or an inverted base at the 3' end of the RNA. Such modifications are routinely incorporated into oligonucleotides and these oligonucleotides have been shown to have a higher Tm (i.e., higher target binding affinity) than 2'-deoxyoligonucleotides against a given target.

A number of nucleotide and nucleoside modifications have been shown to make the oligonucleotide into which they are incorporated more resistant to nuclease digestion than the native oligodeoxynucleotide; these modified oligos survive intact for a longer time than unmodified oligonucleotides. Specific examples of modified oligonucleotides include those comprising modified backbones, for example, phosphorothioates, phosphotriesters, methyl phosphonates, short chain alkyl or cycloalkyl intersugar linkages or short chain heteroatomic or heterocyclic intersugar linkages. Most preferred are oligonucleotides with phosphorothioate backbones and those with heteroatom backbones, particularly CH_2 -NH-O-CH_2, CH,~N(CH_3)~0~CH_2 (known as a methylene(methylimino) or MMI backbone, CH_2 -O-N (CH_3)-CH_2, CH_2 -N (CH_3)-N (CH_3)-CH_2 and O-N (CH_3)- CH_2 -CH_2 backbones, wherein the native phosphodiester backbone is represented as O- P — O- CH,); amide backbones (see De Mesmaeker et al. Ace. Chem. Res. 1995, 28:366-374); morpholino backbone structures (see Summerton and Weller, U.S. Pat. No. 5,034,506); peptide nucleic acid (PNA) backbone (wherein the phosphodiester backbone of the oligonucleotide is replaced with a polyamide backbone, the nucleotides being bound directly or indirectly to the aza nitrogen atoms of the polyamide backbone, see Nielsen et al., Science 1991, 254, 1497). Phosphorus-containing linkages include, but are not limited to, phosphorothioates, chiral phosphorothioates, phosphorodithioates, phosphotriesters, aminoalkylphosphotriesters, methyl and other alkyl phosphonates comprising 3'alkylene phosphonates and chiral phosphonates, phosphinates, phosphoramidates comprising 3'-amino phosphoramidate and aminoalkylphosphoramidates, thionophosphoramidates, thionoalkylphosphonates, thionoalkylphosphotriesters, and boranophosphates having normal 3'-5' linkages, 2'-5' linked analogs of these, and those having inverted polarity wherein the adjacent pairs of nucleoside units are linked 3'-5' to 5'-3' or 2'-5' to 5'-2'; see US patent nos. 3,687,808; 4,469,863; 4,476,301; 5,023,243; 5, 177,196; 5,188,897; 5,264,423; 5,276,019; 5,278,302; 5,286,717; 5,321,131; 5,399,676; 5,405,939; 5,453,496; 5,455, 233; 5,466,677; 5,476,925; 5,519,126; 5,536,821; 5,541,306; 5,550,111; 5,563, 253; 5,571,799; 5,587,361; and 5,625,050.

Morpholino-based oligomeric compounds are described in Dwaine A. Braasch and David R. Corey, Biochemistry, 2002, 41(14), 4503-4510); Genesis, volume 30, issue 3, 2001; Heasman, J., Dev. Biol., 2002, 243, 209-214; Nasevicius et al., Nat. Genet., 2000, 26, 216-220; Lacerra et al., Proc. Natl. Acad. Sci., 2000, 97, 9591-9596; and U.S. Pat. No. 5,034,506, issued Jul. 23, 1991. In some embodiments, the morpholino-based oligomeric compound is a phosphorodiamidate morpholino oligomer (PMO) *(e.g.,* as described in Iverson, Curr. Opin. Mol. Ther., 3:235-238, 2001; and Wang et al., J. Gene Med., 12:354-364, 2010; the disclosures of which are incorporated herein by reference in their entireties).

Cyclohexenyl nucleic acid oligonucleotide mimetics are described in Wang et al., J. Am. Chem. Soc, 2000, 122, 8595-8602.

Modified oligonucleotide backbones that do not include a phosphorus atom therein have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These comprise those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones; and others having mixed N, O, S and CH2 component parts; see US patent nos. 5,034,506; 5,166,315; 5,185,444; 5,214,134; 5,216,141; 5,235,033; 5,264, 562; 5, 264,564; 5,405,938; 5,434,257; 5,466,677; 5,470,967; 5,489,677; 5,541,307; 5,561,225; 5,596, 086; 5,602,240; 5,610,289; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623, 070; 5,663,312; 5,633,360; 5,677,437; and 5,677,439, each of which is herein incorporated by reference.

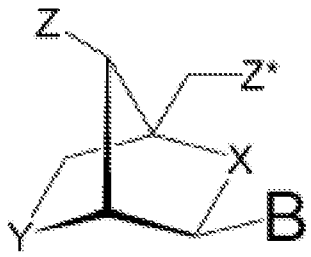
Modified oligonucleotides are also known that include oligonucleotides that are based on or constructed from arabinonucleotide or modified arabinonucleotide residues. Arabinonucleosides are stereoisomers of ribonucleosides, differing only in the configuration at the 2'-position of the sugar ring. In some embodiments, a 2'-arabino modification is 2'-F arabino. In some embodiments, the modified oligonucleotide is 2'-fluoro-D-arabinonucleic acid (FANA) (as described in, for example, Lon et al., Biochem., 41:3457-3467, 2002 and Min et al., Bioorg. Med. Chem. Lett., 12:2651-2654, 2002; the disclosures of which are

incorporated herein by reference in their entireties). Similar modifications can also be made at other positions on the sugar, particularly the 3' position of the sugar on a 3' terminal nucleoside or in 2'-5' linked oligonucleotides and the 5' position of 5' terminal nucleotide.

PCT Publication No. WO 99/67378 discloses arabinonucleic acids (ANA) oligomers and their analogues for improved sequence specific inhibition of gene expression via association to complementary messenger RNA.

Other preferred modifications include ethylene-bridged nucleic acids (ENAs) *(e.g.,* International Patent Publication No. WO 2005/042777, Morita et al., Nucleic Acid Res., Suppl 1:241-242, 2001; Surono et al., Hum. Gene Ther., 15:749-757, 2004; Koizumi, Curr. Opin. Mol. Ther., 8:144-149, 2006 and Horie et al., Nucleic Acids Symp. Ser (Oxf), 49:171-172, 2005; the disclosures of which are incorporated herein by reference in their entireties). Preferred ENAs include, but are not limited to, 2'-0,4'-C-ethylene -bridged nucleic acids.

Examples of LNAs are described in WO/2008/043753 and include compounds of the following general formula.



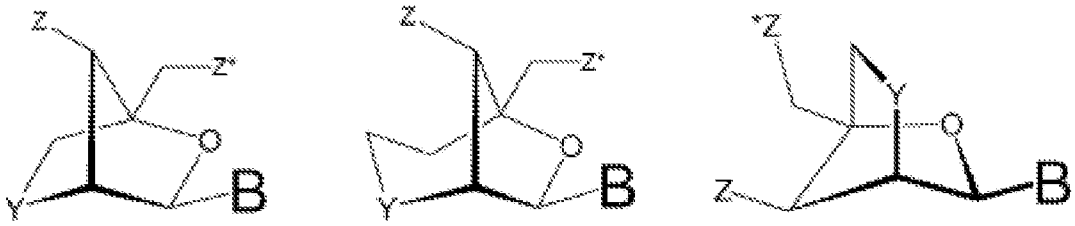
where X and Y are independently selected among the groups -0-,

-S-, -N(H)-, N(R)-, $-CH_2-$ or -CH- (if part of a double bond),

$-CH_2-O-$, $-CH_2-S-$, $-CH_2-N(H)-$, $-CH_2-N(R)-$, $-CH_2-CH_2-$ or $-CH_2-CH-$ (if part of a double bond),

-CH=CH-, where R is selected from hydrogen and Ci-4-alkyl; Z and Z* are independently selected among an internucleoside linkage, a terminal group or a protecting group; B constitutes a natural or non-natural nucleotide base moiety; and the asymmetric groups may be found in either orientation.

Preferably, the LNA used in the oligonucleotides described herein comprises at least one LNA unit according any of the formulas

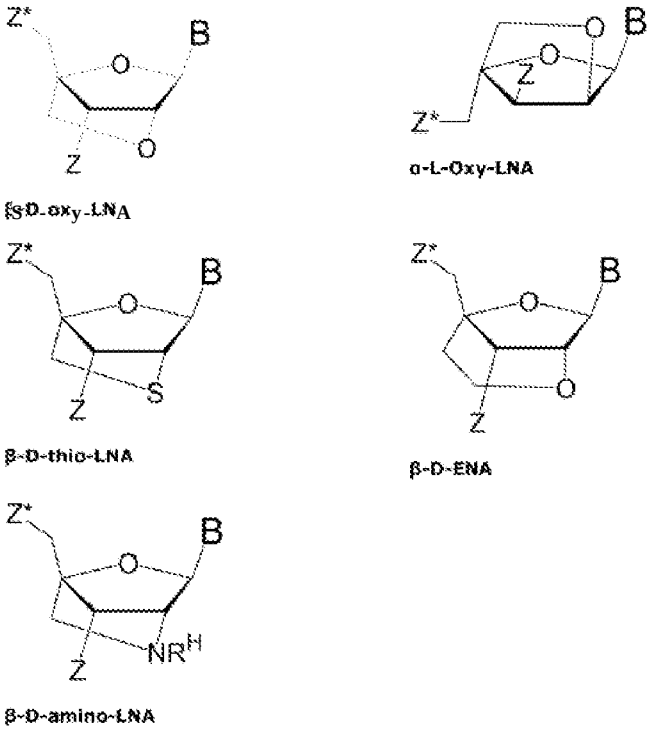


wherein Y is -0-, -S-, -NH-, or N(R^H); Z and Z* are independently selected among an intemucleoside linkage, a terminal group or a protecting group; B constitutes a natural or non-natural nucleotide base moiety, and RH is selected from hydrogen and Ci-4-alkyl.

In some embodiments, the Locked Nucleic Acid (LNA) used in the oligonucleotides described herein comprises at least one Locked Nucleic Acid (LNA) unit according any of the formulas shown in Scheme 2 of PCT/DK2006/000512.

In some embodiments, the LNA used in the oligomer of the invention comprises intemucleoside linkages selected from -0-$P(O)_2$-O-, -0-P(0,S)-0-, -0-$P(S)_2$-O-, -S-P(0) $_2$-0-, -S-P(0,S)-0-, -S-$P(S)_2$-0-, -0-$P(O)_2$-S-, -0-P(0,S)-S-, -S-P(0) $_2$-S-, -0-PO(R^H)-0-, o - PO(OCH_3)-0-, -0-PO(NR^H)-0-, -0-PO(OCH_2CH_2S-R)-O-, -0-PO(BH_3)-0-, -0-PO(NHR^H)-0-, -0-P(0) $_2$-NR^H-, -NR^H-P(0) $_2$-0-, -NR^H-CO-0-, where R^H is selected from hydrogen and Ci_4-alkyl.

Specifically preferred LNA units are shown in scheme 2:



Scheme 2

The term "thio-LNA" comprises a locked nucleotide in which at least one of X or Y in the general formula above is selected from S or -CH_2-S-. Thio-LNA can be in both beta-D and alpha-L-configuration.

The term "amino-LNA" comprises a locked nucleotide in which at least one of X or Y in the general formula above is selected from -N(H)-, N(R)-, CH_2-N(H)-, and -CH_2-N(R)- where R is selected from hydrogen and C_{1-4}-alkyl. Amino-LNA can be in both beta-D and alpha-L-configuration.

The term "oxy-LNA" comprises a locked nucleotide in which at least one of X or Y in the general formula above represents -O- or **-CH_2-O-.** Oxy-LNA can be in both beta-D and alpha-L-configuration.

The term "ena-LNA" comprises a locked nucleotide in which Y in the general formula above is **-CH_2-O-** (where the oxygen atom of **-CH_2-O-** is attached to the 2'-position relative to the base B).

LNAs are described in additional detail herein.

One or more substituted sugar moieties can also be included, *e.g.,* one of the following at the 2' position: OH, SH, SCH_3, F, OCN, OCH_3 OCH_3, OCH_3 $0(CH_2)n$ CH_3, $0(CH_2)n$ NH_2 or $0(CH_2)n$ CH_3 where n is from 1 to about 10; CI to CIO lower alkyl, alkoxyalkoxy, substituted lower alkyl, alkaryl or aralkyl; CI; Br; CN; CF_3 ; OCF_3; 0-, S-, or N-alkyl; 0-, S-, or N-alkenyl; $SOCH_3$; $S0_2$ CH_3; $ON0_2$; $N0_2$; N_3; NH2; heterocycloalkyl; heterocyclo alkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a reporter group; an intercalator; a group for improving the pharmacokinetic properties of an oligonucleotide; or a group for improving the pharmacodynamic properties of an oligonucleotide and other substituents having similar properties. A preferred modification includes 2'-methoxyethoxy [2'-0-$CH_2CH_2OCH_3$, also known as 2'-0-(2-methoxyethyl)] (Martin et al, Helv. Chim. Acta, 1995, 78, 486). Other preferred modifications include 2'-methoxy (2'-0-CH_3), 2'-propoxy (2'-OCH_2 CH_2CH_3) and 2'-fluoro (2'-F). Similar modifications may also be made at other positions on the oligonucleotide, particularly the 3' position of the sugar on the 3' terminal nucleotide and the 5' position of 5' terminal nucleotide. Oligonucleotides may also have sugar mimetics such as cyclobutyls in place of the pentofuranosyl group.

Single stranded oligonucleotides can also include, additionally or alternatively, nucleobase (often referred to in the art simply as "base") modifications or substitutions. As used herein, "unmodified" or "natural" nucleobases include adenine (A), guanine (G), thymine (T), cytosine (C) and uracil (U). Modified nucleobases include nucleobases found only infrequently or transiently in natural nucleic acids, *e.g.,* hypoxanthine, 6-methyladenine, 5-Me pyrimidines, particularly 5-methylcytosine (also referred to as 5-methyl-2' deoxycytosine and often referred to in the art as 5-Me-C), 5-hydroxymethylcytosine (HMC), glycosyl HMC and gentobiosyl HMC, isocytosine, pseudoisocytosine, as well as synthetic nucleobases, *e.g.,* 2-aminoadenine, 2- (methylamino)adenine, 2-(imidazolylalkyl)adenine, 2-(aminoalklyamino)adenine or other hetero substituted alkyladenines, 2-thiouracil, 2-thiothymine, 5-bromouracil, 5-hydroxymethyluracil, 5-propynyluracil, 8-azaguanine, 7-deazaguanine, N6 (6-aminohexyl)adenine, 6-aminopurine, 2-aminopurine, 2-chloro-6-aminopurine and 2,6-diaminopurine or other diaminopurines. See, *e.g.,* Kornberg, "DNA Replication," W. H. Freeman & Co., San Francisco, 1980, pp75-77; and Gebeyehu, G., et al. Nucl. Acids Res., 15:4513 (1987)). A "universal" base known in the art, *e.g.,* inosine, can

also be included. 5-Me-C substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2°C. (Sanghvi, in Crooke, and Lebleu, eds., Antisense Research and Applications, CRC Press, Boca Raton, 1993, pp. 276-278) and may be used as base substitutions.

It is not necessary for all positions in a given oligonucleotide to be uniformly modified, and in fact more than one of the modifications described herein may be incorporated in a single oligonucleotide or even at within a single nucleoside within an oligonucleotide.

In some embodiments, both a sugar and an internucleoside linkage, i.e., the backbone, of the nucleotide units are replaced with novel groups. The base units are maintained for hybridization with an appropriate nucleic acid target compound. One such oligomeric compound, an oligonucleotide mimetic that has been shown to have excellent hybridization properties, is referred to as a peptide nucleic acid (PNA). In PNA compounds, the sugar-backbone of an oligonucleotide is replaced with an amide containing backbone, for example, an aminoethylglycine backbone. The nucleobases are retained and are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone. Representative United States patents that teach the preparation of PNA compounds include, but are not limited to, US patent nos. 5,539,082; 5,714,331; and 5,719,262, each of which is herein incorporated by reference. Further teaching of PNA compounds can be found in Nielsen et al, Science, 1991, 254, 1497-1500.

Single stranded oligonucleotides can also include one or more nucleobase (often referred to in the art simply as "base") modifications or substitutions. As used herein, "unmodified" or "natural" nucleobases comprise the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U). Modified nucleobases comprise other synthetic and natural nucleobases such as 5-methylcytosine (5-me-C), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-halouracil and cytosine, 5-propynyl uracil and cytosine, 6-azo uracil, cytosine and thymine, 5-uracil (pseudo-uracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8- thioalkyl, 8-hydroxyl and other 8-substituted adenines and guanines, 5-halo particularly 5- bromo, 5-trifluoromethyl and other

5-substituted uracils and cytosines, 7-methylquanine and 7-methyladenine, 8-azaguanine and 8-azaadenine, 7-deazaguanine and 7-deazaadenine and 3- deazaguanine and 3-deazaadenine.

Further, nucleobases comprise those disclosed in United States Patent No. 3,687,808, those disclosed in "The Concise Encyclopedia of Polymer Science And Engineering", pages 858-859, Kroschwitz, ed. John Wiley & Sons, 1990;, those disclosed by Englisch et al., Angewandle Chemie, International Edition, 1991, 30, page 613, and those disclosed by Sanghvi, Chapter 15, Antisense Research and Applications," pages 289- 302, Crooke, and Lebleu, eds., CRC Press, 1993. Certain of these nucleobases are particularly useful for increasing the binding affinity of the oligomeric compounds of the invention. These include 5-substituted pyrimidines, 6-azapyrimidines and N-2, N-6 and 0-6 substituted purines, comprising 2-aminopropyladenine, 5-propynyluracil and 5- propynylcytosine. 5-methylcytosine substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2<0>C (Sanghvi, et al., eds, "Antisense Research and Applications," CRC Press, Boca Raton, 1993, pp. 276-278) and are presently preferred base substitutions, even more particularly when combined with 2'-0-methoxyethyl sugar modifications. Modified nucleobases are described in US patent nos. 3,687,808, as well as 4,845,205; 5,130,302; 5,134,066; 5,175, 273; 5, 367,066; 5,432,272; 5,457,187; 5,459,255; 5,484,908; 5,502,177; 5,525,711; 5,552,540; 5,587,469; 5,596,091; 5,614,617; 5,750,692, and 5,681,941, each of which is herein incorporated by reference.

In some embodiments, the single stranded oligonucleotides are chemically linked to one or more moieties or conjugates that enhance the activity, cellular distribution, or cellular uptake of the oligonucleotide. For example, one or more single stranded oligonucleotides, of the same or different types, can be conjugated to each other; or single stranded oligonucleotides can be conjugated to targeting moieties with enhanced specificity for a cell type or tissue type. Such moieties include, but are not limited to, lipid moieties such as a cholesterol moiety (Letsinger et al., Proc. Natl. Acad. Sci. USA, 1989, 86, 6553-6556), cholic acid (Manoharan et al., Bioorg. Med. Chem. Let., 1994, 4, 1053-1060), a thioether, *e.g.,* hexyl-S- tritylthiol (Manoharan et al, Ann. N. Y. Acad. Sci., 1992, 660, 306-309; Manoharan et al., Bioorg. Med. Chem. Let., 1993, 3, 2765-2770), a thiocholesterol (Oberhauser et al., Nucl. Acids Res., 1992, 20, 533-538), an aliphatic chain, *e.g.,* dodecandiol or undecyl residues (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 triethylammonium 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 (Mancharan et al., Nucleosides & Nucleotides, 1995, 14, 969-973), or adamantane acetic acid (Manoharan et al., Tetrahedron Lett., 1995, 36, 3651-3654), a palmityl moiety (Mishra et al., Biochim. Biophys. Acta, 1995, 1264, 229-237), or an octadecylamine or hexylamino-carbonyl-t oxycholesterol moiety (Crooke et al., J. Pharmacol. Exp. Ther., 1996, 277, 923-937). See also US patent nos. 4,828,979; 4,948,882; 5,218,105; 5,525,465; 5,541,313; 5,545,730; 5,552, 538; 5,578,717, 5,580,731; 5,580,731; 5,591,584; 5,109,124; 5,118,802; 5,138,045; 5,414,077; 5,486, 603; 5,512,439; 5,578,718; 5,608,046; 4,587,044; 4,605,735; 4,667,025; 4,762, 779; 4,789,737; 4,824,941; 4,835,263; 4,876,335; 4,904,582; 4,958,013; 5,082, 830; 5,112,963; 5,214,136; 5,082,830; 5,112,963; 5,214,136; 5, 245,022; 5,254,469; 5,258,506; 5,262,536; 5,272,250; 5,292,873; 5,317,098; 5,371,241, 5,391, 723; 5,416,203, 5,451,463; 5,510,475; 5,512,667; 5,514,785; 5, 565,552; 5,567,810; 5,574,142; 5,585,481; 5,587,371; 5,595,726; 5,597,696; 5,599,923; 5,599, 928 and 5,688,941, each of which is herein incorporated by reference.

These moieties or conjugates can include conjugate groups covalently bound to functional groups such as primary or secondary hydroxyl groups. Conjugate groups of the invention include intercalators, reporter molecules, polyamines, polyamides, polyethylene glycols, polyethers, groups that enhance the pharmacodynamic properties of oligomers, and groups that enhance the pharmacokinetic properties of oligomers. Typical conjugate groups include cholesterols, lipids, phospholipids, biotin, phenazine, folate, phenanthridine, anthraquinone, acridine, fluoresceins, rhodamines, coumarins, and dyes. Groups that enhance the pharmacodynamic properties, in the context of this invention, include groups that improve uptake, enhance resistance to degradation, and/or strengthen sequence-specific hybridization with the target nucleic acid. Groups that enhance the pharmacokinetic properties, in the context of this invention, include groups that improve uptake, distribution, metabolism or excretion of the compounds of the present invention. Representative conjugate groups are disclosed in International Patent Application No. PCT/US92/09196, filed Oct. 23, 1992, and U.S. Pat. No. 6,287,860, which are incorporated herein by reference. Conjugate moieties include, but are not limited to, lipid moieties such as a cholesterol moiety, cholic acid, a

thioether, *e.g.,* hexyl-5-tritylthiol, a thiocholesterol, an aliphatic chain, *e.g.,* dodecandiol or undecyl residues, a phospholipid, *e.g.,* di-hexadecyl-rac- glycerol or triethylammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate, a polyamine or a polyethylene glycol chain, or adamantane acetic acid, a palmityl moiety, or an octadecylamine or hexylamino-carbonyl-oxy cholesterol moiety. See, *e.g.,* U.S. Pat. Nos. 4,828,979; 4,948,882; 5,218,105; 5,525,465; 5,541,313; 5,545,730; 5,552,538; 5,578,717, 5,580,731; 5,580,731; 5,591,584; 5,109,124; 5,118,802; 5,138,045; 5,414,077; 5,486,603; 5,512,439; 5,578,718; 5,608,046; 4,587,044; 4,605,735; 4,667,025; 4,762,779; 4,789,737; 4,824,941; 4,835,263; 4,876,335; 4,904,582; 4,958,013; 5,082,830; 5,112,963; 5,214,136; 5,082,830; 5,112,963; 5,214,136; 5,245,022; 5,254,469; 5,258,506; 5,262,536; 5,272,250; 5,292,873; 5,317,098; 5,371,241, 5,391,723; 5,416,203, 5,451,463; 5,510,475; 5,512,667; 5,514,785; 5,565,552; 5,567,810; 5,574,142; 5,585,481; 5,587,371; 5,595,726; 5,597,696; 5,599,923; 5,599,928 and 5,688,941.

In some embodiments, single stranded oligonucleotide modification include modification of the 5' or 3' end of the oligonucleotide. In some embodiments, the 3' end of the oligonucleotide comprises a hydroxyl group or a thiophosphate. It should be appreciated that additional molecules *(e.g.* a biotin moiety or a fluorophor) can be conjugated to the 5' or 3' end of the single stranded oligonucleotide. In some embodiments, the single stranded oligonucleotide comprises a biotin moiety conjugated to the 5' nucleotide.

In some embodiments, the single stranded oligonucleotide comprises locked nucleic acids (LNA), ENA modified nucleotides, 2'-0-methyl nucleotides, or 2'-fluoro-deoxyribonucleotides. In some embodiments, the single stranded oligonucleotide comprises alternating deoxyribonucleotides and 2'-fluoro-deoxyribonucleotides. In some embodiments, the single stranded oligonucleotide comprises alternating deoxyribonucleotides and 2'-0-methyl nucleotides. In some embodiments, the single stranded oligonucleotide comprises alternating deoxyribonucleotides and ENA modified nucleotides. In some embodiments, the single stranded oligonucleotide comprises alternating deoxyribonucleotides and locked nucleic acid nucleotides. In some embodiments, the single stranded oligonucleotide comprises alternating locked nucleic acid nucleotides and 2'-0-methyl nucleotides.

In some embodiments, the 5' nucleotide of the oligonucleotide is a deoxyribonucleotide. In some embodiments, the 5' nucleotide of the oligonucleotide is a locked nucleic acid nucleotide. In some embodiments, the nucleotides of the oligonucleotide

comprise deoxyribonucleotides flanked by at least one locked nucleic acid nucleotide on each of the 5' and 3' ends of the deoxyribonucleotides. In some embodiments, the nucleotide at the 3' position of the oligonucleotide has a 3' hydroxyl group or a 3' thiophosphate.

In some embodiments, the single stranded oligonucleotide comprises phosphorothioate internucleotide linkages. In some embodiments, the single stranded oligonucleotide comprises phosphorothioate internucleotide linkages between at least two nucleotides. In some embodiments, the single stranded oligonucleotide comprises phosphorothioate internucleotide linkages between all nucleotides.

It should be appreciated that the single stranded oligonucleotide can have any combination of modifications as described herein.

The oligonucleotide may comprise a nucleotide sequence having one or more of the following modification patterns.

(a) (X)Xxxxxx, (X)xXxxxx, (X)xxXxxx, (X)xxxXxx, (X)xxxxXx and (X)xxxxxX,

(b) (X)XXxxxx, (X)XxXxxx, (X)XxxXxx, (X)XxxxXx, (X)XxxxxX, (X)xXXxxx, (X)xXxXxx, (X)xXxxXx, (X)xXxxxX, (X)xxXXxx, (X)xxXxXx, (X)xxXxxX, (X)xxxXXx, (X)xxxXxX and (X)xxxxXX,

(c) (X)XXXxxx, (X)xXXXxx, (X)xxXXXx, (X)xxxXXX, (X)XXxXxx, (X)XXxxXx, (X)XXxxxX, (X)xXXxXx, (X)xXXxxX, (X)xxXXxX, (X)XxXXxx, (X)XxxXXx (X)XxxxXX, (X)xXxXXx, (X)xXxxXX, (X)xxXxXX, (X)xXxXxX and (X)XxXxXx,

(d) (X)xxXXX, (X)xXxXXX, (X)xXXxXX, (X)xXXXxX, (X)xXXXXx, (X)XxxXXXX, (X)XxXxXX, (X)XxXXxX, (X)XxXXx, (X)XXxxXX, (X)XXxXxX, (X)XXxXXx, (X)XXXxxX, (X)XXXxXx, and (X)XXXXxx,

(e) (X)xXXXXX, (X)XxXXXX, (X)XXxXXX, (X)XXXxXX, (X)XXXXxX and (X)XXXXXx, and

(f) XXXXXX, XxXXXXX, XXxXXXX, XXXxXXX, XXXXxXX, XXXXXxX and XXXXXXx, in which "X" denotes a nucleotide analogue, (X) denotes an optional nucleotide analogue, and "x" denotes a DNA or RNA nucleotide unit. Each of the above listed patterns may appear one or more times within an oligonucleotide, alone or in combination with any of the other disclosed modification patterns.

Methods for Modulating Gene Expression

In one aspect, the invention relates to methods for modulating gene expression in a cell *(e.g.,* a cell for which UTRN levels are reduced *(e.g.,* a muscle cell)) for research purposes *(e.g.,* to study the function of the gene in the cell). In another aspect, the invention relates to methods for modulating gene expression in a cell *(e.g.,* a cell for which UTRN levels are reduced) for gene or epigenetic therapy. The cells can be *in vitro, ex vivo,* or *in vivo (e.g.,* in a subject who has a disease resulting from reduced expression of UTRN, *(e.g.,* a muscular dystrophy, including DMD, BMD, and myotonic dystrophy)). In some embodiments, methods for modulating gene expression in a cell comprise delivering a single stranded oligonucleotide as described herein. In some embodiments, delivery of the single stranded oligonucleotide to the cell results in a level of expression of gene that is at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 200% or more greater than a level of expression of gene in a control cell to which the single stranded oligonucleotide has not been delivered. In certain embodiments, delivery of the single stranded oligonucleotide to the cell results in a level of expression of gene that is at least 50% greater than a level of expression of gene in a control cell to which the single stranded oligonucleotide has not been delivered.

In another aspect of the invention, methods comprise administering to a subject *(e.g.* a human) a composition comprising a single stranded oligonucleotide as described herein to increase protein levels in the subject. In some embodiments, the increase in protein levels is at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 200%, or more, higher than the amount of a protein in the subject before administering.

As another example, to increase expression of UTRN in a cell, the methods include introducing into the cell a single stranded oligonucleotide that is sufficiently complementary to a PRC2-associated region *(e.g.,* of a long non-coding RNA) that maps to a genomic position encompassing or in proximity to the UTRN gene.

In another aspect of the invention provides methods of treating a condition *(e.g.,* MD) associated with decreased levels of expression of UTRN in a subject, the method comprising administering a single stranded oligonucleotide as described herein.

A subject can include a non-human mammal, *e.g.* mouse, rat, guinea pig, rabbit, cat, dog, goat, cow, or horse. In preferred embodiments, a subject is a human. Single stranded oligonucleotides have been employed as therapeutic moieties in the treatment of disease

states in animals, including humans. Single stranded oligonucleotides can be useful therapeutic modalities that can be configured to be useful in treatment regimes for the treatment of cells, tissues and animals, especially humans.

For therapeutics, an animal, preferably a human, suspected of having MD is treated by administering single stranded oligonucleotide in accordance with this invention. For example, in one non-limiting embodiment, the methods comprise the step of administering to the animal in need of treatment, a therapeutically effective amount of a single stranded oligonucleotide as described herein.

Formulation, Delivery, And Dosing

The oligonucleotides described herein can be formulated for administration to a subject for treating muscular dystrophies, including DMD, BMD, and myotonic dystrophy. It should be understood that the formulations, compositions and methods can be practiced with any of the oligonucleotides disclosed herein.

The formulations may conveniently be presented in unit dosage form and may be prepared by any methods well known in the art of pharmacy. The amount of active ingredient *(e.g.*, an oligonucleotide or compound of the invention) which can be combined with a carrier material to produce a single dosage form will vary depending upon the host being treated, the particular mode of administration, *e.g.*, intradermal or inhalation. The amount of active ingredient which can be combined with a carrier material to produce a single dosage form will generally be that amount of the compound which produces a therapeutic effect, *e.g.* tumor regression.

Pharmaceutical formulations of this invention can be prepared according to any method known to the art for the manufacture of pharmaceuticals. Such formulations can contain sweetening agents, flavoring agents, coloring agents and preserving agents. A formulation can be admixtured with nontoxic pharmaceutically acceptable excipients which are suitable for manufacture. Formulations may comprise one or more diluents, emulsifiers, preservatives, buffers, excipients, etc. and may be provided in such forms as liquids, powders, emulsions, lyophilized powders, sprays, creams, lotions, controlled release formulations, tablets, pills, gels, on patches, in implants, etc.

A formulated single stranded oligonucleotide composition can assume a variety of states. In some examples, the composition is at least partially crystalline, uniformly crystalline, and/or anhydrous *(e.g.,* less than 80, 50, 30, 20, or 10% water). In another example, the single stranded oligonucleotide is in an aqueous phase, *e.g.,* in a solution that includes water. The aqueous phase or the crystalline compositions can, *e.g.,* be incorporated into a delivery vehicle, *e.g.,* a liposome (particularly for the aqueous phase) or a particle *(e.g.,* a microparticle as can be appropriate for a crystalline composition). Generally, the single stranded oligonucleotide composition is formulated in a manner that is compatible with the intended method of administration.

In some embodiments, the composition is prepared by at least one of the following methods: spray drying, lyophilization, vacuum drying, evaporation, fluid bed drying, or a combination of these techniques; or sonication with a lipid, freeze-drying, condensation and other self-assembly.

A single stranded oligonucleotide preparation can be formulated or administered (together or separately) in combination with another agent, *e.g.,* another therapeutic agent or an agent that stabilizes a single stranded oligonucleotide, *e.g.,* a protein that complexes with single stranded oligonucleotide. Still other agents include chelators, *e.g.,* EDTA *(e.g.,* to remove divalent cations such as Mg^{2+}), salts, RNAse inhibitors *(e.g.,* a broad specificity RNAse inhibitor such as RNAsin) and so forth.

In one embodiment, the single stranded oligonucleotide preparation includes another single stranded oligonucleotide, *e.g.,* a second single stranded oligonucleotide that modulates expression of a second gene or a second single stranded oligonucleotide that modulates expression of the first gene. Still other preparation can include at least 3, 5, ten, twenty, fifty, or a hundred or more different single stranded oligonucleotide species. Such single stranded oligonucleotides can mediated gene expression with respect to a similar number of different genes. In one embodiment, the single stranded oligonucleotide preparation includes at least a second therapeutic agent *(e.g.,* an agent other than an oligonucleotide).

Route of Delivery

A composition that includes a single stranded oligonucleotide can be delivered to a subject by a variety of routes. Exemplary routes include: intravenous, intradermal, topical,

rectal, parenteral, anal, intravaginal, intranasal, pulmonary, ocular. The term "therapeutically effective amount" is the amount of oligonucleotide present in the composition that is needed to provide the desired level of UTRN expression in the subject to be treated to give the anticipated physiological response. The term "physiologically effective amount" is that amount delivered to a subject to give the desired palliative or curative effect. The term "pharmaceutically acceptable carrier" means that the carrier can be administered to a subject with no significant adverse toxicological effects to the subject.

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

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

The route and site of administration may be chosen to enhance targeting. For example, to target muscle cells, intramuscular injection into the muscles of interest would be a logical choice. Lung cells might be targeted by administering the single stranded oligonucleotide in aerosol form. The vascular endothelial cells could be targeted by coating a balloon catheter with the single stranded oligonucleotide and mechanically introducing the oligonucleotide.

Topical administration refers to the delivery to a subject by contacting the formulation directly to a surface of the subject. The most common form of topical delivery is to the skin,

but a composition disclosed herein can also be directly applied to other surfaces of the body, *e.g.,* to the eye, a mucous membrane, to surfaces of a body cavity or to an internal surface. As mentioned above, the most common topical delivery is to the skin. The term encompasses several routes of administration including, but not limited to, topical and transdermal. These modes of administration typically include penetration of the skin's permeability barrier and efficient delivery to the target tissue or stratum. Topical administration can be used as a means to penetrate the epidermis and dermis and ultimately achieve systemic delivery of the composition. Topical administration can also be used as a means to selectively deliver oligonucleotides to the epidermis or dermis of a subject, or to specific strata thereof, or to an underlying tissue.

Formulations for topical administration may include transdermal patches, ointments, lotions, creams, gels, drops, suppositories, sprays, liquids and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable. Coated condoms, gloves and the like may also be useful.

Transdermal delivery is a valuable route for the administration of lipid soluble therapeutics. The dermis is more permeable than the epidermis and therefore absorption is much more rapid through abraded, burned or denuded skin. Inflammation and other physiologic conditions that increase blood flow to the skin also enhance transdermal adsorption. Absorption via this route may be enhanced by the use of an oily vehicle (inunction) or through the use of one or more penetration enhancers. Other effective ways to deliver a composition disclosed herein via the transdermal route include hydration of the skin and the use of controlled release topical patches. The transdermal route provides a potentially effective means to deliver a composition disclosed herein for systemic and/or local therapy. In addition, iontophoresis (transfer of ionic solutes through biological membranes under the influence of an electric field), phonophoresis or sonophoresis (use of ultrasound to enhance the absorption of various therapeutic agents across biological membranes, notably the skin and the cornea), and optimization of vehicle characteristics relative to dose position and retention at the site of administration may be useful methods for enhancing the transport of topically applied compositions across skin and mucosal sites.

Both the oral and nasal membranes offer advantages over other routes of administration. For example, oligonucleotides administered through these membranes may

have a rapid onset of action, provide therapeutic plasma levels, avoid first pass effect of hepatic metabolism, and avoid exposure of the oligonucleotides to the hostile gastrointestinal (GI) environment. Additional advantages include easy access to the membrane sites so that the oligonucleotide can be applied, localized and removed easily.

In oral delivery, compositions can be targeted to a surface of the oral cavity, *e.g.,* to sublingual mucosa which includes the membrane of ventral surface of the tongue and the floor of the mouth or the buccal mucosa which constitutes the lining of the cheek. The sublingual mucosa is relatively permeable thus giving rapid absorption and acceptable bioavailability of many agents. Further, the sublingual mucosa is convenient, acceptable and easily accessible.

A pharmaceutical composition of single stranded oligonucleotide may also be administered to the buccal cavity of a human being by spraying into the cavity, without inhalation, from a metered dose spray dispenser, a mixed micellar pharmaceutical formulation as described above and a propellant. In one embodiment, the dispenser is first shaken prior to spraying the pharmaceutical formulation and propellant into the buccal cavity.

Compositions for oral administration include powders or granules, suspensions or solutions in water, syrups, slurries, emulsions, elixirs or non-aqueous media, tablets, capsules, lozenges, or troches. In the case of tablets, carriers that can be used include lactose, sodium citrate and salts of phosphoric acid. Various disintegrants such as starch, and lubricating agents such as magnesium stearate, sodium lauryl sulfate and talc, are commonly used in tablets. For oral administration in capsule form, useful diluents are lactose and high molecular weight polyethylene glycols. When aqueous suspensions are required for oral use, the nucleic acid compositions can be combined with emulsifying and suspending agents. If desired, certain sweetening and/or flavoring agents can be added.

Parenteral administration includes intravenous drip, subcutaneous, intraperitoneal or intramuscular injection, intrathecal or intraventricular administration. In some embodiments, parental administration involves administration directly to the site of disease *(e.g.* injection into a tumor).

Formulations for parenteral administration may include sterile aqueous solutions which may also contain buffers, diluents and other suitable additives. Intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a

reservoir. For intravenous use, the total concentration of solutes should be controlled to render the preparation isotonic.

Any of the single stranded oligonucleotides described herein can be administered to ocular tissue. For example, the compositions can be applied to the surface of the eye or nearby tissue, *e.g.,* the inside of the eyelid. For ocular administration, ointments or droppable liquids may be delivered by ocular delivery systems known to the art such as applicators or eye droppers. Such compositions can include mucomimetics such as hyaluronic acid, chondroitin sulfate, hydroxypropyl methylcellulose or poly(vinyl alcohol), preservatives such as sorbic acid, EDTA or benzylchronium chloride, and the usual quantities of diluents and/or carriers. The single stranded oligonucleotide can also be administered to the interior of the eye, and can be introduced by a needle or other delivery device which can introduce it to a selected area or structure.

Pulmonary delivery compositions can be delivered by inhalation by the patient of a dispersion so that the composition, preferably single stranded oligonucleotides, within the dispersion can reach the lung where it can be readily absorbed through the alveolar region directly into blood circulation. Pulmonary delivery can be effective both for systemic delivery and for localized delivery to treat diseases of the lungs.

Pulmonary delivery can be achieved by different approaches, including the use of nebulized, aerosolized, micellular and dry powder-based formulations. Delivery can be achieved with liquid nebulizers, aerosol-based inhalers, and dry powder dispersion devices. Metered-dose devices are preferred. One of the benefits of using an atomizer or inhaler is that the potential for contamination is minimized because the devices are self-contained. Dry powder dispersion devices, for example, deliver agents that may be readily formulated as dry powders. A single stranded oligonucleotide composition may be stably stored as lyophilized or spray-dried powders by itself or in combination with suitable powder carriers. The delivery of a composition for inhalation can be mediated by a dosing timing element which can include a timer, a dose counter, time measuring device, or a time indicator which when incorporated into the device enables dose tracking, compliance monitoring, and/or dose triggering to a patient during administration of the aerosol medicament.

The term "powder" means a composition that consists of finely dispersed solid particles that are free flowing and capable of being readily dispersed in an inhalation device

and subsequently inhaled by a subject so that the particles reach the lungs to permit penetration into the alveoli. Thus, the powder is said to be "respirable." Preferably the average particle size is less than about 10 μιη in diameter preferably with a relatively uniform spheroidal shape distribution. More preferably the diameter is less than about 7.5 μ m and most preferably less than about 5.0 μ m. Usually the particle size distribution is between about 0.1 μ m and about 5 μ m in diameter, particularly about 0.3 μ m to about 5 μ m.

The term "dry" means that the composition has a moisture content below about 10% by weight (% w) water, usually below about 5% w and preferably less it than about 3% w. A dry composition can be such that the particles are readily dispersible in an inhalation device to form an aerosol.

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

Suitable pH adjusters or buffers include organic salts prepared from organic acids and bases, such as sodium citrate, sodium ascorbate, and the like; sodium citrate is preferred. Pulmonary administration of a micellar single stranded oligonucleotide formulation may be achieved through metered dose spray devices with propellants such as tetrafluoroethane, heptafluoroethane, dimethylfluoropropane, tetrafluoropropane, butane, isobutane, dimethyl ether and other non-CFC and CFC propellants.

Exemplary devices include devices which are introduced into the vasculature, *e.g.,* devices inserted into the lumen of a vascular tissue, or which devices themselves form a part of the vasculature, including stents, catheters, heart valves, and other vascular devices. These devices, *e.g.,* catheters or stents, can be placed in the vasculature of the lung, heart, or leg.

Other devices include non-vascular devices, *e.g.,* devices implanted in the peritoneum, or in organ or glandular tissue, *e.g.,* artificial organs. The device can release a therapeutic substance in addition to a single stranded oligonucleotide, *e.g.,* a device can release insulin.

In one embodiment, unit doses or measured doses of a composition that includes single stranded oligonucleotide are dispensed by an implanted device. The device can

include a sensor that monitors a parameter within a subject. For example, the device can include pump, *e.g.*, and, optionally, associated electronics.

Tissue, *e.g.*, cells or organs can be treated with a single stranded oligonucleotide, ex vivo and then administered or implanted in a subject. The tissue can be autologous, allogeneic, or xenogeneic tissue. *E.g.*, tissue can be treated to reduce graft v. host disease . In other embodiments, the tissue is allogeneic and the tissue is treated to treat a disorder characterized by unwanted gene expression in that tissue. *E.g.*, tissue, *e.g.*, hematopoietic cells, *e.g.*, bone marrow hematopoietic cells, can be treated to inhibit unwanted cell proliferation. Introduction of treated tissue, whether autologous or transplant, can be combined with other therapies. In some implementations, the single stranded oligonucleotide treated cells are insulated from other cells, *e.g.*, by a semi-permeable porous barrier that prevents the cells from leaving the implant, but enables molecules from the body to reach the cells and molecules produced by the cells to enter the body. In one embodiment, the porous barrier is formed from alginate.

In one embodiment, a contraceptive device is coated with or contains a single stranded oligonucleotide. Exemplary devices include condoms, diaphragms, IUD (implantable uterine devices, sponges, vaginal sheaths, and birth control devices.

Dosage

In one aspect, the invention features a method of administering a single stranded oligonucleotide (e.g., as a compound or as a component of a composition) to a subject *(e.g.*, a human subject). In one embodiment, the unit dose is between about 10 mg and 25 mg per kg of bodyweight. In one embodiment, the unit dose is between about 1 mg and 100 mg per kg of bodyweight. In one embodiment, the unit dose is between about 0.1 mg and 500 mg per kg of bodyweight. In some embodiments, the unit dose is more than 0.001, 0.005, 0.01, 0.05, 0.1, 0.5, 1, 2, 5, 10, 25, 50 or 100 mg per kg of bodyweight.

The defined amount can be an amount effective to treat or prevent a disease or disorder, *e.g.*, a disease or disorder associated with the UTRN. The unit dose, for example, can be administered by injection *(e.g.*, intravenous or intramuscular), an inhaled dose, or a topical application.

In some embodiments, the unit dose is administered daily. In some embodiments, less frequently than once a day, *e.g.,* less than every 2, 4, 8 or 30 days. In another embodiment, the unit dose is not administered with a frequency *(e.g.,* not a regular frequency). For example, the unit dose may be administered a single time. In some embodiments, the unit dose is administered more than once a day, *e.g.,* once an hour, two hours, four hours, eight hours, twelve hours, etc.

In one embodiment, a subject is administered an initial dose and one or more maintenance doses of a single stranded oligonucleotide. The maintenance dose or doses are generally lower than the initial dose, *e.g.,* one-half less of the initial dose. A maintenance regimen can include treating the subject with a dose or doses ranging from 0.0001 to 100 mg/kg of body weight per day, *e.g.,* 100, 10, 1, 0.1, 0.01, 0.001, or 0.0001 mg per kg of bodyweight per day. The maintenance doses may be administered no more than once every 1, 5, 10, or 30 days. Further, the treatment regimen may last for a period of time which will vary depending upon the nature of the particular disease, its severity and the overall condition of the patient. In some embodiments the dosage may be delivered no more than once per day, *e.g.,* no more than once per 24, 36, 48, or more hours, *e.g.,* no more than once for every 5 or 8 days. Following treatment, the patient can be monitored for changes in his condition and for alleviation of the symptoms of the disease state. The dosage of the oligonucleotide may either be increased in the event the patient does not respond significantly to current dosage levels, or the dose may be decreased if an alleviation of the symptoms of the disease state is observed, if the disease state has been ablated, or if undesired side-effects are observed.

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

In some embodiments, the oligonucleotide pharmaceutical composition includes a plurality of single stranded oligonucleotide species. In another embodiment, the single stranded oligonucleotide species has sequences that are non-overlapping and non-adjacent to another species with respect to a naturally occurring target sequence *(e.g.,* a PRC2-associated

region). In another embodiment, the plurality of single stranded oligonucleotide species is specific for different PRC2-associated regions. In another embodiment, the single stranded oligonucleotide is allele specific. In some cases, a patient is treated with a single stranded oligonucleotide in conjunction with other therapeutic modalities.

Following successful treatment, it may be desirable to have the patient undergo maintenance therapy to prevent the recurrence of the disease state, wherein the compound of the invention is administered in maintenance doses, ranging from 0.0001 mg to 100 mg per kg of body weight.

The concentration of the single stranded oligonucleotide composition is an amount sufficient to be effective in treating or preventing a disorder or to regulate a physiological condition in humans. The concentration or amount of single stranded oligonucleotide administered will depend on the parameters determined for the agent and the method of administration, *e.g.* nasal, buccal, pulmonary. For example, nasal formulations may tend to require much lower concentrations of some ingredients in order to avoid irritation or burning of the nasal passages. It is sometimes desirable to dilute an oral formulation up to 10-100 times in order to provide a suitable nasal formulation.

Certain factors may influence the dosage required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of a single stranded oligonucleotide can include a single treatment or, preferably, can include a series of treatments. It will also be appreciated that the effective dosage of a single stranded oligonucleotide used for treatment may increase or decrease over the course of a particular treatment. For example, the subject can be monitored after administering a single stranded oligonucleotide composition. Based on information from the monitoring, an additional amount of the single stranded oligonucleotide composition can be administered.

Dosing is dependent on severity and responsiveness of the disease condition to be treated, with the course of treatment lasting from several days to several months, or until a cure is effected or a diminution of disease state is achieved. Optimal dosing schedules can be calculated from measurements of UTRN expression levels in the body of the patient. Persons of ordinary skill can easily determine optimum dosages, dosing methodologies and repetition

rates. Optimum dosages may vary depending on the relative potency of individual compounds, and can generally be estimated based on EC50s found to be effective in in vitro and in vivo animal models. In some embodiments, the animal models include transgenic animals that express a human UTRN. In another embodiment, the composition for testing includes a single stranded oligonucleotide that is complementary, at least in an internal region, to a sequence that is conserved between UTRN in the animal model and the UTRN in a human.

In one embodiment, the administration of the single stranded oligonucleotide composition is parenteral, *e.g.* intravenous *(e.g.,* as a bolus or as a diffusible infusion), intradermal, intraperitoneal, intramuscular, intrathecal, intraventricular, intracranial, subcutaneous, transmucosal, buccal, sublingual, endoscopic, rectal, oral, vaginal, topical, pulmonary, intranasal, urethral or ocular. Administration can be provided by the subject or by another person, *e.g.,* a health care provider. The composition can be provided in measured doses or in a dispenser which delivers a metered dose. Selected modes of delivery are discussed in more detail below.

Kits

In certain aspects of the invention, kits are provided, comprising a container housing a composition comprising a single stranded oligonucleotide. In some embodiments, the composition is a pharmaceutical composition comprising a single stranded oligonucleotide and a pharmaceutically acceptable carrier. In some embodiments, the individual components of the pharmaceutical composition may be provided in one container. Alternatively, it may be desirable to provide the components of the pharmaceutical composition separately in two or more containers, *e.g.,* one container for single stranded oligonucleotides, and at least another for a carrier compound. The kit may be packaged in a number of different configurations such as one or more containers in a single box. The different components can be combined, *e.g.,* according to instructions provided with the kit. The components can be combined according to a method described herein, *e.g.,* to prepare and administer a pharmaceutical composition. The kit can also include a delivery device.

The present invention is further illustrated by the following Examples, which in no way should be construed as further limiting. The entire contents of all of the references (including literature references, issued patents, published patent applications, and co-pending patent applications) cited throughout this application are hereby expressly incorporated by reference.

EXAMPLES

The invention is further described in the following examples, which do not limit the scope of the invention described in the claims.

MATERIALS AND METHODS:

Real Time PCR

RNA was harvested from the cells using Promega SV 96 Total RNA Isolation system or Trizol omitting the DNAse step. In separate pilot experiments, 50 ng of RNA was determined to be sufficient template for the reverse transcriptase reaction. RNA harvested from cells was normalized so that 50ng of RNA was input to each reverse transcription reaction. For the few samples that were too dilute to reach this limit, the maximum input volume was added. Reverse transcriptase reaction was performed using the Superscript II kit and real time PCR performed on cDNA samples using icycler SYBR green chemistry (Biorad). A baseline level of mRNA expression for UTRN was determined through quantitative PCR as outlined above. Baseline levels were also determined for mRNA of various housekeeping genes which are constitutively expressed. A "control" housekeeping gene with approximately the same level of baseline expression as the target gene was chosen for comparison purposes.

Cell Culture

Human hepatocyte Hep3B, human hepatocyte HepG2 cells, mouse hepatoma Hepal-6 cells, and human renal proximal tubule epithelial cells (RPTEC) were cultured using

conditions known in the art (see, *e.g.* Current Protocols in Cell Biology). Details of the cell lines used in the experiments described herein are provided in Table 5.

Table 5. Cell lines

Cell Line	Source	Species	Gender	Type	Tissue	Status	Culture Conditions
RD RMS	ATCC	human	F	rhabdomyosarcoma	skeletal muscle	immortalized	DMEM + 10% FBS
HSKM	Gibco	human	M	muscle	skeletal muscle	normal	DMEM + 10% FBS
SK-N-AS	ATCC	human	F	neuroblast	brain	immortalized	MEM + 10% FBS
am002fDMD	DVBiologics	human	M	muscle	skeletal muscle	normal	M-gro + supplement

Oligonucleotide design

Oligonucleotides were designed within PRC2-interacting regions in order to upregulate UTRN. The sequence and structure of each oligonucleotide is shown in Table 2. The following table provides a description of the nucleotide analogs, modifications and intranucleotide linkages used for certain oligonucleotides tested and described in Table 2.

Table 3: Oligonucleotide Modifications

Symbol	Feature Description
bio	5' biotin
dAs	DNA w/3' thiophosphate
dCs	DNA w/3' thiophosphate
dGs	DNA w/3' thiophosphate
dTs	DNA w/3' thiophosphate
dG	DNA w/3' phosphate
dU	deoxyuridine w/3' phosphate
enaAs	ENA w/3' thiophosphate
enaCs	ENA w/3' thiophosphate
enaGs	ENA w/3' thiophosphate
enaTs	ENA w/3' thiophosphate
fluAs	2'-fluoro w/3' thiophosphate
fluCs	2'-fluoro w/3' thiophosphate

Symbol	Feature Description
fluGs	2'-fluoro w/3' thiophosphate
fluUs	2'-fluoro w/3' thiophosphate
InaAs	LNA w/3' thiophosphate
InaCs	LNA w/3' thiophosphate
InaGs	LNA w/3' thiophosphate
InaTs	LNA w/3' thiophosphate
omeAs	2'-OMe w/3' thiophosphate
omeCs	2'-OMe w/3' thiophosphate
omeGs	2'-OMe w/3' thiophosphate
omeTs	2'-OMe w/3' thiophosphate
InaAs-Sup	LNA w/3' thiophosphate at 3' terminus
InaCs-Sup	LNA w/3' thiophosphate at 3' terminus
InaGs-Sup	LNA w/3' thiophosphate at 3' terminus
InaTs-Sup	LNA w/3' thiophosphate at 3' terminus
InaA-Sup	LNA w/3' OH at 3' terminus
InaC-Sup	LNA w/3' OH at 3' terminus
InaG-Sup	LNA w/3' OH at 3' terminus
InaT-Sup	LNA w/3' OH at 3' terminus
omeA-Sup	2'-OMe w/3' OH at 3' terminus
omeC-Sup	2'-OMe w/3' OH at 3' terminus
omeG-Sup	2'-OMe w/3' OH at 3' terminus
omeU-Sup	2'-OMe w/3' OH at 3' terminus
dAs-Sup	DNA w/3' thiophosphate at 3' terminus
dCs-Sup	DNA w/3' thiophosphate at 3' terminus
dGs-Sup	DNA w/3' thiophosphate at 3' terminus
dTs-Sup	DNA w/3' thiophosphate at 3' terminus
dA-Sup	DNA w/3' OH at 3' terminus
dC-Sup	DNA w/3' OH at 3' terminus
dG-Sup	DNA w/3' OH at 3' terminus

In vitro transfection of cells with oligonucleotides

Cells were seeded into each well of 24-well plates at a density of 25,000 cells per 500uL and transfections were performed with Lipofectamine and the single stranded oligonucleotides. Control wells contained Lipofectamine alone. At 48 hours post-transfection, approximately 200 uL of cell culture supernatants were stored at -80 C for ELISA. At 48 hours post-transfection, RNA was harvested from the cells and quantitative PCR was carried out as outlined above. The percent induction of target mRNA expression by

each oligonucleotide was determined by normalizing mRNA levels in the presence of the oligonucleotide to the mRNA levels in the presence of control (Lipofectamine alone). This was compared side-by-side with the increase in mRNA expression of the "control" housekeeping gene.

RESULTS:

In vitro delivery of single stranded oligonucleotides upregulated UTRN expression

Oligonucleotides were designed as candidates for upregulating UTRN expression. A total of 65 single stranded oligonucleotides were designed to be complementary to a PRC2-interacting region within a sequence as set forth in SEQ ID NO: 1 or 2. Each of the oligonucleotides was tested in at least duplicate. The sequence and structural features of the oligonucleotides are set forth in Table 2. Briefly, cells were transfected in vitro with each of the oligonucleotides as described above. UTRN expression in cells following treatment was evaluated by qRT-PCR. Oligonucleotides that upregulated UTRN expression were identified. Further details are outlined in Table 2.

Tables

Table 1: Hexamers that are not seed sequences of human miRNAs

AAAAAA, AAAAAG, AAAACA, AAAAGA, AAAAGC, AAAAGG, AAAAUA, AAACAA, AAACAC, AAACAG, AAACAU, AAACCC, AAACCU, AAACGA, AAACGC, AAACGU, AAACUA, AAACUC, AAACUU, AAAGAU, AAAGCC, AAAGGA, AAAGGG, AAAGUC, AAAUAC, AAAUAU, AAAUCG, AAAUCU, AAAUGC, AAAUGU, AAAUUA, AAAUUG, AACAAC, AACAAG, AACAAU, AACACA, AACACG, AACAGA, AACAGC, AACAGG, AACAUC, AACAUG, AACCAA, AACCAC, AACCAG, AACCAU, AACCCC, AACCCG, AACCGA, AACCGC, AACCGG, AACCUA, AACCUU, AACGAA, AACGAC, AACGAG, AACGAU, AACGCU, AACGGG, AACGGU, AACGUA, AACGUC, AACGUG, AACGUU, AACUAU, AACUCA, AACUCC, AACUCG, AACUGA, AACUGC, AACUGU, AACU UA, AACUUC, AACU UG, AACUUU, AAGAAA, AAGAAG, AAGAAU, AAGACG, AAGAGA, AAGAGC, AAGAGG, AAGAGU, AAGAUU, AAGCAA, AAGCAC, AAGCAG, AAGCAU, AAGCCA, AAGCCC, AAGCCG, AAGCCU, AAGCGA, AAGCGG, AAGCGU, AAGCUA, AAGGAA, AAGGAC, AAGGCU, AAGGGC, AAGGGU, AAGGUU, AAGUAA, AAGUAC, AAGUAU, AAGUCC, AAGUCG, AAGUGA, AAGUGG, AAGUUA, AAGU UU, AAUAAA, AAUAAC, AAUAAG, AAUAAU, AAUACA, AAUACC, AAUACG, AAUAGA, AAUAGC, AAUAGG, AAUAGU, AAUAUC, AAUAU U, AAUCAA, AAUCAU, AAUCCA, AAUCCC, AAUCCG, AAUCGA, AAUCGC, AAUCGU, AAUCUA, AAUCUG, AAUCUU, AAUGAA, AAUGAC, AAUGAG, AAUGAU, AAUGCG, AAUGCU, AAUGGA, AAUGGU, AAUGUA, AAUGUC, AAUGUG, AAUUAA, AAUUAC, AAUUAG, AAU UCC, AAU UCG, AAUUGA, AAUUGG, AAU UGU, AAUUUC, AAU UUG, ACAAAA, ACAAAC, ACAAAG, ACAAAU,

ACAACC, ACAACG, ACAACU, ACAAGA, ACAAGC, ACAAGU, ACAAUC, ACAAUG, ACAAUU, ACACAG, ACACCA, ACACCC, ACACCG, ACACCU, ACACGA, ACACGC, ACACGU, ACACUC, ACACUG, ACACUU, ACAGAA, ACAGAC, ACAGCC, ACAGCG, ACAGCU, ACAGGG, ACAGUC, ACAGUG, ACAGU U, ACAUAA, ACAUAC, ACAUCC, ACAUCG, ACAUCU, ACAUGA, ACAUGC, ACAUGU, ACAU UG, ACAU UU, ACCAAA, ACCAAC, ACCAAG, ACCAAU, ACCACC, ACCACG, ACCAGA, ACCAGU, ACCAUA, ACCAUG, ACCAU U, ACCCAA, ACCCAC, ACCCCA, ACCCCG, ACCCGA, ACCCGC, ACCCUA, ACCCUC, ACCCUU, ACCGAA, ACCGAC, ACCGAU, ACCGCA, ACCGCC, ACCGCG, ACCGCU, ACCGGA, ACCGGC, ACCGGU, ACCGUA, ACCGUC, ACCGUG, ACCGUU, ACCUAA, ACCUAC, ACCUAG, ACCUAU, ACCUCA, ACCUCC, ACCUCG, ACCUCU, ACCUGA, ACCUGC, ACCUGU, ACCUUA, ACCUUC, ACCUU U, ACGAAA, ACGAAC, ACGAAG, ACGAAU, ACGACA, ACGACC, ACGACG, ACGACU, ACGAGA, ACGAGC, ACGAGG, ACGAGU, ACGAUA, ACGAUC, ACGAUG, ACGAUU, ACGCAA, ACGCAG, ACGCAU, ACGCCC, ACGCCG, ACGCCU, ACGCGA, ACGCGG, ACGCGU, ACGCUA, ACGCUG, ACGCUU, ACGGAA, ACGGAC, ACGGAG, ACGGAU, ACGGCC, ACGGCG, ACGGCU, ACGGGC, ACGGGG, ACGGGU, ACGGUA, ACGGUC, ACGGUG, ACGGUU, ACGUAA, ACGUAC, ACGUAU, ACGUCC, ACGUCG, ACGUCU, ACGUGA, ACGUGC, ACGUGG, ACGUGU, ACGUUA, ACGU UC, ACGUUG, ACGUU U, A CUAAA, ACUAAG, ACUAAU, ACUACA, ACUACC, ACUACG, ACUACU, ACUAGG, ACUAUC, ACUAUG, ACUAUU, ACUCAU, ACUCCC, ACUCCG, ACUCCU, ACUCGA, ACUCGC, ACUCGG, ACUCUC, ACUCUU, ACUGAG, ACUGAU, ACUGCC, ACUGCG, ACUGCU, ACUGGG, ACUGGU, ACUGUC, ACUUAA, ACU UAC, ACUUAU, ACU UCA, ACUUCC, ACUUCG, ACUUCU, ACUUGA, ACU UGC, ACU UGU, ACUUUA, ACU UUC, ACUU UG, AGAAAA, AGAAAC, AGAAAG, AGAACC, AGAACG, AGAACU, AGAAGC, AGAAGU, AGAAUA, AGAAUC, AGAAUG, AGAAUU, AGACAA, AGACAC, AGACAU, AGACCA, AGACCC, AGACCG, AGACCU, AGACGA, AGACGC, AGACGU, AGACUA, AGACUC, AGACUU, AGAGAC, AGAGAG, AGAGAU, AGAGCC, AGAGCG, AGAGCU, AGAGGC, AGAGGG, AGAGGU, AGAGUA, AGAGUU, AGAUAC, AGAUAG, AGAUAU, AGAUCC, AGAUCG, AGAUCU, AGAUGA, AGAUGC, AGAUGG, AGAU UA, AGAU UC, AGAUUG, AGAUU U, AGCAAC, AGCACA, AGCACG, AGCACU, AGCAGA, AGCAUA, AGCAUC, AGCAUG, AGCCAA, AGCCAU, AGCCCA, AGCCGA, AGCCGC, AGCCGG, AGCCGU, AGCCUA, AGCCUC, AGCGAA, AGCGAG, AGCGAU, AGCGCA, AGCGCC, AGCGCG, AGCGCU, AGCGGA, AGCGGC, AGCGGU, AGCGUA, AGCGUC, AGCGUG, AGCGUU, AGCUAA, AGCUAC, AGCUAG, AGCUAU, AGCUCA, AGCUCC, AGCUCG, AGCUCU, AGCUGA, AGCUGG, AGCUGU, AGCU UC, AGCUU U, AGGAAU, AGGACC, AGGACG, AGGAGA, AGGAGU, AGGAUA, AGGCAA, AGGCAU, AGGCCG, AGGCGA, AGGCGC, AGGCGG, AGGCUA, AGGCUC, AGGCUU, AGGGAC, AGGGAU, AGGGGA, AGGGGU, AGGGUA, AGGGUG, AGGUAA, AGGUAC, AGGUCA, AGGUCC, AGGUCU, AGGUGA, AGGUGC, AGGUGG, AGGUGU, AGGU UC, AGGUUG, AGUAAA, AGUAAG, AGUAAU, AGUACA, AGUACG, AGUAGC, AGUAGG, AGUAUA, AGUAUC, AGUAUG, AGUAUU, AGUCAA, AGUCAC, AGUCAG, AGUCAU, AGUCCA, AGUCCG, AGUCCU, AGUCGA, AGUCGC, AGUCGG, AGUCGU, AGUCUA, AGUCUC, AGUCUG, AGUCU U, AGUGAA, AGUGAC, AGUGCG, AGUGGG, AGUGUC, AGU UAA, AGU UAC, AGUUAG, AGUUCC, AGU UCG, AGUUGA, AGUUGC, AGUUGU, AGUUUA, AGUUUC, AGUU UG, AGU UU U, AUAAAC, AUAAAU, AUAACA, AUAACC, AUAACG, AUAACU, AUAAGA, AUAAGC, AUAAGG, AUAAGU, AUAAUC, AUAAUG, AUAAUU, AUACAC, AUACAG, AUACAU, AUACCA, AUACCC, AUACCG, AUACGA, AUACGC, AUACGG, AUACGU, AUACUA, AUACUC, AUACUG, AUACUU, AUAGAA, AUAGAC, AUAGAU, AUAGCA, AUAGCG, AUAGCU, AUAGGA, AUAGGU, AUAGUA, AUAGUC, AUAGUG, AUAGUU, AUAUAC, AUAUAG, AUAUCC, AUAUCG, AUAUCU, AUAUGA, AUAUGC, AUAUGG, AUAUGU, AUAUUC, AUAU UG, AUAUU U, AUCAAA, AUCAAC, AUCAAG, AUCAAU,

AUCACA, AUCACC, AUCACG, AUCAGC, AUCAGG, AUCCAA, AUCCAU, AUCCCC, AUCCCG, AUCCGA, AUCCGC, AUCCGG, AUCCUA, AUCCUC, AUCCUG, AUCGAA, AUCGAC, AUCGAG, AUCGAU, AUCGCA, AUCGCC, AUCGCG, AUCGCU, AUCGGC, AUCGGG, AUCGGU, AUCGUC, AUCGUG, AUCGU U, AUCUAA, AUCUAC, AUCUAG, AUCUAU, AUCUCC, AUCUCG, AUCUGU, AUCUUG, AUCUU U, AUGAAA, AUGAAC, AUGAAG, AUGAAU, AUGACC, AUGACU, AUGAGG, AUGAGU, AUGAUA, AUGAUC, AUGAU U, AUGCAA, AUGCAG, AUGCCA, AUGCCC, AUGCCG, AUGCGA, AUGCGG, AUGCGU, AUGCUC, AUGCUU, AUGGAC, AUGGCC, AUGGGA, AUGGGC, AUGGGU, AUGGUC, AUGGUG, AUGUAC, AUGUAU, AUGUCA, AUGUCC, AUGUCG, AUGUGU, AUGUUA, AUGUUC, AUUAAA, AUUAAC, AUUAAG, AUUAAU, AUUACA, AUUACC, AUUACG, AUUACU, AUUAGA, AUUAGC, AUUAGG, AUUAGU, AUUAUA, AUUAUC, AUUAUG, AUUCAC, AUUCCA, AUUCCG, AUUCCU, AUUCGA, AUUCGC, AUUCGG, AUUCGU, AUUCUA, AUUCUC, AUUCU U, AUUGAA, AUUGAC, AUUGAU, AUUGCC, AUUGCG, AUUGCU, AUUGGA, AUUGGC, AUUGGG, AUUGGU, AUUGUA, AUUGUC, AUUGUG, AUUGU U, AUUUAA, AUUUAG, AUUUAU, AUU UCC, AUU UCG, AUU UCU, AUUUGA, AUUUGC, AUUUGU, AUUUUA, AUUUUC, AUU UUG, AUU UUU, CAAAAG, CAAACA, CAAACC, CAAACG, CAAACU, CAAAGA, CAAAGG, CAAAUA, CAAAUU, CAACAC, CAACAU, CAACCA, CAACCC, CAACCG, CAACGA, CAACGC, CAACGG, CAACGU, CAACUA, CAACUC, CAACUG, CAACUU, CAAGAA, CAAGAC, CAAGAU, CAAGCA, CAAGCC, CAAGCG, CAAGCU, CAAGGA, CAAGGG, CAAGUC, CAAGUG, CAAGU U, CAAUAA, CAAUAC, CAAUAG, CAAUCC, CAAUCG, CAAUCU, CAAUGA, CAAUGC, CAAUGG, CAAUGU, CAAU UC, CAAU UG, CAAU UU, CACAAU, CACACA, CACACG, CACACU, CACAGA, CACAGC, CACAGG, CACAUA, CACAUC, CACAUU, CACCAA, CACCAC, CACCAU, CACCCA, CACCCC, CACCCG, CACCGA, CACCGC, CACCGG, CACCGU, CACCUA, CACCU U, CACGAA, CACGAC, CACGAG, CACGAU, CACGCA, CACGCC, CACGCU, CACGGA, CACGGC, CACGGG, CACGG U, CACGUA, CACGUC, CACGUG, CACGU U, CACUAA, CACUAG, CACUAU, CACUCA, CACUCG, CACUGA, CACUGC, CACUGG, CACUUA, CACU UC, CACU UU, CAGAAA, CAGAAG, CAGAAU, CAGACC, CAGACG, CAGAGC, CAGAUA, CAGAUC, CAGCCG, CAGCCU, CAGCGA, CAGCGC, CAGCGG, CAGCGU, CAGCUC, CAGCUU, CAGGAU, CAGGGG, CAGGGU, CAGGUA, CAGGUC, CAGGUU, CAGUAC, CAGUCG, CAGU UG, CAUAAA, CAUAAC, CAUAAG, CAUAAU, CAUACA, CAUACC, CAUACG, CAUACU, CAUAGA, CAUAGG, CAUAGU, CAUAUA, CAUAUC, CAUAUG, CAUCAA, CAUCAC, CAUCAG, CAUCAU, CAUCCA, CAUCCC, CAUCCG, CAUCGA, CAUCGC, CAUCGG, CAUCGU, CAUCUA, CAUCUC, CAUCUG, CAUCUU, CAUGAA, CAUGAC, CAUGAG, CAUGAU, CAUGCA, CAUGCC, CAUGCG, CAUGCU, CAUGGC, CAUGGG, CAUGGU, CAUGUA, CAUGUC, CAUGUU, CAU UAA, CAUUAC, CAUUAG, CAUUCA, CAU UCC, CAU UCG, CAU UCU, CAU UGA, CAU UGG, CAUU UC, CAU UUG, CAUU UU, CCAAAA, CCAAAC, CCAAAG, CCAAAU, CCAACA, CCAACC, CCAACG, CCAACU, CCAAGA, CCAAGC, CCAAGG, CCAAUC, CCAAUG, CCAAU U, CCACAA, CCACAC, CCACAG, CCACAU, CCACCA, CCACCC, CCACCG, CCACCU, CCACGA, CCACGC, CCACGG, CCACGU, CCACUA, CCACUC, CCACUU, CCAGAA, CCAGAC, CCAGAG, CCAGCC, CCAGGU, CCAGUC, CCAGUU, CCAUAA, CCAUAC, CCAUAG, CCAUAU, CCAUCA, CCAUCC, CCAUCU, CCAUGA, CCAUGC, CCAUGG, CCAUUC, CCAUUG, CCAUU U, CCCAAC, CCCAAG, CCCAAU, CCCACA, CCCAGA, CCCAGC, CCCAGU, CCCAUA, CCCAUC, CCCAUG, CCCAUU, CCCCAA, CCCCAG, CCCCAU, CCCCCC, CCCCCG, CCCCCU, CCCCGA, CCCCGC, CCCCGU, CCCCUA, CCCCUC, CCCGAA, CCCGAC, CCCGAU, CCCGCA, CCCGCU, CCCGGA, CCCGGC, CCCGUA, CCCGUG, CCCGU U, CCCUAA, CCCUAG, CCCUCA, CCCUCU, CCCUGC, CCCUUA, CCCU UC, CCCU UU, CCGAAA, CCGAAC, CCGAAU, CCGACA, CCGACC, CCGACG, CCGACU, CCGAGA, CCGAGG, CCGAGU, CCGAUA, CCGAUC, CCGAUG, CCGAU U, CCGCAA,

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UGCUGU, UGCUUA, UGCUUU, UGGAAC, UGGAAG, UGGAGC, UGGAUC, UGGAUU, UGGCAA, UGGCAC, UGGCAG, UGGCCG, UGGCCU, UGGCGA, UGGCGC, UGGCGU, UGGCUA, UGGCUC, UGGCUU, UGGGAA, UGGGCA, UGGGCC, UGGGGC, UGGGUC, UGGUAA, UGGUAG, UGGUAU, UGGUCC, UGGUCG, UGGUCU, UGGUGA, UGGUGC, UGGUGG, UGGUGU, UGGUUA, UGGUUG, UGUAAA, UGUAAC, UGUAAG, UGUACC, UGUACG, UGUACU, UGUAGA, UGUAGC, UGUAGU, UGUAUC, UGUAUU, UGUCAA, UGUCAC, UGUCAG, UGUCAU, UGUCCA, UGUCCC, UGUCCG, UGUCGA, UGUCGC, UGUCGG, UGUCGU, UGUCUA, UGUCUC, UGUGAC, UGUGAG, UGUGAU, UGUGCA, UGUGGU, UGUGUA, UGUGUU, UGUUAC, UGUUAG, UGUUAU, UGUUCA, UGUUCC, UGUUCG, UGUUGG, UGUUGU, UGUUUA, UGUUUC, UGUUUG, UGUUUU, UUAAAA, UUAAAC, UUAAAG, UUAAAU, UUAACC, UUAACG, UUAACU, UUAAGU, UUAAUA, UUAAUC, UUAAUG, UUAAUU, UUACAA, UUACAC, UUACAG, UUACAU, UUACCA, UUACCC, UUACCG, UUACCU, UUACGA, UUACGC, UUACGG, UUACGU, UUACUA, UUACUC, UUACUG, UUACUU, UUAGAA, UUAGAC, UUAGCC, UUAGCG, UUAGCU, UUAGGC, UUAGGU, UUAGUA, UUAGUC, UUAGUU, UUAUAA, UUAUAC, UUAUAG, UUAUAU, UUAUCC, UUAUCG, UUAUCU, UUAUGA, UUAUGG, UUAUGU, UUAUUA, UUAUUC, UUAUUG, UUAUUU, UUCAAC, UUCAAU, UUCACA, UUCACC, UUCACG, UUCACU, UUCAGC, UUCAGG, UUCAGU, UUCAUA, UUCAUC, UUCAUG, UUCAUU, UUCCAA, UUCCCA, UUCCCG, UUCCGA, UUCCGU, UUCCUU, UUCGAA, UUCGAC, UUCGAG, UUCGAU, UUCGCA, UUCGCC, UUCGCG, UUCGCU, UUCGGA, UUCGGC, UUCGGG, UUCGGU, UUCGUA, UUCGUC, UUCGUG, UUCGUU, UUCUAC, UUCUAG, UUCUCA, UUCUCG, UUCUGG, UUCUUA, UUCUUU, UUGAAA, UUGAAC, UUGAAG, UUGAAU, UUGACC, UUGACG, UUGACU, UUGAGA, UUGAGC, UUGAGU, UUGAUA, UUGAUC, UUGAUG, UUGAUU, UUGCAA, UUGCAC, UUGCAG, UUGCAU, UUGCCC, UUGCCG, UUGCGA, UUGCGC, UUGCGG, UUGCGU, UUGCUA, UUGCUC, UUGCUG, UUGCUU, UUGGAA, UUGGAG, UUGGCC, UUGGCG, UUGGCU, UUGGGC, UUGGGU, UUGGUA, UUGGUG, UUGUAA, UUGUAC, UUGUCA, UUGUCG, UUGUCU, UUGUGC, UUGUGG, UUGUUA, UUGUUG, UUGUUU, UUUAAA, UUUAAC, UUUAAG, UUUAAU, UUUACA, UUUACC, UUUACG, UUUACU, UUUAGA, UUUAGC, UUUAGG, UUUAGU, UUUAUA, UUUAUC, UUUAUG, UUUAUU, UUUCAU, UUUCCA, UUUCCG, UUUCCU, UUUCGA, UUUCGC, UUUCGG, UUUCGU, UUUCUA, UUUCUC, UUUCUG, UUUCUU, UUUGAA, UUUGAC, UUUGAG, UUUGAU, UUUGCC, UUUGCU, UUUGGA, UUUGGC, UUUGGG, UUUGGU, UUUGUA, UUUGUC, UUUGUU, UUUUAA, UUUUAG, UUUUAU, UUUUCC, UUUUCG, UUUUCU, UUUUGA, UUUUGC, UUUUGG, UUUUGU, UUUUUA, UUUUUC, UUUUUU

Table 2: Oligonucleotide sequences made for testing.

SeqID	Oligo Name	Avg RQ	Avg RQ SE	Expt #	Target	[oligo]	cell line	Time (hr)	Assay Type
313770	UTRN-01 mOl	0.56722359	0.19874762	1092	UTRN-69	10000	HSKM	240	qRTPCR
5776	UTRN-02 mOl	0.67184319	0.02092561	1092	UTRN-69	10000	HSKM	240	qRTPCR
5781	UTRN-03 mOl	0.67120255	0.02923406	1092	UTRN-69	10000	HSKM	240	qRTPCR
32192	UTRN-04 m01	0.47381841	0.07845869	1092	UTRN-69	10000	HSKM	240	qRTPCR
39558	UTRN-	0.379107	0.0109907	1092	UTRN-	10000	HSKM	240	qRTPCR

	05 mOl	82	8		69				
45784	UTRN-06m01	0.57173237	0.07542375	1092	UTRN-69	10000	HSKM	240	qRTPCR
60002	UTRN-07 mOl	0.81935385	0.2957031	1092	UTRN-69	10000	HSKM	240	qRTPCR
60035	UTRN-08 mOl	0.47643682	0.00956236	1092	UTRN-69	10000	HSKM	240	qRTPCR
60038	UTRN-09 mOl	0.27641668	0.02978163	1092	UTRN-69	10000	HSKM	240	qRTPCR
336679	UTRN-lOmOl	0.4548524	0.04438911	1092	UTRN-69	10000	HSKM	240	qRTPCR
62709	UTRN-11 mOl	0.31515099	0.08650396	1092	UTRN-69	10000	HSKM	240	qRTPCR
64394	UTRN-12 mOl	0.33957971	0.07934133	1092	UTRN-69	10000	HSKM	240	qRTPCR
64407	UTRN-13 mOl	0.48259158	0.02130792	1092	UTRN-69	10000	HSKM	240	qRTPCR
68368	UTRN-14m01	0.5186531	0.04635273	1092	UTRN-69	10000	HSKM	240	qRTPCR
68420	UTRN-15 mOl	0.40961743	0.01198532	1092	UTRN-69	10000	HSKM	240	qRTPCR
68424	UTRN-16m01	0.58260161	0.08279854	1092	UTRN-69	10000	HSKM	240	qRTPCR
225662	UTRN-51 mOl	0.40878698	0.0396697	1092	UTRN-69	10000	HSKM	240	qRTPCR
229456	UTRN-52 mOl	0.52805355	0.09271042	1092	UTRN-69	10000	HSKM	240	qRTPCR
436557	UTRN-53 mOl	0.60486934	0.01210078	1092	UTRN-69	10000	HSKM	240	qRTPCR
238467	UTRN-54m01	0.48843878	0.08898362	1092	UTRN-69	10000	HSKM	240	qRTPCR
242264	UTRN-55 mOl	0.44606685	0.11570192	1092	UTRN-69	10000	HSKM	240	qRTPCR
251939	UTRN-56m01	0.62479703	0.10459768	1092	UTRN-69	10000	HSKM	240	qRTPCR
453443	UTRN-57 mOl	0.62712277	0.10181988	1092	UTRN-69	10000	HSKM	240	qRTPCR
453483	UTRN-58 mOl	0.60355641	0.06283768	1092	UTRN-69	10000	HSKM	240	qRTPCR
456038	UTRN-59 mOl	0.55331257	0.00333395	1092	UTRN-69	10000	HSKM	240	qRTPCR
272301	UTRN-60m01	0.68004552	0.04014439	1092	UTRN-69	10000	HSKM	240	qRTPCR
276749	UTRN-61 mOl	0.40554491	0.04428404	1092	UTRN-69	10000	HSKM	240	qRTPCR
289697	UTRN-	0.575474	0.1091810	1092	UTRN-	10000	HSKM	240	qRTPCR

	62 mOl	05	6		69				
292490	UTRN-63 mOl	1.22451016	0.1400616	1092	UTRN-69	10000	HSKM	240	qRTPCR
292535	UTRN-64m01	0.35813772	0.02632312	1092	UTRN-69	10000	HSKM	240	qRTPCR
292541	UTRN-65 mOl	0.5783448	0.14263157	1092	UTRN-69	10000	HSKM	240	qRTPCR
	Ctrl Un	1	0.15624566	1092	UTRN-69	10000	HSKM	240	qRTPCR
313770	UTRN-01 mOl	0.80889119	0.22465479	1092	UTRN-02	10000	HSKM	240	qRTPCR
5776	UTRN-02 mOl	0.40448717	0.06346895	1092	UTRN-02	10000	HSKM	240	qRTPCR
5781	UTRN-03 mOl	0.42883333	0.01903559	1092	UTRN-02	10000	HSKM	240	qRTPCR
32192	UTRN-04m01	0.58600693	0.04983107	1092	UTRN-02	10000	HSKM	240	qRTPCR
39558	UTRN-05 mOl	0.44668903	0.03733429	1092	UTRN-02	10000	HSKM	240	qRTPCR
45784	UTRN-06m01	0.60263964	0.05898416	1092	UTRN-02	10000	HSKM	240	qRTPCR
60002	UTRN-07 mOl	0.65881688	0.15865717	1092	UTRN-02	10000	HSKM	240	qRTPCR
60035	UTRN-08 mOl	0.45969974	0.02226413	1092	UTRN-02	10000	HSKM	240	qRTPCR
60038	UTRN-09 mOl	0.28578991	0.05386535	1092	UTRN-02	10000	HSKM	240	qRTPCR
336679	UTRN-lOmOl	0.42517389	0.07119164	1092	UTRN-02	10000	HSKM	240	qRTPCR
62709	UTRN-11 mOl	0.26632703	0.08404946	1092	UTRN-02	10000	HSKM	240	qRTPCR
64394	UTRN-12 mOl	0.24238335	0.08508889	1092	UTRN-02	10000	HSKM	240	qRTPCR
64407	UTRN-13 mOl	0.3867596	0.02251739	1092	UTRN-02	10000	HSKM	240	qRTPCR
68368	UTRN-14m01	0.5047263	0.06510318	1092	UTRN-02	10000	HSKM	240	qRTPCR
68420	UTRN-15 mOl	0.35145444	0.00360596	1092	UTRN-02	10000	HSKM	240	qRTPCR
68424	UTRN-16m01	0.25078544	0.0448786	1092	UTRN-02	10000	HSKM	240	qRTPCR
225662	UTRN-51 mOl	0.42594611	0.01741836	1092	UTRN-02	10000	HSKM	240	qRTPCR
229456	UTRN-52 mOl	0.45785694	0.0993462	1092	UTRN-02	10000	HSKM	240	qRTPCR
436557	UTRN-	0.529350	0.0707348	1092	UTRN-	10000	HSKM	240	qRTPCR

	53 mOl	15	5		02				
238467	UTRN-54m01	0.38557612	0.10392575	1092	UTRN-02	10000	HSKM	240	qRTPCR
242264	UTRN-55 mOl	0.38539574	0.08982757	1092	UTRN-02	10000	HSKM	240	qRTPCR
251939	UTRN-56m01	0.52757689	0.07069548	1092	UTRN-02	10000	HSKM	240	qRTPCR
453443	UTRN-57 mOl	0.60576249	0.08631879	1092	UTRN-02	10000	HSKM	240	qRTPCR
453483	UTRN-58 mOl	1.16594129	0.207295	1092	UTRN-02	10000	HSKM	240	qRTPCR
456038	UTRN-59 mOl	0.74009641	0.06482759	1092	UTRN-02	10000	HSKM	240	qRTPCR
272301	UTRN-60m01	0.56858603	0.01375065	1092	UTRN-02	10000	HSKM	240	qRTPCR
276749	UTRN-61 mOl	0.34556947	0.01341551	1092	UTRN-02	10000	HSKM	240	qRTPCR
289697	UTRN-62 mOl	0.57219193	0.11079267	1092	UTRN-02	10000	HSKM	240	qRTPCR
292490	UTRN-63 mOl	1.76162269	0.37735928	1092	UTRN-02	10000	HSKM	240	qRTPCR
292535	UTRN-64m01	0.42586244	0.13429	1092	UTRN-02	10000	HSKM	240	qRTPCR
292541	UTRN-65 mOl	0.49257532	0.18416443	1092	UTRN-02	10000	HSKM	240	qRTPCR
	Ctrl Un	1	0.12734144	1092	UTRN-02	10000	HSKM	240	qRTPCR
313770	UTRN-01 mOl	0.67362339	0.2232522	1092	UTRN-16	10000	HSKM	240	qRTPCR
5776	UTRN-02 mOl	0.59489089	0.01623233	1092	UTRN-16	10000	HSKM	240	qRTPCR
5781	UTRN-03 mOl	0.60756352	0.02120997	1092	UTRN-16	10000	HSKM	240	qRTPCR
32192	UTRN-04m01	0.84579108	0.07082459	1092	UTRN-16	10000	HSKM	240	qRTPCR
39558	UTRN-05 mOl	0.52590671	0.02640074	1092	UTRN-16	10000	HSKM	240	qRTPCR
45784	UTRN-06m01	0.55979289	0.09669573	1092	UTRN-16	10000	HSKM	240	qRTPCR
60002	UTRN-07 mOl	0.82437207	0.13621597	1092	UTRN-16	10000	HSKM	240	qRTPCR
60035	UTRN-08 mOl	1.02069162	0.15643042	1092	UTRN-16	10000	HSKM	240	qRTPCR
60038	UTRN-09 mOl	0.52400801	0.11892967	1092	UTRN-16	10000	HSKM	240	qRTPCR
336679	UTRN-	0.666533	0.0057863	1092	UTRN-	10000	HSKM	240	qRTPCR

	lOmOl	72	5		16				
62709	UTRN-11 mOl	0.46489043	0.11377591	1092	UTRN-16	10000	HSKM	240	qRTPCR
64394	UTRN-12 mOl	0.29381633	0.10236692	1092	UTRN-16	10000	HSKM	240	qRTPCR
64407	UTRN-13 mOl	0.43332498	0.02180279	1092	UTRN-16	10000	HSKM	240	qRTPCR
68368	UTRN-14m01	0.60192704	0.07793789	1092	UTRN-16	10000	HSKM	240	qRTPCR
68420	UTRN-15 mOl	0.50850314	0.02026773	1092	UTRN-16	10000	HSKM	240	qRTPCR
68424	UTRN-16m01	0.79338782	0.14011627	1092	UTRN-16	10000	HSKM	240	qRTPCR
225662	UTRN-51 mOl	0.61828072	0.03135995	1092	UTRN-16	10000	HSKM	240	qRTPCR
229456	UTRN-52 mOl	0.67684173	0.11544636	1092	UTRN-16	10000	HSKM	240	qRTPCR
436557	UTRN-53 mOl	0.66132939	0.00638037	1092	UTRN-16	10000	HSKM	240	qRTPCR
238467	UTRN-54m01	0.52348932	0.13255186	1092	UTRN-16	10000	HSKM	240	qRTPCR
242264	UTRN-55 mOl	0.43640996	0.072764	1092	UTRN-16	10000	HSKM	240	qRTPCR
251939	UTRN-56m01	0.63988557	0.11520213	1092	UTRN-16	10000	HSKM	240	qRTPCR
453443	UTRN-57 mOl	0.93462493	0.18712741	1092	UTRN-16	10000	HSKM	240	qRTPCR
453483	UTRN-58 mOl	0.75940222	0.0719666	1092	UTRN-16	10000	HSKM	240	qRTPCR
456038	UTRN-59 mOl	0.83102612	0.09768756	1092	UTRN-16	10000	HSKM	240	qRTPCR
272301	UTRN-60m01	0.90452397	0.03259764	1092	UTRN-16	10000	HSKM	240	qRTPCR
276749	UTRN-61 mOl	0.43497163	0.04443017	1092	UTRN-16	10000	HSKM	240	qRTPCR
289697	UTRN-62 mOl	0.52034725	0.08101528	1092	UTRN-16	10000	HSKM	240	qRTPCR
292490	UTRN-63 mOl	2.09680006	0.29037971	1092	UTRN-16	10000	HSKM	240	qRTPCR
292535	UTRN-64m01	0.47456584	0.04190501	1092	UTRN-16	10000	HSKM	240	qRTPCR
292541	UTRN-65 mOl	0.67792191	0.14377542	1092	UTRN-16	10000	HSKM	240	qRTPCR
	Ctrl Un	1	0.06312076	1092	UTRN-16	10000	HSKM	240	qRTPCR
313770	UTRN-	0.757577	0.0651988	1093	UTRN-	10	SK-N-	96	qRTPCR

	01 mOl	5	2		16		AS		
5776	UTRN-02 mOl	0.85222427	0.10789825	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
5781	UTRN-03 mOl	1.01396082	0.09810241	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
32192	UTRN-04m01	1.03810301	0.03479278	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
39558	UTRN-05 mOl	0.83811001	0.07880378	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
45784	UTRN-06m01	0.83497824	0.07648946	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
60002	UTRN-07 mOl	0.96839775	0.01027857	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
60035	UTRN-08 mOl	0.75617386	0.07285202	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
60038	UTRN-09 mOl	0.7312052	0.10368988	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
336679	UTRN-lOmOl	0.79199888	0.02149166	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
62709	UTRN-11 mOl	0.83242213	0.06016044	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
64394	UTRN-12 mOl	0.64519349	0.01424472	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
64407	UTRN-13 mOl	1.11054003	0.18126866	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
68368	UTRN-14m01	0.88642258	0.02610345	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
68420	UTRN-15 mOl	0.97809677	0.03996164	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
68424	UTRN-16m01	1.05603303	0.0221464	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
82947	UTRN-17 mOl	0.86484877	0.03445718	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
85204	UTRN-18 mOl	0.87523415	0.06143543	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
89541	UTRN-19 mOl	0.81075428	0.06133622	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
355024	UTRN-20m01	0.88311212	0.09117433	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
99210	UTRN-21 mOl	0.74490634	0.07508644	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
101919	UTRN-22 mOl	1.02899798	0.08963731	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
101994	UTRN-23 mOl	0.68475403	0.07475312	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
103832	UTRN-	1.163646	0.0205931	1093	UTRN-	10	SK-N-	96	qRTPCR

	24 m01	8	7		16		AS		
103833	UTRN-25 mOl	1.0058327	0.07356244	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
103853	UTRN-26 m01	0.9156987 3	0.04941268	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
103933	UTRN-27 mOl	1.0264325 9	0.09834793	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
117420	UTRN-28 mOl	0.8944546 2	0.06128667	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
120115	UTRN-29 mOl	1.4876180 3	0.15210318	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
120121	UTRN-30 m01	0.9962421 7	0.09012073	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
	Ctrl Un	1.1593515 7	0.09751773	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
	Ctrl Lipo	1	0.15131056	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
362061	UTRN-31 mOl	0.8950112 9	0.10526106	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
372488	UTRN-32 mOl	0.9193177 9	0.04115957	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
372542	UTRN-33 mOl	0.9257933	0.10415883	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
376352	UTRN-34 m01	0.9140217 7	0.11538068	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
139243	UTRN-35 mOl	0.6441603 2	0.02961176	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
143189	UTRN-36 m01	0.7944654 5	0.08975342	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
151630	UTRN-37 mOl	1.0822911 9	0.15428042	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
166370	UTRN-38 mOl	0.7317089 6	0.11684001	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
166372	UTRN-39 mOl	0.8373646 3	0.04842828	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
169368	UTRN-40 m01	1.0057193 1	0.09657045	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
399345	UTRN-41 mOl	0.6679405 6	0.12852317	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
412519	UTRN-42 mOl	0.8097281 3	0.03420812	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
412600	UTRN-43 mOl	0.9318418 1	0.0330165	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
414862	UTRN-44 m01	0.7780304	0.0640387	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
195707	UTRN-	0.764635	0.1129499	1093	UTRN-	10	SK-N-	96	qRTPCR

	45 mOl	6	8		16		AS		
422943	UTRN-46 m01	1.03916407	0.18471623	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
422946	UTRN-47 mOl	0.78047667	0.05266601	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
210674	UTRN-48 mOl	0.69055555	0.00272025	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
426032	UTRN-49 mOl	0.9731503	0.09896712	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
225629	UTRN-50 m01	0.65724116	0.02090648	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
225662	UTRN-51 mOl	0.87698771	0.12228726	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
229456	UTRN-52 mOl	1.08973844	0.09000559	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
436557	UTRN-53 mOl	0.81611016	0.03686041	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
238467	UTRN-54 m01	0.93870312	0.06965803	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
242264	UTRN-55 mOl	0.82889014	0.17454161	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
251939	UTRN-56 m01	1.13435171	0.17819815	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
453443	UTRN-57 mOl	1.3064641	0.26025914	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
453483	UTRN-58 mOl	0.84810601	0.11631749	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
456038	UTRN-59 mOl	0.74549699	0.03267881	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
272301	UTRN-60 m01	1.19595592	0.13571268	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
	Ctrl Un	1.05713903	0.11259158	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
	Ctrl Lipo	1	0.08245938	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
276749	UTRN-61 mOl	1.03127416	0.10921988	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
289697	UTRN-62 mOl	1.044169	0.03233713	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
292490	UTRN-63 mOl	1.52465937	0.09572692	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
292535	UTRN-64 m01	1.1321036	0.05236107	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
292541	UTRN-65 mOl	1.08228927	0.13345192	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
	Ctrl	1	0.0570959	1093	UTRN-	10	SK-N-	96	qRTPCR

	Lipo		7		16		AS		
	Ctrl Un	1.47130024	0.02213981	1093	UTRN-16	10	SK-N-AS	96	qRTPCR
313770	UTRN-01 mOl	0.60984478	0.06309994	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
5776	UTRN-02 mOl	0.89147593	0.13375976	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
5781	UTRN-03 mOl	0.61855672	0.02207853	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
32192	UTRN-04 m01	1.28418183	0.15451636	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
39558	UTRN-05 mOl	0.52634941	0.02812606	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
45784	UTRN-06 m01	0.71111335	0.08563004	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
60002	UTRN-07 mOl	0.99729465	0.11235194	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
60035	UTRN-08 mOl	0.86387159	0.18316087	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
60038	UTRN-09 mOl	0.72007659	0.24804121	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
336679	UTRN-l OmOl	0.86416247	0.34064684	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
62709	UTRN-11 mOl	0.8083888	0.08325476	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
64394	UTRN-12 mOl	0.66395045	0.0899959	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
64407	UTRN-13 mOl	1.67089265	0.2291624	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
68368	UTRN-14 m01	1.025824	0.22573532	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
68420	UTRN-15 mOl	0.73754467	0.09940368	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
68424	UTRN-16 m01	0.94217145	0.1721728	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
82947	UTRN-17 mOl	0.58124677	0.04563767	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
85204	UTRN-18 mOl	0.61668486	0.05784673	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
89541	UTRN-19 mOl	0.54982484	0.09185093	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
355024	UTRN-20 m01	0.67455874	0.19009293	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
99210	UTRN-21 mOl	0.58343685	0.04620854	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
101919	UTRN-	1.484405	0.2677884	1093	UTRN-	30	SK-N-	96	qRTPCR

	22 mOl	99	3		16		AS		
101994	UTRN-23 mOl	0.81907189	0.0273814	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
103832	UTRN-24 m01	1.25868392	0.17591054	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
103833	UTRN-25 mOl	1.0311567	0.11744487	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
103853	UTRN-26 m01	0.72249989	0.11346444	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
103933	UTRN-27 mOl	1.18559662	0.06292947	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
117420	UTRN-28 mOl	1.61312748	0.02476836	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
120115	UTRN-29 mOl	1.0051088	0.15356527	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
120121	UTRN-30 m01	0.92694391	0.13136339	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
	Ctrl Un	1.05582073	0.16466874	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
	Ctrl Lipo	1	0.101077	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
362061	UTRN-31 mOl	0.50511184	0.01784854	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
372488	UTRN-32 mOl	0.80809669	0.00211969	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
372542	UTRN-33 mOl	0.65771104	0.06565461	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
376352	UTRN-34 m01	0.5431115	0.02628406	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
139243	UTRN-35 mOl	0.56264098	0.05675936	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
143189	UTRN-36 m01	0.57779435	0.02631325	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
151630	UTRN-37 mOl	0.50337944	0.05884767	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
166370	UTRN-38 mOl	0.32025952	0.01286791	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
166372	UTRN-39 mOl	0.60714523	0.02373014	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
169368	UTRN-40 m01	1.12335489	0.19727474	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
399345	UTRN-41 mOl	0.49256976	0.04675795	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
412519	UTRN-42 mOl	0.68909557	0.03904239	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
412600	UTRN-	0.964888	0.2058873	1093	UTRN-	30	SK-N-	96	qRTPCR

	43 mOl	78	4		16		AS		
414862	UTRN-44 m01	0.52495952	0.08382155	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
195707	UTRN-45 mOl	0.73795336	0.05541599	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
422943	UTRN-46 m01	0.74085667	0.06637287	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
422946	UTRN-47 mOl	0.42761568	0.01772915	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
210674	UTRN-48 mOl	0.58780787	0.02910385	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
426032	UTRN-49 mOl	0.72965664	0.02867856	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
225629	UTRN-50 m01	0.40395121	0.03201391	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
225662	UTRN-51 mOl	0.83099737	0.12029916	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
229456	UTRN-52 mOl	0.77073083	0.16512396	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
436557	UTRN-53 mOl	0.48278404	0.01573001	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
238467	UTRN-54 m01	0.49363203	0.08427735	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
242264	UTRN-55 mOl	0.69749568	0.03277514	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
251939	UTRN-56 m01	0.59481116	0.07476238	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
453443	UTRN-57 mOl	1.08275204	0.0676891	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
453483	UTRN-58 mOl	0.37405908	0.03151226	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
456038	UTRN-59 mOl	0.34267879	0.04428324	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
272301	UTRN-60 m01	0.77142847	0.04819709	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
	Ctrl Un	0.77092848	0.16407024	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
	Ctrl Lipo	1	0.1342955	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
276749	UTRN-61 mOl	0.65483288	0.07342203	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
289697	UTRN-62 mOl	0.98337602	0.13676097	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
292490	UTRN-63 mOl	2.58061127	0.15400488	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
292535	UTRN-	0.883720	0.0301472	1093	UTRN-	30	SK-N-	96	qRTPCR

	64 m01	96	1		16		AS		
292541	UTRN-65 mOl	0.9736869	0.04890107	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
	Ctrl Lipo	1	0.08104028	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
	Ctrl Un	1.20258604	0.15138558	1093	UTRN-16	30	SK-N-AS	96	qRTPCR
313770	UTRN-01 mOl	0.32616792	0.02185726	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
5776	UTRN-02 mOl	1.01669863	0.0462533	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
5781	UTRN-03 mOl	0.70233657	0.0250169	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
32192	UTRN-04 m01	1.59956172	0.13696613	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
39558	UTRN-05 mOl	0.58957401	0.02802524	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
45784	UTRN-06 m01	1.0334611	0.00777542	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
60002	UTRN-07 mOl	0.76143058	0.02768371	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
60035	UTRN-08 mOl	0.39512861	0.00936128	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
60038	UTRN-09 mOl	0.34012174	0.01623502	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
336679	UTRN-l OmOl	0.38868099	0.01886348	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
62709	UTRN-11 mOl	0.50986245	0.03047854	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
64394	UTRN-12 mOl	0.60028491	0.00721445	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
64407	UTRN-13 mOl	0.72114801	0.0075241	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR

68368	UTRN-14 m01	1.12622763	0.03367478	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
68420	UTRN-15 mOl	0.53891452	0.01936459	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
68424	UTRN-16 m01	1.11183444	0.04790854	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
82947	UTRN-17 mOl	0.82497461	0.03386966	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
85204	UTRN-18 mOl	0.79359523	0.03608986	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
89541	UTRN-19 mOl	0.28545383	0.01787595	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
355024	UTRN-20 m01	0.92181838	0.08353234	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
99210	UTRN-21 mOl	0.64207739	0.02593464	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
101919	UTRN-22 mOl	1.37266809	0.03108759	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
101994	UTRN-23 mOl	0.58216388	0.02158436	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
103832	UTRN-24 m01	1.45704637	0.04091926	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
276749	UTRN-61 mOl	0.62942509	0.01705386	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
289697	UTRN-62 mOl	1.01437442	0.08211814	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
292490	UTRN-63 mOl	1.40856666	0.13479916	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
292535	UTRN-64 m01	0.58443353	0.02574256	1094	UTRN-16	50	amOO 2fDMD	96	qRTPCR
292541	UTRN-65 mOl	0.44749637	0.019656	1094	UTRN-16	50	amOO 2fDM	96	qRTPCR

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	Ctrl Un	1.293983 42	0.010621	1094	UTRN-16	50	amOO 2fDM D	96	qRTPCR
	Ctrl Lipo	1	0.0266363	1094	UTRN-16	50	amOO 2fDM D	96	qRTPCR
313770	UTRN-01 mOl	0.200063 44	0.0479847 1	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
5776	UTRN-02 mOl	0.375427 54	0.0685709 6	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
5781	UTRN-03 mOl	0.318321 93	0.0594546 6	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
32192	UTRN-04 m01	1.031831 23	0.0823938 9	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
39558	UTRN-05 mOl	0.968771 2	0.0399313 6	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
45784	UTRN-06 m01	0.835151 8	0.0399697	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
60002	UTRN-07 mOl	0.447966 1	0.0293348 1	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
60035	UTRN-08 mOl	0.520033 64	0.0187217 6	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
60038	UTRN-09 mOl	0.324561 03	0.0119251 6	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
336679	UTRN-l OmOl	0.581292 19	0.0235723 1	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
62709	UTRN-11 mOl	0.492435 56	0.0206654 4	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
64394	UTRN-12 mOl	0.631436 65	0.0387497 3	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
64407	UTRN-13 mOl	1.143554 59	0.0568240 8	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR

68368	UTRN-14 m01	0.42045044	0.05763665	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
68420	UTRN-15 mOl	0.68441644	0.05478663	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
68424	UTRN-16 m01	0.58821005	0.04014146	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
82947	UTRN-17 mOl	0.36863122	0.03598423	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
85204	UTRN-18 mOl	0.66171976	0.0178607	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
89541	UTRN-19 mOl	0.11822583	0.01493743	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
355024	UTRN-20 m01	0.70082483	0.07992993	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
99210	UTRN-21 mOl	0.71340219	0.05198843	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
101919	UTRN-22 mOl	0.45449951	0.04236762	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
101994	UTRN-23 mOl	0.63994873	0.02817303	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
103832	UTRN-24 m01	0.88092337	0.05871034	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
276749	UTRN-61 mOl	0.23006675	0.03780199	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
289697	UTRN-62 mOl	1.12844673	0.17967005	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
292490	UTRN-63 mOl	0.18433323	0.03485563	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
292535	UTRN-64 m01	0.17433798	0.01365184	1094	UTRN-69	50	amOO 2fDMD	96	qRTPCR
292541	UTRN-65 mOl	0.50196292	0.0491373	1094	UTRN-69	50	amOO 2fDM	96	qRTPCR

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	Ctrl Un	2.136450 92	0.0973056 5	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
	Ctrl Lipo	1	0.1015793 1	1094	UTRN-69	50	amOO 2fDM D	96	qRTPCR
313770	UTRN-01 mOl	0.270160 57	0.0537116	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
5776	UTRN-02 mOl	0.437558 94	0.0576139 5	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
5781	UTRN-03 mOl	0.412494 59	0.0294363 1	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
32192	UTRN-04 m01	1.115190 83	0.0743017 4	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
39558	UTRN-05 mOl	1.011592 92	0.0262187	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
45784	UTRN-06 m01	0.899692 33	0.0106237 4	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
60002	UTRN-07 mOl	0.551755 58	0.0488109 3	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
60035	UTRN-08 mOl	0.582255 9	0.0366705 9	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
60038	UTRN-09 mOl	0.352455 32	0.04133	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
336679	UTRN-l OmOl	0.550474 95	0.0220726 8	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
62709	UTRN-11 mOl	0.417839 56	0.0209482	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
64394	UTRN-12 mOl	0.533388 75	0.0270747	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR
64407	UTRN-13 mOl	1.172305 76	0.0810883 9	1094	UTRN-02	50	amOO 2fDM D	96	qRTPCR

68368	UTRN-14 m01	0.54787389	0.09693453	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
68420	UTRN-15 mOl	0.71271868	0.06754801	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
68424	UTRN-16 m01	0.29579555	0.02408746	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
82947	UTRN-17 mOl	0.36760298	0.03225722	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
85204	UTRN-18 mOl	0.71687906	0.02515345	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
89541	UTRN-19 mOl	0.1380875	0.01926532	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
355024	UTRN-20 m01	0.7078851	0.04532949	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
99210	UTRN-21 mOl	0.68991983	0.03857872	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
101919	UTRN-22 mOl	0.49654219	0.05756049	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
101994	UTRN-23 mOl	0.64166664	0.03200979	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
103832	UTRN-24 m01	0.86083828	0.08223742	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
276749	UTRN-61 mOl	0.36924754	0.03271067	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
289697	UTRN-62 mOl	1.30122081	0.21051853	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
292490	UTRN-63 mOl	0.24329494	0.01817197	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
292535	UTRN-64 m01	0.17744299	0.01532655	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
292541	UTRN-65 mOl	0.55237323	0.01848998	1094	UTRN-02	50	amOO 2fDM	96	qRTPCR

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	Ctrl Un	2.36606122	0.10116289	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
	Ctrl Lipo	1	0.07587432	1094	UTRN-02	50	amOO 2fDMD	96	qRTPCR
313770	UTRN-01 mOl	0.23166392	0.03986326	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
5776	UTRN-02 mOl	0.7562623	0.03218152	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
5781	UTRN-03 mOl	0.68206196	0.07354295	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
32192	UTRN-04 m01	1.38957133	0.07032511	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
39558	UTRN-05 mOl	0.77569544	0.02262853	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
45784	UTRN-06 m01	1.43617331	0.02530774	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
60002	UTRN-07 mOl	0.99220334	0.07921071	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
60035	UTRN-08 mOl	0.46517717	0.03573208	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
60038	UTRN-09 mOl	0.46125504	0.00935883	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
336679	UTRN-l OmOl	0.68754121	0.02920918	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
62709	UTRN-11 mOl	0.60949652	0.06010728	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
64394	UTRN-12 mOl	0.44118491	0.01910906	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR
64407	UTRN-13 mOl	1.03529403	0.07129539	1095	UTRN-16	50	amOO 2fDMD	168	qRTPCR

68368	UTRN-14 m01	0.997852 37	0.0027716 9	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
68420	UTRN-15 mOl	0.582290 01	0.0343304 3	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
68424	UTRN-16 m01	1.077852 44	0.0508851 4	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
82947	UTRN-17 mOl	1.133088 49	0.0872718 6	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
85204	UTRN-18 mOl	0.888279 48	0.0255301 1	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
89541	UTRN-19 mOl	0.437855 75	0.0362509 2	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
355024	UTRN-20 m01	1.036151 97	0.1072805 8	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
99210	UTRN-21 mOl	0.849358 9	0.0210921 7	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
101919	UTRN-22 mOl	1.134063 58	0.0784872 1	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
101994	UTRN-23 mOl	0.785376 51	0.0378730 8	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
103832	UTRN-24 m01	1.579593 87	0.0211809 7	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
276749	UTRN-61 mOl	0.276964 13	0.0278247	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
289697	UTRN-62 mOl	1.025834 43	0.0913287 7	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
292490	UTRN-63 mOl	1.363210 54	0.0227907 4	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
292535	UTRN-64 m01	0.802721 69	0.0355891 9	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
292541	UTRN-65 mOl	0.451381 21	0.0395210 7	1095	UTRN-16	50	amOO 2fDM	168	qRTPCR

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	Ctrl Un	1.059252 62	0.0576024 7	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
	Ctrl Lipo	1	0.0305738 6	1095	UTRN-16	50	amOO 2fDM D	168	qRTPCR
313770	UTRN-01 mOl	0.750553 97	0.0519179 1	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
5776	UTRN-02 mOl	0.932678 94	0.0836112 7	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
5781	UTRN-03 mOl	0.845937 5	0.0689847 9	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
32192	UTRN-04 m01	0.948068 81	0.0072707 6	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
39558	UTRN-05 mOl	0.855485 43	0.0268599 5	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
45784	UTRN-06 m01	0.876722 97	0.0858836 9	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
60002	UTRN-07 mOl	0.919232 87	0.0376135 8	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
60035	UTRN-08 mOl	0.852685 62	0.0176562 1	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
60038	UTRN-09 mOl	0.755969 14	0.0363114 3	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
336679	UTRN-l OmOl	0.846415 68	0.1015263 5	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
62709	UTRN-11 mOl	0.696953 09	0.030787	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
64394	UTRN-12 mOl	0.763276 96	0.0411056	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
64407	UTRN-13 mOl	0.821724 28	0.0442925	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR

68368	UTRN-14 m01	0.765373 62	0.0185059 8	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
68420	UTRN-15 mOl	0.782522 29	0.0222246 1	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
68424	UTRN-16 m01	0.900370 16	0.0457554 4	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
82947	UTRN-17 mOl	0.959084 59	0.0731709 5	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
85204	UTRN-18 mOl	0.806000 73	0.0568940 5	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
89541	UTRN-19 mOl	0.690837 38	0.0348385 2	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
355024	UTRN-20 m01	0.827973 69	0.0732032 7	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
99210	UTRN-21 mOl	0.927943 61	0.0290955 7	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
101919	UTRN-22 mOl	0.799957 75	0.0647240 3	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
101994	UTRN-23 mOl	0.803951 9	0.0761958 3	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
103832	UTRN-24 m01	0.835080 16	0.0262635 1	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
103833	UTRN-25 mOl	0.944663 45	0.0775039 2	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
103853	UTRN-26 m01	0.807983 64	0.0336117 2	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
103933	UTRN-27 mOl	0.879840 23	0.0214700 1	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
117420	UTRN-28 mOl	0.732057 2	0.07556	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
120115	UTRN-29 mOl	1.131345 23	0.0226549 7	1096	UTRN-16	30	amOO 2fDM	240	qRTPCR

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120121	UTRN-30 m01	0.79490416	0.06953964	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
	Ctrl Un	0.84394069	0.04916997	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
	Ctrl Lipo	1	0.06926976	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
362061	UTRN-31 mOl	0.9709284	0.01153552	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
372488	UTRN-32 mOl	1.06867182	0.02106709	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
372542	UTRN-33 mOl	1.082223	0.02532558	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
376352	UTRN-34 m01	1.00992377	0.06565572	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
139243	UTRN-35 mOl	1.00400191	0.13229164	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
143189	UTRN-36 m01	1.15434692	0.08027218	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
151630	UTRN-37 mOl	0.97730844	0.05076649	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
166370	UTRN-38 mOl	1.12892012	0.07118998	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
166372	UTRN-39 mOl	1.10114938	0.07594277	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
169368	UTRN-40 m01	1.21178408	0.08044384	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
399345	UTRN-41 mOl	1.0417129	0.03344421	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR
412519	UTRN-42 mOl	1.07744408	0.06857424	1096	UTRN-16	30	amOO 2fDMD	240	qRTPCR

412600	UTRN-43 mOl	0.924578 66	0.0319588 5	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
414862	UTRN-44 m01	1.055441 15	0.0300824 5	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
195707	UTRN-45 mOl	0.980526 64	0.0909284 9	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
422943	UTRN-46 m01	1.098925 13	0.0198460 4	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
422946	UTRN-47 mOl	0.794970 43	0.0248972 8	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
210674	UTRN-48 mOl	0.889197 09	0.0168988	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
426032	UTRN-49 mOl	0.930483 26	0.0302888 3	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
225629	UTRN-50 m01	0.997402 07	0.0540456	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
225662	UTRN-51 mOl	1.014453 04	0.0609220 2	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
229456	UTRN-52 mOl	1.078299 75	0.0960239 3	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
436557	UTRN-53 mOl	0.922433 19	0.0495010 7	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
238467	UTRN-54 m01	1.044947 04	0.0842068 7	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
242264	UTRN-55 mOl	0.961382 08	0.0238776	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
251939	UTRN-56 m01	0.918689 51	0.0278237 3	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
453443	UTRN-57 mOl	0.879552 84	0.0417934 7	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
453483	UTRN-58 mOl	0.941436 9	0.0542119 4	1096	UTRN-16	30	amOO 2fDM	240	qRTPCR

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456038	UTRN-59 mOl	0.97625584	0.05408032	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
272301	UTRN-60 m01	1.23338031	0.11033036	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
	Ctrl Un	0.96551729	0.04747653	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
	Ctrl Lipo	1	0.0303013	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
276749	UTRN-61 mOl	0.96970978	0.01935113	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
289697	UTRN-62 mOl	1.10260017	0.06256634	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
292490	UTRN-63 mOl	1.22965464	0.08170049	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
292535	UTRN-64 m01	1.14528961	0.02605831	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
292541	UTRN-65 mOl	1.12304054	0.0494786	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
	Ctrl Lipo	1	0.0328001	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
	Ctrl Un	1.06036423	0.07916255	1096	UTRN-16	30	amOO 2fDM D	240	qRTPCR
313770	UTRN-01 mOl	0.67462825	0.08165038	1097	UTRN-16	30	amOO 2fDM D	144	qRTPCR
5776	UTRN-02 mOl	1.0040793	0.03792203	1097	UTRN-16	30	amOO 2fDM D	144	qRTPCR
5781	UTRN-03 mOl	1.05073108	0.06995556	1097	UTRN-16	30	amOO 2fDM D	144	qRTPCR
32192	UTRN-04 m01	1.21889789	0.04939547	1097	UTRN-16	30	amOO 2fDM D	144	qRTPCR

39558	UTRN-05 mOl	0.97204726	0.02800328	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
45784	UTRN-06 m01	1.19749167	0.11502609	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
60002	UTRN-07 mOl	1.05892638	0.03195538	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
60035	UTRN-08 mOl	0.96059417	0.13090996	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
60038	UTRN-09 mOl	0.79396118	0.02398773	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
336679	UTRN-l OmOl	1.1137313	0.08926529	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
62709	UTRN-11 mOl	1.03710375	0.02946032	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
64394	UTRN-12 mOl	1.07733712	0.03880175	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
64407	UTRN-13 mOl	1.11772016	0.04658961	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
68368	UTRN-14 m01	1.07447243	0.06712376	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
68420	UTRN-15 mOl	1.10416183	0.01446185	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
68424	UTRN-16 m01	1.22784073	0.01283689	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
82947	UTRN-17 mOl	1.13231879	0.02632991	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
85204	UTRN-18 mOl	1.18971985	0.07744601	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
89541	UTRN-19 mOl	1.06468745	0.04841277	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
355024	UTRN-20 m01	1.28469255	0.08438321	1097	UTRN-16	30	amOO 2fDM	144	qRTPCR

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99210	UTRN-21 mOl	1.2761479	0.02407821	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
101919	UTRN-22 mOl	1.34357124	0.03731536	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
101994	UTRN-23 mOl	0.95200968	0.03605078	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
103832	UTRN-24 m01	1.22036161	0.01059834	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
103833	UTRN-25 mOl	1.26356309	0.09774877	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
103853	UTRN-26 m01	1.08808616	0.04569736	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
103933	UTRN-27 mOl	1.03276149	0.04356174	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
117420	UTRN-28 mOl	1.24524138	0.01823423	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
120115	UTRN-29 mOl	1.39018159	0.02601533	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
120121	UTRN-30 m01	1.08224781	0.03837067	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
	Ctrl Un	1.03242662	0.04553206	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
	Ctrl Lipo	1	0.04378138	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
362061	UTRN-31 mOl	0.76844471	0.02706795	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
372488	UTRN-32 mOl	1.08294629	0.02698451	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
372542	UTRN-33 mOl	1.41025624	0.02528352	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR

376352	UTRN-34 m01	1.16630314	0.0576001	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
139243	UTRN-35 mOl	0.91507564	0.03123946	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
143189	UTRN-36 m01	0.97742097	0.00384429	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
151630	UTRN-37 mOl	1.13551038	0.02995458	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
166370	UTRN-38 mOl	0.95864002	0.07166238	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
166372	UTRN-39 mOl	1.0509856	0.01855711	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
169368	UTRN-40 m01	1.12206678	0.02649287	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
399345	UTRN-41 mOl	1.11991272	0.04296588	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
412519	UTRN-42 mOl	1.0642452	0.06414741	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
412600	UTRN-43 mOl	1.09166311	0.03507153	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
414862	UTRN-44 m01	1.22016214	0.02217895	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
195707	UTRN-45 mOl	1.17726461	0.01617406	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
422943	UTRN-46 m01	1.21931609	0.05796389	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
422946	UTRN-47 mOl	1.09650056	0.07741785	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
210674	UTRN-48 mOl	1.19915402	0.0338564	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
426032	UTRN-49 mOl	1.13219977	0.03432322	1097	UTRN-16	30	amOO 2fDM	144	qRTPCR

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225629	UTRN-50 m01	1.17482362	0.07479833	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
225662	UTRN-51 mOl	0.86280779	0.0230224	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
229456	UTRN-52 mOl	1.10025011	0.0429719	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
436557	UTRN-53 mOl	1.01849372	0.02944671	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
238467	UTRN-54 m01	0.93011546	0.0506212	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
242264	UTRN-55 mOl	0.928550 5	0.02965249	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
251939	UTRN-56 m01	1.02614832	0.05760928	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
453443	UTRN-57 mOl	0.99500772	0.00717961	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
453483	UTRN-58 mOl	1.03468366	0.03962052	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
456038	UTRN-59 mOl	1.00688925	0.04965703	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
272301	UTRN-60 m01	0.992163 1	0.01799872	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
	Ctrl Un	1.08692556	0.04802467	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
	Ctrl Lipo	1	0.04148875	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
276749	UTRN-61 mOl	0.95657363	0.07952758	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
289697	UTRN-62 mOl	1.27556793	0.08315062	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR

292490	UTRN-63 mOl	1.16339533	0.08677085	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
292535	UTRN-64 m01	1.36654512	0.04898731	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
292541	UTRN-65 mOl	0.86254085	0.06740933	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
	Ctrl Lipo	1	0.07402642	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
	Ctrl Un	1.69636888	0.10587351	1097	UTRN-16	30	amOO 2fDMD	144	qRTPCR
313770	UTRN-01 mOl	0.58076529	0.03039882	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
5776	UTRN-02 mOl	0.96881503	0.08147278	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
5781	UTRN-03 mOl	0.8233217	0.04011316	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
32192	UTRN-04 m01	1.16671325	0.06652984	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
39558	UTRN-05 mOl	0.80244274	0.03208655	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
45784	UTRN-06 m01	1.1712878	0.03151455	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
60002	UTRN-07 mOl	0.89575232	0.02762414	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
60035	UTRN-08 mOl	0.5689325	0.01841599	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
60038	UTRN-09 mOl	0.46116762	0.02018062	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
336679	UTRN-l OmOl	0.59071506	0.02036091	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
62709	UTRN-11 mOl	0.45292364	0.05621024	1098	UTRN-16	30	amOO 2fDM	96	qRTPCR

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64394	UTRN-12 mOl	0.59036933	0.02970165	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
64407	UTRN-13 mOl	0.47978013	0.04345336	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
68368	UTRN-14 m01	1.09580674	0.02423345	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
68420	UTRN-15 mOl	0.74264079	0.03365387	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
68424	UTRN-16 m01	0.87712391	0.05397445	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
82947	UTRN-17 mOl	1.08253115	0.02494187	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
85204	UTRN-18 mOl	0.76472603	0.03441017	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
89541	UTRN-19 mOl	0.44534113	0.02299761	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
355024	UTRN-20 m01	0.79603848	0.06100838	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
99210	UTRN-21 mOl	0.55112051	0.01090463	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
101919	UTRN-22 mOl	1.10907773	0.01134182	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
101994	UTRN-23 mOl	0.7410306	0.04264853	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
103832	UTRN-24 m01	1.19776254	0.04344756	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
103833	UTRN-25 mOl	1.40237149	0.04131397	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
103853	UTRN-26 m01	0.88496235	0.02236041	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR

103933	UTRN-27 mOl	0.51259821	0.02670704	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
117420	UTRN-28 mOl	0.85318924	0.01188527	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
120115	UTRN-29 mOl	1.4078235	0.0069635	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
120121	UTRN-30 m01	0.97599956	0.03751087	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
	Ctrl Un	1.05179276	0.06427556	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
	Ctrl Lipo	1	0.07413322	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
362061	UTRN-31 mOl	0.87482409	0.03160046	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
372488	UTRN-32 mOl	0.90578907	0.04281746	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
372542	UTRN-33 mOl	0.79508229	0.04767849	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
376352	UTRN-34 m01	1.12394667	0.10893678	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
139243	UTRN-35 mOl	0.63887247	0.02591518	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
143189	UTRN-36 m01	1.02155885	0.07088794	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
151630	UTRN-37 mOl	0.70881548	0.06529816	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
166370	UTRN-38 mOl	0.50209162	0.03139329	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
166372	UTRN-39 mOl	0.82631739	0.00543354	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
169368	UTRN-40 m01	0.87845259	0.02260314	1098	UTRN-16	30	amOO 2fDM	96	qRTPCR

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399345	UTRN-41 mOl	0.70623726	0.01080899	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
412519	UTRN-42 mOl	1.01312974	0.03339384	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
412600	UTRN-43 mOl	0.92072992	0.04505221	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
414862	UTRN-44 m01	0.57355729	0.03685588	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
195707	UTRN-45 mOl	0.79911892	0.01900042	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
422943	UTRN-46 m01	0.93613873	0.01779705	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
422946	UTRN-47 mOl	0.4587612	0.02411369	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
210674	UTRN-48 mOl	0.74859068	0.02362965	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
426032	UTRN-49 mOl	0.66580214	0.02139001	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
225629	UTRN-50 m01	0.83019627	0.02025208	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
225662	UTRN-51 mOl	0.46833508	0.01039709	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
229456	UTRN-52 mOl	0.70892642	0.00242912	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
436557	UTRN-53 mOl	0.64888575	0.03688872	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
238467	UTRN-54 m01	0.8529075	0.03343083	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR
242264	UTRN-55 mOl	0.52305543	0.04356075	1098	UTRN-16	30	amOO 2fDMD	96	qRTPCR

251939	UTRN-56 m01	0.66743863	0.05307766	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
453443	UTRN-57 mOl	0.91013296	0.06546661	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
453483	UTRN-58 mOl	0.6125509	0.02627138	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
456038	UTRN-59 mOl	0.99789605	0.06465815	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
272301	UTRN-60 m01	0.91755307	0.06594373	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
	Ctrl Un	0.89152675	0.0402528	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
	Ctrl Lipo	1	0.06455142	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
276749	UTRN-61 mOl	0.67867922	0.02399703	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
289697	UTRN-62 mOl	1.04840944	0.02365808	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
292490	UTRN-63 mOl	1.00338618	0.0808448	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
292535	UTRN-64 m01	0.77127007	0.03101058	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
292541	UTRN-65 mOl	0.59484854	0.0342936	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
	Ctrl Lipo	1	0.09383278	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
	Ctrl Un	0.95433212	0.05764991	1098	UTRN-16	30	amOO 2fDM D	96	qRTPCR
313770	UTRN-01 mOl	1.09999355	0.0522105	1099	UTRN-16	50	amOO 2fDM D	16	qRTPCR
5776	UTRN-02 mOl	0.98048522	0.05829249	1099	UTRN-16	50	amOO 2fDM	16	qRTPCR

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5781	UTRN-03 mOl	1.11018609	0.09057436	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
32192	UTRN-04 m01	1.04324326	0.05874548	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
39558	UTRN-05 mOl	0.90267337	0.02384534	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
45784	UTRN-06 m01	0.95957965	0.02440134	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
60002	UTRN-07 mOl	1.06633244	0.06683347	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
60035	UTRN-08 mOl	1.03379791	0.07644067	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
60038	UTRN-09 mOl	1.19128452	0.06345743	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
336679	UTRN-l OmOl	1.04590735	0.02568251	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
62709	UTRN-11 mOl	1.3006283	0.09566221	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
64394	UTRN-12 mOl	1.32164316	0.07336719	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
64407	UTRN-13 mOl	1.02457735	0.0099744	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
68368	UTRN-14 m01	0.89786302	0.02932433	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
68420	UTRN-15 mOl	1.04929606	0.02858814	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
68424	UTRN-16 m01	1.0167624	0.04978825	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
82947	UTRN-17 mOl	1.33820211	0.16165828	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR

85204	UTRN-18 mOl	1.08174251	0.03029958	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
89541	UTRN-19 mOl	1.2124862	0.03538288	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
355024	UTRN-20 m01	1.18707808	0.08658924	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
99210	UTRN-21 mOl	1.06985407	0.00459959	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
101919	UTRN-22 mOl	1.02001321	0.00982358	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
101994	UTRN-23 mOl	1.07309486	0.03530298	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
103832	UTRN-24 m01	1.15223004	0.02317344	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
103833	UTRN-25 mOl	1.07729047	0.08903163	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
103853	UTRN-26 m01	1.05670588	0.03993355	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
103933	UTRN-27 mOl	0.92230239	0.13830922	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
117420	UTRN-28 mOl	1.0269754	0.18269877	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
120115	UTRN-29 mOl	0.95740501	0.13717197	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
120121	UTRN-30 m01	0.91015254	0.01477685	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
	Ctrl Un	1.17147479	0.06069851	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
	Ctrl Lipo	1	0.01155989	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
362061	UTRN-31 mOl	0.84129209	0.0551895	1099	UTRN-16	50	amOO 2fDM	16	qRTPCR

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372488	UTRN-32 mOl	0.87401238	0.05711907	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
372542	UTRN-33 mOl	1.00773219	0.136912	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
376352	UTRN-34 m01	0.88581399	0.0883952	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
139243	UTRN-35 mOl	0.81977584	0.0747876	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
143189	UTRN-36 m01	0.90303543	0.0639527	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
151630	UTRN-37 mOl	0.85852205	0.06571187	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
166370	UTRN-38 mOl	0.79791465	0.04599394	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
166372	UTRN-39 mOl	0.70577426	0.02258757	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
169368	UTRN-40 m01	0.86132342	0.07520493	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
399345	UTRN-41 mOl	0.95686499	0.04826801	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
412519	UTRN-42 mOl	0.91846716	0.06735625	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
412600	UTRN-43 mOl	0.90545962	0.0764699	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
414862	UTRN-44 m01	0.87250314	0.04934873	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
195707	UTRN-45 mOl	0.90958	0.0321877	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
422943	UTRN-46 m01	0.77236631	0.02358972	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR

422946	UTRN-47 mOl	0.79566678	0.0195359	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
210674	UTRN-48 mOl	0.92591552	0.0686307	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
426032	UTRN-49 mOl	0.91753186	0.11107633	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
225629	UTRN-50 m01	0.90366093	0.05020314	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
225662	UTRN-51 mOl	0.84773763	0.01225047	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
229456	UTRN-52 mOl	0.93886586	0.03206633	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
436557	UTRN-53 mOl	0.99264254	0.07123769	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
238467	UTRN-54 m01	0.78797951	0.05217497	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
242264	UTRN-55 mOl	0.77050873	0.04398832	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
251939	UTRN-56 m01	0.89266966	0.05871496	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
453443	UTRN-57 mOl	0.92906018	0.07248755	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
453483	UTRN-58 mOl	0.94497021	0.04599071	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
456038	UTRN-59 mOl	0.94970793	0.0624258	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
272301	UTRN-60 m01	0.8175283	0.00629294	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
	Ctrl Un	0.8823963	0.05212196	1099	UTRN-16	50	amOO2fDMD	16	qRTPCR
	Ctrl Lipo	1	0.11512636	1099	UTRN-16	50	amOO2fDM	16	qRTPCR

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276749	UTRN-61 mOl	0.84129209	0.0551895	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
289697	UTRN-62 mOl	0.87401238	0.05711907	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
292490	UTRN-63 mOl	1.00773219	0.136912	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
292535	UTRN-64 m01	0.88581399	0.08839522	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
292541	UTRN-65 mOl	0.81977584	0.0747876	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
497808	unc-232 ml2	0.90303543	0.0639527	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
497809	unc-293 ml2	0.85852205	0.06571187	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
497808	unc-232 mOl	0.79791465	0.04599394	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
497809	unc-293 mOl	0.70577426	0.02258757	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
	Ctrl Un	0.8823963	0.05212196	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR
	Ctrl Lipo	1	0.11512636	1099	UTRN-16	50	amOO 2fDMD	16	qRTPCR

Table 4: Formatted sequences

OligoID	Base Sequence	Formatted Sequence	SeqID
UTRN-01 mOl	CATCGTAGGAAGTTG	lnaCs;omeAs;lnaTs;omeCs;lnaGs;omeUs;lnaAs;omeGs;lnaGs;omeAs;lnaAs;omeGs;lnaTs;omeUs;lnaG-Sup	313770
UTRN-02 mOl	CCGGTATCATGGAGG	lnaCs;omeCs;lnaGs;omeGs;lnaTs;omeAs;lnaTs;omeCs;lnaAs;omeUs;lnaGs;omeGs;lnaAs;omeGs;lnaG-Sup	5776
UTRN-03	CAACACCGGTAT	lnaCs;omeAs;lnaAs;omeCs;lnaAs;omeCs;lnaCs;omeGs;lna	5781

mOl	CAT	Gs;omeUs;lnaAs;omeUs;lnaCs;omeAs;lnaT-Sup	
UTRN-04 mOl	CCGAACATCACCCAC	lnaCs;omeCs;lnaGs;omeAs;lnaAs;omeCs;lnaAs;omeUs;lnaCs;omeAs;lnaCs;omeCs;lnaCs;omeAs;lnaC-Sup	32192
UTRN-05 mOl	GGACTTCTGGACGAC	lnaGs;omeGs;lnaAs;omeCs;lnaTs;omeUs;lnaCs;omeUs;lnaGs;omeGs;lnaAs;omeCs;lnaGs;omeAs;lnaC-Sup	39558
UTRN-06 mOl	CCAAAACCTAGCGTT	lnaCs;omeCs;lnaAs;omeAs;lnaAs;omeAs;lnaCs;omeCs;lnaTs;omeAs;lnaGs;omeCs;lnaGs;omeUs;lnaT-Sup	45784
UTRN-07 mOl	CTTTTGTGACGTCCC	lnaCs;omeUs;lnaTs;omeUs;lnaTs;omeGs;lnaTs;omeGs;lnaAs;omeCs;lnaGs;omeUs;lnaCs;omeCs;lnaC-Sup	60002
UTRN-08 mOl	CCCGATATGATGCAC	lnaCs;omeCs;lnaCs;omeGs;lnaAs;omeUs;lnaAs;omeUs;lnaGs;omeAs;lnaTs;omeGs;lnaCs;omeAs;lnaC-Sup	60035
UTRN-09 mOl	ATCCCCGATATGATG	lnaAs;omeUs;lnaCs;omeCs;lnaCs;omeCs;lnaGs;omeAs;lnaTs;omeAs;lnaTs;omeGs;lnaAs;omeUs;lnaG-Sup	60038
UTRN-10 mOl	CCACCGACATAAGTG	lnaCs;omeCs;lnaAs;omeCs;lnaCs;omeGs;lnaAs;omeCs;lnaAs;omeUs;lnaAs;omeAs;lnaGs;omeUs;lnaG-Sup	336679
UTRN-11 mOl	CTCTCCGATGCCAAG	lnaCs;omeUs;lnaCs;omeUs;lnaCs;omeCs;lnaGs;omeAs;lnaTs;omeGs;lnaCs;omeCs;lnaAs;omeAs;lnaG-Sup	62709
UTRN-12 mOl	GGCGTCTATGGTGAC	lnaGs;omeGs;lnaCs;omeGs;lnaTs;omeCs;lnaTs;omeAs;lnaTs;omeGs;lnaGs;omeUs;lnaGs;omeAs;lnaC-Sup	64394
UTRN-13 mOl	CTACCTCACGGATGG	lnaCs;omeUs;lnaAs;omeCs;lnaCs;omeUs;lnaCs;omeAs;lnaCs;omeGs;lnaGs;omeAs;lnaTs;omeGs;lnaG-Sup	64407
UTRN-14 mOl	GAGTTTCAGCTCGGG	lnaGs;omeAs;lnaGs;omeUs;lnaTs;omeUs;lnaCs;omeAs;lnaGs;omeCs;lnaTs;omeCs;lnaGs;omeGs;lnaG-Sup	68368
UTRN-15 mOl	AACGCAATCTGATAG	lnaAs;omeAs;lnaCs;omeGs;lnaCs;omeAs;lnaAs;omeUs;lnaCs;omeUs;lnaGs;omeAs;lnaTs;omeAs;lnaG-Sup	68420
UTRN-16 mOl	CTCCAACGCAATCTG	lnaCs;omeUs;lnaCs;omeCs;lnaAs;omeAs;lnaCs;omeGs;lnaCs;omeAs;lnaAs;omeUs;lnaCs;omeUs;lnaG-Sup	68424
UTRN-17 mOl	CATTTCGGAAGTGTC	lnaCs;omeAs;lnaTs;omeUs;lnaTs;omeCs;lnaGs;omeGs;lnaAs;omeAs;lnaGs;omeUs;lnaGs;omeUs;lnaC-Sup	82947
UTRN-18 mOl	TTATTCGATGCCACC	lnaTs;omeUs;lnaAs;omeUs;lnaTs;omeCs;lnaGs;omeAs;lnaTs;omeGs;lnaCs;omeCs;lnaAs;omeCs;lnaC-Sup	85204
UTRN-19 mOl	CAATTCCCGCTAAGG	lnaCs;omeAs;lnaAs;omeUs;lnaTs;omeCs;lnaCs;omeCs;lnaGs;omeCs;lnaTs;omeAs;lnaAs;omeGs;lnaG-Sup	89541
UTRN-20 mOl	CTAATCTTCGAAGTG	lnaCs;omeUs;lnaAs;omeAs;lnaTs;omeCs;lnaTs;omeUs;lnaCs;omeGs;lnaAs;omeAs;lnaGs;omeUs;lnaG-Sup	355024
UTRN-21 mOl	CTCGAATTCTATTAC	lnaCs;omeUs;lnaCs;omeGs;lnaAs;omeAs;lnaTs;omeUs;lnaCs;omeUs;lnaAs;omeUs;lnaTs;omeAs;lnaC-Sup	99210
UTRN-22 mOl	GGAGATCACGGGTTC	lnaGs;omeGs;lnaAs;omeGs;lnaAs;omeUs;lnaCs;omeAs;lnaCs;omeGs;lnaGs;omeGs;lnaTs;omeUs;lnaC-Sup	101919
UTRN-23 mOl	CATTTGCCTGCGTAA	lnaCs;omeAs;lnaTs;omeUs;lnaTs;omeGs;lnaCs;omeCs;lnaTs;omeGs;lnaCs;omeGs;lnaTs;omeAs;lnaA-Sup	101994
UTRN-24 mOl	CGATTATCTGCCGGG	lnaCs;omeGs;lnaAs;omeUs;lnaTs;omeAs;lnaTs;omeCs;lnaTs;omeGs;lnaCs;omeCs;lnaGs;omeGs;lnaG-Sup	103832
UTRN-25 mOl	GCGATTATCTGCCGG	lnaGs;omeCs;lnaGs;omeAs;lnaTs;omeUs;lnaAs;omeUs;lnaCs;omeUs;lnaGs;omeCs;lnaCs;omeGs;lnaG-Sup	103833
UTRN-26	CCAAGCTCTCGA	lnaCs;omeCs;lnaAs;omeAs;lnaGs;omeCs;lnaTs;omeCs;lna	103853

mOl	ATC	Ts;omeCs;lnaGs;omeAs;lnaAs;omeUs;lnaC-Sup	
UTRN-27 mOl	GATCTTCATATCG GC	lnaGs;omeAs;lnaTs;omeCs;lnaTs;omeUs;lnaCs;omeAs;lna Ts;omeAs;lnaTs;omeCs;lnaGs;omeGs;lnaC-Sup	103933
UTRN-28 mOl	CAGGTACGAACT CGG	lnaCs;omeAs;lnaGs;omeGs;lnaTs;omeAs;lnaCs;omeGs;lna As;omeAs;lnaCs;omeUs;lnaCs;omeGs;lnaG-Sup	117420
UTRN-29 mOl	GCGTTACTGATGT CT	lnaGs;omeCs;lnaGs;omeUs;lnaTs;omeAs;lnaCs;omeUs;lna Gs;omeAs;lnaTs;omeGs;lnaTs;omeCs;lnaT-Sup	120115
UTRN-30 mOl	CCAAAAGCGTTA CTG	lnaCs;omeCs;lnaAs;omeAs;lnaAs;omeAs;lnaGs;omeCs;lna Gs;omeUs;lnaTs;omeAs;lnaCs;omeUs;lnaG-Sup	120121
UTRN-31 mOl	TTTAAACCAACG C TG	lnaTs;omeUs;lnaTs;omeAs;lnaAs;omeAs;lnaCs;omeCs;lna As;omeAs;lnaCs;omeGs;lnaCs;omeUs;lnaG-Sup	362061
UTRN-32 mOl	CACCGATCTGCAT TC	lnaCs;omeAs;lnaCs;omeCs;lnaGs;omeAs;lnaTs;omeCs;lna Ts;omeGs;lnaCs;omeAs;lnaTs;omeUs;lnaC-Sup	372488
UTRN-33 mOl	GGAGTCATACGA TGC	lnaGs;omeGs;lnaAs;omeGs;lnaTs;omeCs;lnaAs;omeUs;lna As;omeCs;lnaGs;omeAs;lnaTs;omeGs;lnaC-Sup	372542
UTRN-34 mOl	CTCATGATAACCG TG	lnaCs;omeUs;lnaCs;omeAs;lnaTs;omeGs;lnaAs;omeUs;lna As;omeAs;lnaCs;omeCs;lnaGs;omeUs;lnaG-Sup	376352
UTRN-35 mOl	GAATATAGAGTC GAG	lnaGs;omeAs;lnaAs;omeUs;lnaAs;omeUs;lnaAs;omeGs;ln aAs;omeGs;lnaTs;omeCs;lnaGs;omeAs;lnaG-Sup	139243
UTRN-36 mOl	CCAATTCGGTGA ATG	lnaCs;omeCs;lnaAs;omeAs;lnaTs;omeUs;lnaCs;omeGs;lna Gs;omeUs;lnaGs;omeAs;lnaAs;omeUs;lnaG-Sup	143189
UTRN-37 mOl	CCCATCTACATAC GC	lnaCs;omeCs;lnaCs;omeAs;lnaTs;omeCs;lnaTs;omeAs;lnaC s;omeAs;lnaTs;omeAs;lnaCs;omeGs;lnaC-Sup	151630
UTRN-38 mOl	CCGATTAATTTAC CC	lnaCs;omeCs;lnaGs;omeAs;lnaTs;omeUs;lnaAs;omeAs;lna Ts;omeUs;lnaTs;omeAs;lnaCs;omeCs;lnaC-Sup	166370
UTRN-39 mOl	CCCCGATTAATTT AC	lnaCs;omeCs;lnaCs;omeCs;lnaGs;omeAs;lnaTs;omeUs;lna As;omeAs;lnaTs;omeUs;lnaTs;omeAs;lnaC-Sup	166372
UTRN-40 mOl	AATGAAACAGCG TAG	lnaAs;omeAs;lnaTs;omeGs;lnaAs;omeAs;lnaAs;omeCs;lna As;omeGs;lnaCs;omeGs;lnaTs;omeAs;lnaG-Sup	169368
UTRN-41 mOl	CTGAGTTATCGTA AA	lnaCs;omeUs;lnaGs;omeAs;lnaGs;omeUs;lnaTs;omeAs;lna Ts;omeCs;lnaGs;omeUs;lnaAs;omeAs;lnaA-Sup	399345
UTRN-42 mOl	AGAAGTTAAACG CTG	lnaAs;omeGs;lnaAs;omeAs;lnaGs;omeUs;lnaTs;omeAs;lna As;omeAs;lnaCs;omeGs;lnaCs;omeUs;lnaG-Sup	412519
UTRN-43 mOl	CTTCAACTTACGG GA	lnaCs;omeUs;lnaTs;omeCs;lnaAs;omeAs;lnaCs;omeUs;lna Ts;omeAs;lnaCs;omeGs;lnaGs;omeGs;lnaA-Sup	412600
UTRN-44 mOl	GCCTTAACGATTT AC	lnaGs;omeCs;lnaCs;omeUs;lnaTs;omeAs;lnaAs;omeCs;lna Gs;omeAs;lnaTs;omeUs;lnaTs;omeAs;lnaC-Sup	414862
UTRN-45 mOl	CTGTTTCCGTCAA TG	lnaCs;omeUs;lnaGs;omeUs;lnaTs;omeUs;lnaCs;omeCs;lna Gs;omeUs;lnaCs;omeAs;lnaAs;omeUs;lnaG-Sup	195707
UTRN-46 mOl	TGAGTCGCTTAAT TC	lnaTs;omeGs;lnaAs;omeGs;lnaTs;omeCs;lnaGs;omeCs;lna Ts;omeUs;lnaAs;omeAs;lnaTs;omeUs;lnaC-Sup	422943
UTRN-47 mOl	GTCGCTTAATTCA AA	lnaGs;omeUs;lnaCs;omeGs;lnaCs;omeUs;lnaTs;omeAs;lna As;omeUs;lnaTs;omeCs;lnaAs;omeAs;lnaA-Sup	422946
UTRN-48 mOl	CTAAGGCGAAAT CTC	lnaCs;omeUs;lnaAs;omeAs;lnaGs;omeGs;lnaCs;omeGs;lna As;omeAs;lnaAs;omeUs;lnaCs;omeUs;lnaC-Sup	210674
UTRN-49	CTCGGACTCTACT	lnaCs;omeUs;lnaCs;omeGs;lnaGs;omeAs;lnaCs;omeUs;lna	426032

mOl	TG	Cs;omeUs;lnaAs;omeCs;lnaTs;omeUs;lnaG-Sup	
UTRN-50 mOl	CTTTAACTCCCGTCT	lnaCs;omeUs;lnaTs;omeUs;lnaAs;omeAs;lnaCs;omeUs;lnaCs;omeCs;lnaCs;omeGs;lnaTs;omeCs;lnaT-Sup	225629
UTRN-51 mOl	GTCGACAGCATTCAG	lnaGs;omeUs;lnaCs;omeGs;lnaAs;omeCs;lnaAs;omeGs;lnaCs;omeAs;lnaTs;omeUs;lnaCs;omeAs;lnaG-Sup	225662
UTRN-52 mOl	TTTACCCAATCGATG	lnaTs;omeUs;lnaTs;omeAs;lnaCs;omeCs;lnaCs;omeAs;lnaAs;omeUs;lnaCs;omeGs;lnaAs;omeUs;lnaG-Sup	229456
UTRN-53 mOl	GTAGCTCGATCAATC	lnaGs;omeUs;lnaAs;omeGs;lnaCs;omeUs;lnaCs;omeGs;lnaAs;omeUs;lnaCs;omeAs;lnaAs;omeUs;lnaC-Sup	436557
UTRN-54 mOl	CATCTAGCTGGCGAG	lnaCs;omeAs;lnaTs;omeCs;lnaTs;omeAs;lnaGs;omeCs;lnaTs;omeGs;lnaGs;omeCs;lnaGs;omeAs;lnaG-Sup	238467
UTRN-55 mOl	GGATCTTTGCCACGG	lnaGs;omeGs;lnaAs;omeUs;lnaCs;omeUs;lnaTs;omeUs;lnaGs;omeCs;lnaCs;omeAs;lnaCs;omeGs;lnaG-Sup	242264
UTRN-56 mOl	ACGACAACAGTACTG	lnaAs;omeCs;lnaGs;omeAs;lnaCs;omeAs;lnaAs;omeCs;lnaAs;omeGs;lnaTs;omeAs;lnaCs;omeUs;lnaG-Sup	251939
UTRN-57 mOl	CTGAATAATGTACGT	lnaCs;omeUs;lnaGs;omeAs;lnaAs;omeUs;lnaAs;omeAs;lnaTs;omeGs;lnaTs;omeAs;lnaCs;omeGs;lnaT-Sup	453443
UTRN-58 mOl	AAATCCGAAGACTAC	lnaAs;omeAs;lnaAs;omeUs;lnaCs;omeCs;lnaGs;omeAs;lnaAs;omeGs;lnaAs;omeCs;lnaTs;omeAs;lnaC-Sup	453483
UTRN-59 mOl	GTTGTCGATCACCTC	lnaGs;omeUs;lnaTs;omeGs;lnaTs;omeCs;lnaGs;omeAs;lnaTs;omeCs;lnaAs;omeCs;lnaCs;omeUs;lnaC-Sup	456038
UTRN-60 mOl	CTATTAAGTAGCCGT	lnaCs;omeUs;lnaAs;omeUs;lnaTs;omeAs;lnaAs;omeGs;lnaTs;omeAs;lnaGs;omeCs;lnaCs;omeGs;lnaT-Sup	272301
UTRN-61 mOl	GTAACCAAGTCGAGG	lnaGs;omeUs;lnaAs;omeAs;lnaCs;omeCs;lnaAs;omeAs;lnaGs;omeUs;lnaCs;omeGs;lnaAs;omeGs;lnaG-Sup	276749
UTRN-62 mOl	CAGACGTGTGATGGG	lnaCs;omeAs;lnaGs;omeAs;lnaCs;omeGs;lnaTs;omeGs;lnaTs;omeGs;lnaAs;omeUs;lnaGs;omeGs;lnaG-Sup	289697
UTRN-63 mOl	CACCATTGATTCGGG	lnaCs;omeAs;lnaCs;omeCs;lnaAs;omeUs;lnaTs;omeGs;lnaAs;omeUs;lnaTs;omeCs;lnaGs;omeGs;lnaG-Sup	292490
UTRN-64 mOl	GCGAGTAGCTCAGTG	lnaGs;omeCs;lnaGs;omeAs;lnaGs;omeUs;lnaAs;omeGs;lnaCs;omeUs;lnaCs;omeAs;lnaGs;omeUs;lnaG-Sup	292535
UTRN-65 mOl	GATCAAGCGAGTAGC	lnaGs;omeAs;lnaTs;omeCs;lnaAs;omeAs;lnaGs;omeCs;lnaGs;omeAs;lnaGs;omeUs;lnaAs;omeGs;lnaC-Sup	292541
UTRN-112 m08	CCCCGATCTATTCTC	lnaCs;lnaCs;lnaCs;dCs;dGs;dAs;dTs;dCs;dTs;dAs;dTs;dTs;lnaCs;lnaTs;lnaC-Sup	497729
UTRN-113 m08	CCCGATCTATTCTCC	lnaCs;lnaCs;lnaCs;dGs;dAs;dTs;dCs;dTs;dAs;dTs;dTs;dCs;lnaTs;lnaCs;lnaC-Sup	497730
UTRN-114 m08	CCGATCTATTCTCCA	lnaCs;lnaCs;lnaGs;dAs;dTs;dCs;dTs;dAs;dTs;dTs;dCs;dTs;lnaCs;lnaCs;lnaA-Sup	497731
UTRN-115 m08	GCGCGATGCTGAACT	lnaGs;lnaCs;lnaGs;dCs;dGs;dAs;dTs;dGs;dCs;dTs;dGs;dAs;lnaAs;lnaCs;lnaT-Sup	497732
UTRN-116 m08	CTGCGAACAGCAATG	lnaCs;lnaTs;lnaGs;dCs;dGs;dAs;dAs;dCs;dAs;dGs;dCs;dAs;lnaAs;lnaTs;lnaG-Sup	497733
UTRN-117 m08	TGCGAACAGCAATGG	lnaTs;lnaGs;lnaCs;dGs;dAs;dAs;dCs;dAs;dGs;dCs;dAs;dAs;lnaTs;lnaGs;lnaG-Sup	497734
UTRN-	GCGAACAGCAAT	lnaGs;lnaCs;lnaGs;dAs;dAs;dCs;dAs;dGs;dCs;dAs;dAs;dTs;l	497735

118 m08	GGC	naGs;lnaGs;lnaC-Sup	
UTRN-119 m08	AGTTCTGGCCAGTGA	lnaAs;lnaGs;lnaTs;dTs;dCs;dTs;dGs;dGs;dCs;dCs;dAs;dGs;lnaTs;lnaGs;lnaA-Sup	497736
UTRN-120 m08	AGAAGTGTTATTGGA	lnaAs;lnaGs;lnaAs;dAs;dGs;dTs;dGs;dTs;dTs;dAs;dTs;dTs;lnaGs;lnaGs;lnaA-Sup	497737
UTRN-121 m08	GAAGTGTTATTGGAC	lnaGs;lnaAs;lnaAs;dGs;dTs;dGs;dTs;dTs;dAs;dTs;dTs;dGs;lnaGs;lnaAs;lnaC-Sup	497738
UTRN-122 m08	GGTAGACTTGCGCTA	lnaGs;lnaGs;lnaTs;dAs;dGs;dAs;dCs;dTs;dTs;dGs;dCs;dGs;lnaCs;lnaTs;lnaA-Sup	497739
UTRN-123 m08	TAGACTTGCGCTACA	lnaTs;lnaAs;lnaGs;dAs;dCs;dTs;dTs;dGs;dCs;dGs;dCs;dTs;lnaAs;lnaCs;lnaA-Sup	497740
UTRN-124 m08	AGACTTGCGCTACAT	lnaAs;lnaGs;lnaAs;dCs;dTs;dTs;dGs;dCs;dGs;dCs;dTs;dAs;lnaCs;lnaAs;lnaT-Sup	497741
UTRN-125 m08	GACTTGCGCTACATT	lnaGs;lnaAs;lnaCs;dTs;dTs;dGs;dCs;dGs;dCs;dTs;dAs;dCs;lnaAs;lnaTs;lnaT-Sup	497742
UTRN-126 m08	ACTTGCGCTACATTA	lnaAs;lnaCs;lnaTs;dTs;dGs;dCs;dGs;dCs;dTs;dAs;dCs;dAs;lnaTs;lnaTs;lnaA-Sup	497743
UTRN-127 m08	CTTGCGCTACATTAA	lnaCs;lnaTs;lnaTs;dGs;dCs;dGs;dCs;dTs;dAs;dCs;dAs;dTs;lnaTs;lnaAs;lnaA-Sup	497744
UTRN-128 m08	TTGCGCTACATTAAT	lnaTs;lnaTs;lnaGs;dCs;dGs;dCs;dTs;dAs;dCs;dAs;dTs;dTs;lnaAs;lnaAs;lnaT-Sup	497745
UTRN-129 m08	TGCGCTACATTAATA	lnaTs;lnaGs;lnaCs;dGs;dCs;dTs;dAs;dCs;dAs;dTs;dTs;dAs;lnaAs;lnaTs;lnaA-Sup	497746
UTRN-130 m08	GCGCTACATTAATAT	lnaGs;lnaCs;lnaGs;dCs;dTs;dAs;dCs;dAs;dTs;dTs;dAs;dAs;lnaTs;lnaAs;lnaT-Sup	497747
UTRN-131 m08	GAAAGAACAGAGTGA	lnaGs;lnaAs;lnaAs;dAs;dGs;dAs;dAs;dCs;dAs;dGs;dAs;dGs;lnaTs;lnaGs;lnaA-Sup	497748
UTRN-132 m08	AAAGAACAGAGTGAC	lnaAs;lnaAs;lnaAs;dGs;dAs;dAs;dCs;dAs;dGs;dAs;dGs;dTs;lnaGs;lnaAs;lnaC-Sup	497749
UTRN-133 m08	TCCATTCTGGTTCGG	lnaTs;lnaCs;lnaCs;dAs;dTs;dTs;dCs;dTs;dGs;dGs;dTs;dTs;lnaCs;lnaGs;lnaG-Sup	497750
UTRN-134 m08	CCATTCTGGTTCGGT	lnaCs;lnaCs;lnaAs;dTs;dTs;dCs;dTs;dGs;dGs;dTs;dTs;dCs;lnaGs;lnaGs;lnaT-Sup	497751
UTRN-135 m08	ATTCTGGTTCGGTCT	lnaAs;lnaTs;lnaTs;dCs;dTs;dGs;dGs;dTs;dTs;dCs;dGs;dGs;lnaTs;lnaCs;lnaT-Sup	497752
UTRN-136 m08	TTCTGGTTCGGTCTC	lnaTs;lnaTs;lnaCs;dTs;dGs;dGs;dTs;dTs;dCs;dGs;dGs;dTs;lnaCs;lnaTs;lnaC-Sup	497753
UTRN-112 mOl	CCCCGATCTATTCTC	lnaCs;omeCs;lnaCs;omeCs;lnaGs;omeAs;lnaTs;omeCs;lnaTs;omeAs;lnaTs;omeUs;lnaCs;omeUs;lnaC-Sup	497729
UTRN-113 mOl	CCCGATCTATTCTCC	lnaCs;omeCs;lnaCs;omeGs;lnaAs;omeUs;lnaCs;omeUs;lnaAs;omeUs;lnaTs;omeCs;lnaTs;omeCs;lnaC-Sup	497730
UTRN-114 mOl	CCGATCTATTCTCCA	lnaCs;omeCs;lnaGs;omeAs;lnaTs;omeCs;lnaTs;omeAs;lnaTs;omeUs;lnaCs;omeUs;lnaCs;omeCs;lnaA-Sup	497731
UTRN-115 mOl	GCGCGATGCTGAACT	lnaGs;omeCs;lnaGs;omeCs;lnaGs;omeAs;lnaTs;omeGs;lnaCs;omeUs;lnaGs;omeAs;lnaAs;omeCs;lnaT-Sup	497732
UTRN-	CTGCGAACAGCA	lnaCs;omeUs;lnaGs;omeCs;lnaGs;omeAs;lnaAs;omeCs;lna	497733

116 mOl	ATG	As;omeGs;lnaCs;omeAs;lnaAs;omeUs;lnaG-Sup	
UTRN-117 mOl	TGCGAACAGCAATGG	lnaTs;omeGs;lnaCs;omeGs;lnaAs;omeAs;lnaCs;omeAs;lnaGs;omeCs;lnaAs;omeAs;lnaTs;omeGs;lnaG-Sup	497734
UTRN-118 mOl	GCGAACAGCAATGGC	lnaGs;omeCs;lnaGs;omeAs;lnaAs;omeCs;lnaAs;omeGs;lnaCs;omeAs;lnaAs;omeUs;lnaGs;omeGs;lnaC-Sup	497735
UTRN-119 mOl	AGTTCTGGCCAGTGA	lnaAs;omeGs;lnaTs;omeUs;lnaCs;omeUs;lnaGs;omeGs;lnaCs;omeCs;lnaAs;omeGs;lnaTs;omeGs;lnaA-Sup	497736
UTRN-120 mOl	AGAAGTGTTATTGGA	lnaAs;omeGs;lnaAs;omeAs;lnaGs;omeUs;lnaGs;omeUs;lnaTs;omeAs;lnaTs;omeUs;lnaGs;omeGs;lnaA-Sup	497737
UTRN-121 mOl	GAAGTGTTATTGGAC	lnaGs;omeAs;lnaAs;omeGs;lnaTs;omeGs;lnaTs;omeUs;lnaAs;omeUs;lnaTs;omeGs;lnaGs;omeAs;lnaC-Sup	497738
UTRN-122 mOl	GGTAGACTTGCGCTA	lnaGs;omeGs;lnaTs;omeAs;lnaGs;omeAs;lnaCs;omeUs;lnaTs;omeGs;lnaCs;omeGs;lnaCs;omeUs;lnaA-Sup	497739
UTRN-123 mOl	TAGACTTGCGCTACA	lnaTs;omeAs;lnaGs;omeAs;lnaCs;omeUs;lnaTs;omeGs;lnaCs;omeGs;lnaCs;omeUs;lnaAs;omeCs;lnaA-Sup	497740
UTRN-124 mOl	AGACTTGCGCTACAT	lnaAs;omeGs;lnaAs;omeCs;lnaTs;omeUs;lnaGs;omeCs;lnaGs;omeCs;lnaTs;omeAs;lnaCs;omeAs;lnaT-Sup	497741
UTRN-125 mOl	GACTTGCGCTACATT	lnaGs;omeAs;lnaCs;omeUs;lnaTs;omeGs;lnaCs;omeGs;lnaCs;omeUs;lnaAs;omeCs;lnaAs;omeUs;lnaT-Sup	497742
UTRN-126 mOl	ACTTGCGCTACATTA	lnaAs;omeCs;lnaTs;omeUs;lnaGs;omeCs;lnaGs;omeCs;lnaTs;omeAs;lnaCs;omeAs;lnaTs;omeUs;lnaA-Sup	497743
UTRN-127 mOl	CTTGCGCTACATTAA	lnaCs;omeUs;lnaTs;omeGs;lnaCs;omeGs;lnaCs;omeUs;lnaAs;omeCs;lnaAs;omeUs;lnaTs;omeAs;lnaA-Sup	497744
UTRN-128 mOl	TTGCGCTACATTAAT	lnaTs;omeUs;lnaGs;omeCs;lnaGs;omeCs;lnaTs;omeAs;lnaCs;omeAs;lnaTs;omeUs;lnaAs;omeAs;lnaT-Sup	497745
UTRN-129 mOl	TGCGCTACATTAATA	lnaTs;omeGs;lnaCs;omeGs;lnaCs;omeUs;lnaAs;omeCs;lnaAs;omeUs;lnaTs;omeAs;lnaAs;omeUs;lnaA-Sup	497746
UTRN-130 mOl	GCGCTACATTAATAT	lnaGs;omeCs;lnaGs;omeCs;lnaTs;omeAs;lnaCs;omeAs;lnaTs;omeUs;lnaAs;omeAs;lnaTs;omeAs;lnaT-Sup	497747
UTRN-131 mOl	GAAAGAACAGAGTGA	lnaGs;omeAs;lnaAs;omeAs;lnaGs;omeAs;lnaAs;omeCs;lnaAs;omeGs;lnaAs;omeGs;lnaTs;omeGs;lnaA-Sup	497748
UTRN-132 mOl	AAAGAACAGAGTGAC	lnaAs;omeAs;lnaAs;omeGs;lnaAs;omeAs;lnaCs;omeAs;lnaGs;omeAs;lnaGs;omeUs;lnaGs;omeAs;lnaC-Sup	497749
UTRN-133 mOl	TCCATTCTGGTTCGG	lnaTs;omeCs;lnaCs;omeAs;lnaTs;omeUs;lnaCs;omeUs;lnaGs;omeGs;lnaTs;omeUs;lnaCs;omeGs;lnaG-Sup	497750
UTRN-134 mOl	CCATTCTGGTTCGGT	lnaCs;omeCs;lnaAs;omeUs;lnaTs;omeCs;lnaTs;omeGs;lnaGs;omeUs;lnaTs;omeCs;lnaGs;omeGs;lnaT-Sup	497751
UTRN-135 mOl	ATTCTGGTTCGGTCT	lnaAs;omeUs;lnaTs;omeCs;lnaTs;omeGs;lnaGs;omeUs;lnaTs;omeCs;lnaGs;omeGs;lnaTs;omeCs;lnaT-Sup	497752
UTRN-136 mOl	TTCTGGTTCGGTCTC	lnaTs;omeUs;lnaCs;omeUs;lnaGs;omeGs;lnaTs;omeUs;lnaCs;omeGs;lnaGs;omeUs;lnaCs;omeUs;lnaC-Sup	497753
UTRN-157 m08	CAGTATTATCTACAC	lnaCs;lnaAs;lnaGs;dTs;dAs;dTs;dTs;dAs;dTs;dCs;dTs;dAs;lnaCs;lnaAs;lnaC-Sup	320709
UTRN-158 m08	AGTATTATCTACACT	lnaAs;lnaGs;lnaTs;dAs;dTs;dTs;dAs;dTs;dCs;dTs;dAs;dCs;lnaAs;lnaCs;lnaT-Sup	320710
UTRN-	TATCTACACTGAT	lnaTs;lnaAs;lnaTs;dCs;dTs;dAs;dCs;dAs;dCs;dTs;dGs;dAs;l	320715

159 m08	CT	naTs;lnaCs;lnaT-Sup	
UTRN-160 m08	ATCTACACTGATCTT	lnaAs;lnaTs;lnaCs;dTs;dAs;dCs;dAs;dCs;dTs;dGs;dAs;dTs;lnaCs;lnaTs;lnaT-Sup	320716
UTRN-161 m08	TGCACACTTGGATTC	lnaTs;lnaGs;lnaCs;dAs;dCs;dAs;dCs;dTs;dTs;dGs;dGs;dAs;lnaTs;lnaTs;lnaC-Sup	320742
UTRN-162 m08	GCACACTTGGATTCT	lnaGs;lnaCs;lnaAs;dCs;dAs;dCs;dTs;dTs;dGs;dGs;dAs;dTs;lnaTs;lnaCs;lnaT-Sup	320743
UTRN-163 m08	GGATTCTAACCTGCA	lnaGs;lnaGs;lnaAs;dTs;dTs;dCs;dTs;dAs;dAs;dCs;dCs;dTs;lnaGs;lnaCs;lnaA-Sup	320751
UTRN-164 m08	GATTCTAACCTGCAA	lnaGs;lnaAs;lnaTs;dTs;dCs;dTs;dAs;dAs;dCs;dCs;dTs;dGs;lnaCs;lnaAs;lnaA-Sup	320752
UTRN-165 m08	TTCTAACCTGCAATA	lnaTs;lnaTs;lnaCs;dTs;dAs;dAs;dCs;dCs;dTs;dGs;dCs;dAs;lnaAs;lnaTs;lnaA-Sup	320754
UTRN-166 m08	TCTAACCTGCAATAT	lnaTs;lnaCs;lnaTs;dAs;dAs;dCs;dCs;dTs;dGs;dCs;dAs;dAs;lnaTs;lnaAs;lnaT-Sup	320755
UTRN-167 m08	ATTTTTATCTCTAAA	lnaAs;lnaTs;lnaTs;dTs;dTs;dTs;dAs;dTs;dCs;dTs;dCs;dTs;lnaAs;lnaAs;lnaA-Sup	320821
UTRN-168 m08	GAGTTAGATATCAAG	lnaGs;lnaAs;lnaGs;dTs;dTs;dAs;dGs;dAs;dTs;dAs;dTs;dCs;lnaAs;lnaAs;lnaG-Sup	320838
UTRN-169 m08	AGTTAGATATCAAGG	lnaAs;lnaGs;lnaTs;dTs;dAs;dGs;dAs;dTs;dAs;dTs;dCs;dAs;lnaAs;lnaGs;lnaG-Sup	320839
UTRN-170 m08	CATGGTATTAGATTA	lnaCs;lnaAs;lnaTs;dGs;dGs;dTs;dAs;dTs;dTs;dAs;dGs;dAs;lnaTs;lnaTs;lnaA-Sup	320858
UTRN-171 m08	GGTATTAGATTACAC	lnaGs;lnaGs;lnaTs;dAs;dTs;dTs;dAs;dGs;dAs;dTs;dTs;dAs;lnaCs;lnaAs;lnaC-Sup	320861
UTRN-172 m08	GTATTAGATTACACA	lnaGs;lnaTs;lnaAs;dTs;dTs;dAs;dGs;dAs;dTs;dTs;dAs;dCs;lnaAs;lnaCs;lnaA-Sup	320862
UTRN-173 m08	TATTAGATTACACAA	lnaTs;lnaAs;lnaTs;dTs;dAs;dGs;dAs;dTs;dTs;dAs;dCs;dAs;lnaCs;lnaAs;lnaA-Sup	320863
UTRN-174 m08	TAGATTACACAATAT	lnaTs;lnaAs;lnaGs;dAs;dTs;dTs;dAs;dCs;dAs;dCs;dAs;dAs;lnaTs;lnaAs;lnaT-Sup	320866
UTRN-175 m08	ATCTTATTAGTACTC	lnaAs;lnaTs;lnaCs;dTs;dTs;dAs;dTs;dTs;dAs;dGs;dTs;dAs;lnaCs;lnaTs;lnaC-Sup	320918
UTRN-176 m08	ATTAGTACTCTTCTG	lnaAs;lnaTs;lnaTs;dAs;dGs;dTs;dAs;dCs;dTs;dCs;dTs;dTs;lnaCs;lnaTs;lnaG-Sup	320923
UTRN-177 m08	TTAGTACTCTTCTGT	lnaTs;lnaTs;lnaAs;dGs;dTs;dAs;dCs;dTs;dCs;dTs;dTs;dCs;lnaTs;lnaGs;lnaT-Sup	320924
UTRN-178 m08	AGTACTCTTCTGTAG	lnaAs;lnaGs;lnaTs;dAs;dCs;dTs;dCs;dTs;dTs;dCs;dTs;dGs;lnaTs;lnaAs;lnaG-Sup	320926
UTRN-179 m08	GGAATGGTTCAGACA	lnaGs;lnaGs;lnaAs;dAs;dTs;dGs;dGs;dTs;dTs;dCs;dAs;dGs;lnaAs;lnaCs;lnaA-Sup	320952
UTRN-180 m08	GAATGGTTCAGACAG	lnaGs;lnaAs;lnaAs;dTs;dGs;dGs;dTs;dTs;dCs;dAs;dGs;dAs;lnaCs;lnaAs;lnaG-Sup	320953
UTRN-181 m08	AATGGTTCAGACAGT	lnaAs;lnaAs;lnaTs;dGs;dGs;dTs;dTs;dCs;dAs;dGs;dAs;dCs;lnaAs;lnaGs;lnaT-Sup	320954
UTRN-	GGTTCAGACAGT	lnaGs;lnaGs;lnaTs;dTs;dCs;dAs;dGs;dAs;dCs;dAs;dGs;dTs;l	320957

182 m08	ATC	naAs;lnaTs;lnaC-Sup	
UTRN-183 m08	TGTGGGTGTAAGCAT	lnaTs;lnaGs;lnaTs;dGs;dGs;dGs;dTs;dGs;dTs;dAs;dAs;dGs;lnaCs;lnaAs;lnaT-Sup	320978
UTRN-184 m08	GTGGGTGTAAGCATG	lnaGs;lnaTs;lnaGs;dGs;dGs;dTs;dGs;dTs;dAs;dAs;dGs;dCs;lnaAs;lnaTs;lnaG-Sup	320979
UTRN-185 m08	GTAAGCATGGCCACC	lnaGs;lnaTs;lnaAs;dAs;dGs;dCs;dAs;dTs;dGs;dGs;dCs;dCs;lnaAs;lnaCs;lnaC-Sup	320985
UTRN-186 m08	CTGCTCTGTGCCTGA	lnaCs;lnaTs;lnaGs;dCs;dTs;dCs;dTs;dGs;dTs;dGs;dCs;dCs;lnaTs;lnaGs;lnaA-Sup	321033
UTRN-187 m08	TGCTCTGTGCCTGAG	lnaTs;lnaGs;lnaCs;dTs;dCs;dTs;dGs;dTs;dGs;dCs;dCs;dTs;lnaGs;lnaAs;lnaG-Sup	321034
UTRN-188 m08	CTGAGTAAAGTAGAG	lnaCs;lnaTs;lnaGs;dAs;dGs;dTs;dAs;dAs;dAs;dGs;dTs;dAs;lnaGs;lnaAs;lnaG-Sup	321044
UTRN-189 m08	GTCTTCCCATAACAG	lnaGs;lnaTs;lnaCs;dTs;dTs;dCs;dCs;dCs;dAs;dTs;dAs;dAs;lnaCs;lnaAs;lnaG-Sup	497754
UTRN-190 m08	CCCATAACAGACCTT	lnaCs;lnaCs;lnaCs;dAs;dTs;dAs;dAs;dCs;dAs;dGs;dAs;dCs;lnaCs;lnaTs;lnaT-Sup	497755
UTRN-191 m08	CCATAACAGACCTTC	lnaCs;lnaCs;lnaAs;dTs;dAs;dAs;dCs;dAs;dGs;dAs;dCs;dCs;lnaTs;lnaTs;lnaC-Sup	497756
UTRN-240 m08	CCGCCACTGTCTCGG	lnaCs;lnaCs;lnaGs;dCs;dCs;dAs;dCs;dTs;dGs;dTs;dCs;dTs;lnaCs;lnaGs;lnaG-Sup	497757
UTRN-241 m08	TTTTCGCCGCCACTG	lnaTs;lnaTs;lnaTs;dTs;dCs;dGs;dCs;dCs;dGs;dCs;dCs;dAs;lnaCs;lnaTs;lnaG-Sup	497758
UTRN-242 m08	GTTTTCGCCGCCACT	lnaGs;lnaTs;lnaTs;dTs;dTs;dCs;dGs;dCs;dCs;dGs;dCs;dCs;lnaAs;lnaCs;lnaT-Sup	497759
UTRN-243 m08	AG-T-T-T-C-G-C-C-G-CCAC	lnaAs;lnaGs;lnaTs;dTs;dTs;dTs;dCs;dGs;dCs;dCs;dGs;dCs;lnaCs;lnaAs;lnaC-Sup	497760
UTRN-244 m08	GAG-T-T-T-C-G-C-C-G-CCA	lnaGs;lnaAs;lnaGs;dTs;dTs;dTs;dTs;dCs;dGs;dCs;dCs;dGs;lnaCs;lnaCs;lnaA-Sup	497761
UTRN-245 m08	AGAG-T-T-T-1-C-G-C-CGCC	lnaAs;lnaGs;lnaAs;dGs;dTs;dTs;dTs;dTs;dCs;dGs;dCs;dCs;lnaGs;lnaCs;lnaC-Sup	497762
UTRN-246 m08	GAGAG-T-T-T-1-C-G-C-CGC	lnaGs;lnaAs;lnaGs;dAs;dGs;dTs;dTs;dTs;dTs;dCs;dGs;dCs;lnaCs;lnaGs;lnaC-Sup	497763
UTRN-247 m08	CAGAGAG-T-T-T-T-C-GCC	lnaCs;lnaAs;lnaGs;dAs;dGs;dAs;dGs;dTs;dTs;dTs;dTs;dCs;lnaGs;lnaCs;lnaC-Sup	497764
UTRN-248 m08	CCGCTTACAAGGCAT	lnaCs;lnaCs;lnaGs;dCs;dTs;dTs;dAs;dCs;dAs;dAs;dGs;dGs;lnaCs;lnaAs;lnaT-Sup	497765
UTRN-249 m08	GCTCCGCTTACAAGG	lnaGs;lnaCs;lnaTs;dCs;dCs;dGs;dCs;dTs;dTs;dAs;dCs;dAs;lnaAs;lnaGs;lnaG-Sup	497766
UTRN-250 m08	TGCTCCGCTTACAAG	lnaTs;lnaGs;lnaCs;dTs;dCs;dCs;dGs;dCs;dTs;dTs;dAs;dCs;lnaAs;lnaAs;lnaG-Sup	497767
UTRN-251 m08	-T-T-T-G-C-T-C-C-G-C-T-1AC	lnaTs;lnaTs;lnaTs;dTs;dGs;dCs;dTs;dCs;dCs;dGs;dCs;dTs;lnaTs;lnaAs;lnaC-Sup	497768
UTRN-252 m08	ACGTTGAACCTTGTT	lnaAs;lnaCs;lnaGs;dTs;dTs;dGs;dAs;dAs;dCs;dCs;dTs;dTs;lnaGs;lnaTs;lnaT-Sup	497769
UTRN-	GACGTTGAACCTT	lnaGs;lnaAs;lnaCs;dGs;dTs;dTs;dGs;dAs;dAs;dCs;dCs;dTs;l	497770

253 m08	GT	naTs;lnaGs;lnaT-Sup	
UTRN-254 m08	AGACGTTGAACCTTG	lnaAs;lnaGs;lnaAs;dCs;dGs;dTs;dTs;dGs;dAs;dAs;dCs;dCs;lnaTs;lnaTs;lnaG-Sup	497771
UTRN-255 m08	CAGACGTTGAACCTT	lnaCs;lnaAs;lnaGs;dAs;dCs;dGs;dTs;dTs;dGs;dAs;dAs;dCs;lnaCs;lnaTs;lnaT-Sup	497772
UTRN-256 m08	GCAGACGTTGAACCT	lnaGs;lnaCs;lnaAs;dGs;dAs;dCs;dGs;dTs;dTs;dGs;dAs;dAs;lnaCs;lnaCs;lnaT-Sup	497773
UTRN-257 m08	AATGTCCAAGGCGTG	lnaAs;lnaAs;lnaTs;dGs;dTs;dCs;dCs;dAs;dAs;dGs;dGs;dCs;lnaGs;lnaTs;lnaG-Sup	497774
UTRN-258 m08	GTCGGAATTCTAATG	lnaGs;lnaTs;lnaCs;dGs;dGs;dAs;dAs;dTs;dTs;dCs;dTs;dAs;lnaAs;lnaTs;lnaG-Sup	497775
UTRN-259 m08	AGTCGGAATTCTAAT	lnaAs;lnaGs;lnaTs;dCs;dGs;dGs;dAs;dAs;dTs;dTs;dCs;dTs;lnaAs;lnaAs;lnaT-Sup	497776
UTRN-260 m08	AAGTCGGAATTCTAA	lnaAs;lnaAs;lnaGs;dTs;dCs;dGs;dGs;dAs;dAs;dTs;dTs;dCs;lnaTs;lnaAs;lnaA-Sup	497777
UTRN-261 m08	GAAGTCGGAATTCTA	lnaGs;lnaAs;lnaAs;dGs;dTs;dCs;dGs;dGs;dAs;dAs;dTs;dTs;lnaCs;lnaTs;lnaA-Sup	497778
UTRN-262 m08	AGAAGTCGGAATTCT	lnaAs;lnaGs;lnaAs;dAs;dGs;dTs;dCs;dGs;dGs;dAs;dAs;dTs;lnaTs;lnaCs;lnaT-Sup	497779
UTRN-263 m08	CGTTGCGCTTCTCCC	lnaCs;lnaGs;lnaTs;dTs;dGs;dCs;dGs;dCs;dTs;dTs;dCs;dTs;lnaCs;lnaCs;lnaC-Sup	497780
UTRN-264 m08	GCGTTGCGCTTCTCC	lnaGs;lnaCs;lnaGs;dTs;dTs;dGs;dCs;dGs;dCs;dTs;dTs;dCs;lnaTs;lnaCs;lnaC-Sup	497781
UTRN-265 m08	AGCGTTGCGCTTCTC	lnaAs;lnaGs;lnaCs;dGs;dTs;dTs;dGs;dCs;dGs;dCs;dTs;dTs;lnaCs;lnaTs;lnaC-Sup	497782
UTRN-266 m08	GAGCGTTGCGCTTCT	lnaGs;lnaAs;lnaGs;dCs;dGs;dTs;dTs;dGs;dCs;dGs;dCs;dTs;lnaTs;lnaCs;lnaT-Sup	497783
UTRN-267 m08	TGAGCGTTGCGCTTC	lnaTs;lnaGs;lnaAs;dGs;dCs;dGs;dTs;dTs;dGs;dCs;dGs;dCs;lnaTs;lnaTs;lnaC-Sup	497784
UTRN-268 m08	GCGTGTGAGCGTTGC	lnaGs;lnaCs;lnaGs;dTs;dGs;dTs;dGs;dAs;dGs;dCs;dGs;dTs;lnaTs;lnaGs;lnaC-Sup	497785
UTRN-269 m08	TGCGTGTGAGCGTTG	lnaTs;lnaGs;lnaCs;dGs;dTs;dGs;dTs;dGs;dAs;dGs;dCs;dGs;lnaTs;lnaTs;lnaG-Sup	497786
UTRN-270 m08	GCGGTCTCTTGGTGG	lnaGs;lnaCs;lnaGs;dGs;dTs;dCs;dTs;dCs;dTs;dTs;dGs;dGs;lnaTs;lnaGs;lnaG-Sup	497787
UTRN-271 m08	CGCGGTCTCTTGGTG	lnaCs;lnaGs;lnaCs;dGs;dGs;dTs;dCs;dTs;dCs;dTs;dTs;dGs;lnaGs;lnaTs;lnaG-Sup	497788
UTRN-272 m08	CTGCGCGGTCTCTTG	lnaCs;lnaTs;lnaGs;dCs;dGs;dCs;dGs;dGs;dTs;dCs;dTs;dCs;lnaTs;lnaTs;lnaG-Sup	497789
UTRN-273 m08	ATATTCGCTATGTTT	lnaAs;lnaTs;lnaAs;dTs;dTs;dCs;dGs;dCs;dTs;dAs;dTs;dGs;lnaTs;lnaTs;lnaT-Sup	497790
UTRN-274 m08	TTCAATATATTCGCT	lnaTs;lnaTs;lnaCs;dAs;dAs;dTs;dAs;dTs;dAs;dTs;dTs;dCs;lnaGs;lnaCs;lnaT-Sup	497791
UTRN-275 m08	TTAACGATTCAAATT	lnaTs;lnaTs;lnaAs;dAs;dCs;dGs;dAs;dTs;dTs;dCs;dAs;dAs;lnaAs;lnaTs;lnaT-Sup	497792
UTRN-	AGTTAACGATTCA	lnaAs;lnaGs;lnaTs;dTs;dAs;dAs;dCs;dGs;dAs;dTs;dTs;dCs;l	497793

276 m08	AA	naAs;lnaAs;lnaA-Sup	
UTRN-277 m08	AAGTTAACGATTCAA	lnaAs;lnaAs;lnaGs;dTs;dTs;dAs;dAs;dCs;dGs;dAs;dTs;dTs;lnaCs;lnaAs;lnaA-Sup	497794
UTRN-278 m08	ACTAAGTTAACGATT	lnaAs;lnaCs;lnaTs;dAs;dAs;dGs;dTs;dTs;dAs;dAs;dCs;dGs;lnaAs;lnaTs;lnaT-Sup	497795
UTRN-279 m08	AACTAAGTTAACGAT	lnaAs;lnaAs;lnaCs;dTs;dAs;dAs;dGs;dTs;dTs;dAs;dAs;dCs;lnaGs;lnaAs;lnaT-Sup	497796
UTRN-280 m08	CACTGCGTAAATACA	lnaCs;lnaAs;lnaCs;dTs;dGs;dCs;dGs;dTs;dAs;dAs;dAs;dTs;lnaAs;lnaCs;lnaA-Sup	497797
UTRN-281 m08	GTGTCACTGCGTAAA	lnaGs;lnaTs;lnaGs;dTs;dCs;dAs;dCs;dTs;dGs;dCs;dGs;dTs;lnaAs;lnaAs;lnaA-Sup	497798
UTRN-282 m08	GTCTCGTGCAAGTTG	lnaGs;lnaTs;lnaCs;dTs;dCs;dGs;dTs;dGs;dCs;dAs;dAs;dGs;lnaTs;lnaTs;lnaG-Sup	497799
UTRN-283 m08	ATAATGTCTCGTGCA	lnaAs;lnaTs;lnaAs;dAs;dTs;dGs;dTs;dCs;dTs;dCs;dGs;dTs;lnaGs;lnaCs;lnaA-Sup	497800
UTRN-284 m08	ACGCTACTTGTTCAG	lnaAs;lnaCs;lnaGs;dCs;dTs;dAs;dCs;dTs;dTs;dGs;dTs;dTs;lnaCs;lnaAs;lnaG-Sup	497801
UTRN-285 m08	AACGCTACTTGTTCA	lnaAs;lnaAs;lnaCs;dGs;dCs;dTs;dAs;dCs;dTs;dTs;dGs;dTs;lnaTs;lnaCs;lnaA-Sup	497802
UTRN-286 m08	GAACGCTACTTGTTC	lnaGs;lnaAs;lnaAs;dCs;dGs;dCs;dTs;dAs;dCs;dTs;dTs;dGs;lnaTs;lnaTs;lnaC-Sup	497803
UTRN-287 m08	AGAACGCTACTTGTT	lnaAs;lnaGs;lnaAs;dAs;dCs;dGs;dCs;dTs;dAs;dCs;dTs;dTs;lnaGs;lnaTs;lnaT-Sup	497804
UTRN-288 m08	AAGAACGCTACTTGT	lnaAs;lnaAs;lnaGs;dAs;dAs;dCs;dGs;dCs;dTs;dAs;dCs;dTs;lnaTs;lnaGs;lnaT-Sup	497805
UTRN-289 m08	CCAAGAACGCTACTT	lnaCs;lnaCs;lnaAs;dAs;dGs;dAs;dAs;dCs;dGs;dCs;dTs;dAs;lnaCs;lnaTs;lnaT-Sup	497806
unc-232 ml2	CTACGCGTCGACGGT	lnaCs;dTs;lnaAs;dCs;lnaGs;dCs;lnaGs;dTs;lnaCs;dGs;lnaAs;dCs;lnaGs;dGs;lnaT-Sup	497808
unc-232 mOl	CTACGCGTCGACGGT	lnaCs;omeUs;lnaAs;omeCs;lnaGs;omeCs;lnaGs;omeUs;lnaCs;omeGs;lnaAs;omeCs;lnaGs;omeGs;lnaT-Sup	497808
unc-293 ml2	CCGATTCGCGCGTAA	lnaCs;dCs;lnaGs;dAs;lnaTs;dTs;lnaCs;dGs;lnaCs;dGs;lnaCs;dGs;lnaTs;dAs;lnaA-Sup	497809
unc-293 mOl	CCGATTCGCGCGTAA	lnaCs;omeCs;lnaGs;omeAs;lnaTs;omeUs;lnaCs;omeGs;lnaCs;omeGs;lnaCs;omeGs;lnaTs;omeAs;lnaA-Sup	497809

BRIEF DESCRIPTION OF SEQUENCE LISTING

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
1	chr6	UTRN	144600872	145186170	+
2	chr6	UTRN	144600872	145186170	-
3	chrlO	Utrn	12089985	12593533	-
4	chrlO	Utrn	12089985	12593533	+
5	chr6	UTRN	144610489	144610535	+

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
6	chr6	UTRN	144612994	144613040	+
7	chr6	UTRN	144614120	144614162	+
8	chr6	UTRN	144614968	144615021	+
9	chr6	UTRN	144618862	144618901	+
10	chr6	UTRN	144621690	144621714	+
11	chr6	UTRN	144625028	144625096	+
12	chr6	UTRN	144625129	144625174	+
13	chr6	UTRN	144625319	144625379	+
14	chr6	UTRN	144628965	144629011	+
15	chr6	UTRN	144633818	144633869	+
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17	chr6	UTRN	144658267	144658302	+
18	chr6	UTRN	144685087	144685140	+
19	chr6	UTRN	144695039	144695063	+
20	chr6	UTRN	144699670	144699699	+
21	chr6	UTRN	144704043	144704398	+
22	chr6	UTRN	144706312	144706345	+
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27	chr6	UTRN	144727897	144727947	+
28	chr6	UTRN	144746408	144746448	+
29	chr6	UTRN	144749102	144749152	+
30	chr6	UTRN	144749948	144750026	+
31	chr6	UTRN	144750728	144750789	+
32	chr6	UTRN	144750789	144750853	+
33	chr6	UTRN	144757162	144757214	+
34	chr6	UTRN	144757214	144757274	+
35	chr6	UTRN	144758752	144758807	+
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37	chr6	UTRN	144761513	144761579	+
38	chr6	UTRN	144765456	144765506	+
39	chr6	UTRN	144768420	144768461	+
40	chr6	UTRN	144768737	144768764	+
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42	chr6	UTRN	144774960	144775001	+
43	chr6	UTRN	144779914	144779960	+

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
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45	chr6	UTRN	144780278	144780324	+
46	chr6	UTRN	144783879	144783933	+
47	chr6	UTRN	144783933	144783995	+
48	chr6	UTRN	144800953	144800999	+
49	chr6	UTRN	144802780	144802822	+
50	chr6	UTRN	144803427	144803473	+
51	chr6	UTRN	144803714	144803742	+
52	chr6	UTRN	144803774	144803849	+
53	chr6	UTRN	144806673	144806714	+
54	chr6	UTRN	144808684	144808739	+
55	chr6	UTRN	144808739	144808803	+
56	chr6	UTRN	144809834	144809881	+
57	chr6	UTRN	144811266	144811310	+
58	chr6	UTRN	144814476	144814522	+
59	chr6	UTRN	144815156	144815199	+
60	chr6	UTRN	144820469	144820529	+
61	chr6	UTRN	144832193	144832243	+
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66	chr6	UTRN	144844263	144844304	+
67	chr6	UTRN	144858722	144858798	+
68	chr6	UTRN	144870778	144870817	+
69	chr6	UTRN	144871113	144871154	+
70	chr6	UTRN	144872123	144872165	+
71	chr6	UTRN	144872599	144872669	+
72	chr6	UTRN	144873625	144873662	+
73	chr6	UTRN	144875136	144875182	+
74	chr6	UTRN	144875895	144875938	+
75	chr6	UTRN	144886315	144886378	+
76	chr6	UTRN	144904604	144904645	+
77	chr6	UTRN	144905276	144905300	+
78	chr6	UTRN	144906334	144906358	+
79	chr6	UTRN	144907025	144907055	+
80	chr6	UTRN	144908864	144908908	+
81	chr6	UTRN	144909055	144909078	+

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
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83	chr6	UTRN	144918990	144919013	+
84	chr6	UTRN	144935390	144935427	+
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87	chr6	UTRN	144941551	144941596	+
88	chr6	UTRN	144941700	144941748	+
89	chr6	UTRN	144941856	144941912	+
90	chr6	UTRN	144941912	144941988	+
91	chr6	UTRN	144942080	144942136	+
92	chr6	UTRN	144944667	144944712	+
93	chr6	UTRN	144945160	144945207	+
94	chr6	UTRN	144950918	144950987	+
95	chr6	UTRN	144952595	144952650	+
96	chr6	UTRN	144954758	144954804	+
97	chr6	UTRN	144960952	144960996	+
98	chr6	UTRN	144968386	144968438	+
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100	chr6	UTRN	144985026	144985072	+
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102	chr6	UTRN	144999750	144999785	+
103	chr6	UTRN	144999904	144999956	+
104	chr6	UTRN	145012224	145012561	+
105	chr6	UTRN	145017897	145017969	+
106	chr6	UTRN	145017978	145018021	+
107	chr6	UTRN	145019229	145019261	+
108	chr6	UTRN	145021232	145021278	+
109	chr6	UTRN	145021336	145021382	+
110	chr6	UTRN	145031285	145031331	+
111	chr6	UTRN	145038424	145038467	+
112	chr6	UTRN	145042706	145042751	+
113	chr6	UTRN	145047775	145047820	+
114	chr6	UTRN	145051549	145051592	+
115	chr6	UTRN	145061899	145061941	+
116	chr6	UTRN	145063569	145063615	+
117	chr6	UTRN	145069445	145069497	+
118	chr6	UTRN	145072959	145073005	+
119	chr6	UTRN	145079115	145079162	+

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
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121	chr6	UTRN	145080780	145080816	+
122	chr6	UTRN	145080843	145080885	+
123	chr6	UTRN	145081884	145081930	+
124	chr6	UTRN	145087734	145087827	+
125	chr6	UTRN	145087827	145087911	+
126	chr6	UTRN	145088046	145088124	+
127	chr6	UTRN	145088210	145088245	+
128	chr6	UTRN	145088678	145088723	+
129	chr6	UTRN	145090281	145090327	+
130	chr6	UTRN	145090884	145090934	+
131	chr6	UTRN	145093542	145093591	+
132	chr6	UTRN	145094155	145094199	+
133	chr6	UTRN	145096714	145096756	+
134	chr6	UTRN	145101237	145101284	+
135	chr6	UTRN	145101598	145101642	+
136	chr6	UTRN	145127145	145127194	+
137	chr6	UTRN	145127467	145127507	+
138	chr6	UTRN	145127866	145127929	+
139	chr6	UTRN	145128105	145128160	+
140	chr6	UTRN	145128415	145128460	+
141	chr6	UTRN	145132350	145132397	+
142	chr6	UTRN	145132917	145132974	+
143	chr6	UTRN	145133779	145133802	+
144	chr6	UTRN	145134097	145134169	+
145	chr6	UTRN	145134835	145134881	+
146	chr6	UTRN	145142034	145142135	+
147	chr6	UTRN	145142629	145142676	+
148	chr6	UTRN	145148750	145148806	+
149	chr6	UTRN	145149936	145149984	+
150	chr6	UTRN	145153900	145154300	+
151	chr6	UTRN	145154735	145154782	+
152	chr6	UTRN	145155438	145155468	+
153	chr6	UTRN	145156972	145157019	+
154	chr6	UTRN	145157440	145157555	+
155	chr6	UTRN	145157566	145157621	+
156	chr6	UTRN	145158149	145158194	+
157	chr6	UTRN	145160356	145160409	+

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
158	chr6	UTRN	145161881	145161927	+
159	chr6	UTRN	145167107	145167151	+
160	chr6	UTRN	145167205	145167243	+
161	chr6	UTRN	145168292	145168344	+
162	chr6	UTRN	145169033	145169085	+
163	chr6	UTRN	145169156	145169202	+
164	chr6	UTRN	145169270	145169315	+
165	chr6	UTRN	145171814	145171863	+
166	chr6	UTRN	145173631	145173718	+
167	chr6	UTRN	144608489	144612535	+
168	chr6	UTRN	144610994	144615040	+
169	chr6	UTRN	144612120	144616162	+
170	chr6	UTRN	144612968	144617021	+
171	chr6	UTRN	144616862	144620901	+
172	chr6	UTRN	144619690	144623714	+
173	chr6	UTRN	144623028	144627096	+
174	chr6	UTRN	144623129	144627174	+
175	chr6	UTRN	144623319	144627379	+
176	chr6	UTRN	144626965	144631011	+
177	chr6	UTRN	144631818	144635869	+
178	chr6	UTRN	144631933	144635968	+
179	chr6	UTRN	144656267	144660302	+
180	chr6	UTRN	144683087	144687140	+
181	chr6	UTRN	144693039	144697063	+
182	chr6	UTRN	144697670	144701699	+
183	chr6	UTRN	144702043	144706398	+
184	chr6	UTRN	144704312	144708345	+
185	chr6	UTRN	144704654	144708704	+
186	chr6	UTRN	144719683	144723738	+
187	chr6	UTRN	144720580	144724627	+
188	chr6	UTRN	144722848	144726889	+
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195	chr6	UTRN	144755162	144759214	+

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
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197	chr6	UTRN	144756752	144760807	+
198	chr6	UTRN	144756807	144760864	+
199	chr6	UTRN	144759513	144763579	+
200	chr6	UTRN	144763456	144767506	+
201	chr6	UTRN	144766420	144770461	+
202	chr6	UTRN	144766737	144770764	+
203	chr6	UTRN	144770549	144774627	+
204	chr6	UTRN	144772960	144777001	+
205	chr6	UTRN	144777914	144781960	+
206	chr6	UTRN	144778026	144782070	+
207	chr6	UTRN	144778278	144782324	+
208	chr6	UTRN	144781879	144785933	+
209	chr6	UTRN	144781933	144785995	+
210	chr6	UTRN	144798953	144802999	+
211	chr6	UTRN	144800780	144804822	+
212	chr6	UTRN	144801427	144805473	+
213	chr6	UTRN	144801714	144805742	+
214	chr6	UTRN	144801774	144805849	+
215	chr6	UTRN	144804673	144808714	+
216	chr6	UTRN	144806684	144810739	+
217	chr6	UTRN	144806739	144810803	+
218	chr6	UTRN	144807834	144811881	+
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220	chr6	UTRN	144812476	144816522	+
221	chr6	UTRN	144813156	144817199	+
222	chr6	UTRN	144818469	144822529	+
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224	chr6	UTRN	144833120	144837166	+
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226	chr6	UTRN	144835423	144839465	+
227	chr6	UTRN	144835943	144839989	+
228	chr6	UTRN	144842263	144846304	+
229	chr6	UTRN	144856722	144860798	+
230	chr6	UTRN	144868778	144872817	+
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232	chr6	UTRN	144870123	144874165	+
233	chr6	UTRN	144870599	144874669	+

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
234	chr6	UTRN	144871625	144875662	+
235	chr6	UTRN	144873136	144877182	+
236	chr6	UTRN	144873895	144877938	+
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238	chr6	UTRN	144902604	144906645	+
239	chr6	UTRN	144903276	144907300	+
240	chr6	UTRN	144904334	144908358	+
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242	chr6	UTRN	144906864	144910908	+
243	chr6	UTRN	144907055	144911078	+
244	chr6	UTRN	144908040	144912085	+
245	chr6	UTRN	144916990	144921013	+
246	chr6	UTRN	144933390	144937427	+
247	chr6	UTRN	144936199	144940248	+
248	chr6	UTRN	144939446	144943489	+
249	chr6	UTRN	144939551	144943596	+
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253	chr6	UTRN	144940080	144944136	+
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255	chr6	UTRN	144943160	144947207	+
256	chr6	UTRN	144948918	144952987	+
257	chr6	UTRN	144950595	144954650	+
258	chr6	UTRN	144952758	144956804	+
259	chr6	UTRN	144958952	144962996	+
260	chr6	UTRN	144966386	144970438	+
261	chr6	UTRN	144979668	144983709	+
262	chr6	UTRN	144983026	144987072	+
263	chr6	UTRN	144997637	145001686	+
264	chr6	UTRN	144997750	145001785	+
265	chr6	UTRN	144997904	145001956	+
266	chr6	UTRN	145010224	145014561	+
267	chr6	UTRN	145015897	145019969	+
268	chr6	UTRN	145015978	145020021	+
269	chr6	UTRN	145017229	145021261	+
270	chr6	UTRN	145019232	145023278	+
271	chr6	UTRN	145019336	145023382	+

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
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273	chr6	UTRN	145036424	145040467	+
274	chr6	UTRN	145040706	145044751	+
275	chr6	UTRN	145045775	145049820	+
276	chr6	UTRN	145049549	145053592	+
111	chr6	UTRN	145059899	145063941	+
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280	chr6	UTRN	145070959	145075005	+
281	chr6	UTRN	145077115	145081162	+
282	chr6	UTRN	145077204	145081271	+
283	chr6	UTRN	145078780	145082816	+
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285	chr6	UTRN	145079884	145083930	+
286	chr6	UTRN	145085734	145089827	+
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291	chr6	UTRN	145088281	145092327	+
292	chr6	UTRN	145088884	145092934	+
293	chr6	UTRN	145091542	145095591	+
294	chr6	UTRN	145092155	145096199	+
295	chr6	UTRN	145094714	145098756	+
296	chr6	UTRN	145099237	145103284	+
297	chr6	UTRN	145099598	145103642	+
298	chr6	UTRN	145125145	145129194	+
299	chr6	UTRN	145125467	145129507	+
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301	chr6	UTRN	145126105	145130160	+
302	chr6	UTRN	145126415	145130460	+
303	chr6	UTRN	145130350	145134397	+
304	chr6	UTRN	145130917	145134974	+
305	chr6	UTRN	145131779	145135802	+
306	chr6	UTRN	145132097	145136169	+
307	chr6	UTRN	145132835	145136881	+
308	chr6	UTRN	145140034	145144135	+
309	chr6	UTRN	145140629	145144676	+

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
310	chr6	UTRN	145146750	145150806	+
311	chr6	UTRN	145147936	145151984	+
312	chr6	UTRN	145151900	145156300	+
313	chr6	UTRN	145152735	145156782	+
314	chr6	UTRN	145153438	145157468	+
315	chr6	UTRN	145154972	145159019	+
316	chr6	UTRN	145155440	145159555	+
317	chr6	UTRN	145155566	145159621	+
318	chr6	UTRN	145156149	145160194	+
319	chr6	UTRN	145158356	145162409	+
320	chr6	UTRN	145159881	145163927	+
321	chr6	UTRN	145165107	145169151	+
322	chr6	UTRN	145165205	145169243	+
323	chr6	UTRN	145166292	145170344	+
324	chr6	UTRN	145167033	145171085	+
325	chr6	UTRN	145167156	145171202	+
326	chr6	UTRN	145167270	145171315	+
327	chr6	UTRN	145169814	145173863	+
328	chr6	UTRN	145171631	145175718	+
329	chr6	UTRN	144608031	144608073	-
330	chr6	UTRN	144612926	144612972	-
331	chr6	UTRN	144628552	144628595	-
332	chr6	UTRN	144633946	144633970	-
333	chr6	UTRN	144650739	144650804	-
334	chr6	UTRN	144657045	144657093	-
335	chr6	UTRN	144696995	144697041	-
336	chr6	UTRN	144747612	144747674	-
337	chr6	UTRN	144747879	144747925	-
338	chr6	UTRN	144759816	144759863	-
339	chr6	UTRN	144768238	144768312	-
340	chr6	UTRN	144780036	144780082	-
341	chr6	UTRN	144782886	144782935	-
342	chr6	UTRN	144795766	144795789	-
343	chr6	UTRN	144806556	144806601	-
344	chr6	UTRN	144854365	144854401	-
345	chr6	UTRN	144858769	144858809	-
346	chr6	UTRN	144861763	144861805	-
347	chr6	UTRN	144865560	144865594	-

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
348	chr6	UTRN	144871095	144871118	-
349	chr6	UTRN	144872146	144872179	-
350	chr6	UTRN	144873792	144873815	-
351	chr6	UTRN	144875726	144875775	-
352	chr6	UTRN	144881389	144881429	-
353	chr6	UTRN	144902992	144903093	-
354	chr6	UTRN	144913242	144913292	-
355	chr6	UTRN	144916606	144916629	-
356	chr6	UTRN	144953033	144953075	-
357	chr6	UTRN	144957938	144957985	-
358	chr6	UTRN	144960849	144960900	-
359	chr6	UTRN	144963737	144963802	-
360	chr6	UTRN	144980957	144981000	-
361	chr6	UTRN	144981226	144981271	-
362	chr6	UTRN	144981350	144981396	-
363	chr6	UTRN	144981507	144981542	-
364	chr6	UTRN	144983660	144983707	-
365	chr6	UTRN	145005066	145005095	-
366	chr6	UTRN	145005500	145005548	-
367	chr6	UTRN	145021339	145021384	-
368	chr6	UTRN	145036068	145036136	-
369	chr6	UTRN	145036766	145036820	-
370	chr6	UTRN	145038552	145038606	-
371	chr6	UTRN	145058056	145058096	-
372	chr6	UTRN	145059402	145059450	-
373	chr6	UTRN	145060834	145060905	-
374	chr6	UTRN	145062448	145062475	-
375	chr6	UTRN	145063125	145063160	-
376	chr6	UTRN	145063273	145063302	-
377	chr6	UTRN	145071318	145071359	-
378	chr6	UTRN	145079495	145079543	-
379	chr6	UTRN	145090227	145090266	-
380	chr6	UTRN	145095420	145095465	-
381	chr6	UTRN	145097191	145097232	-
382	chr6	UTRN	145098097	145098128	-
383	chr6	UTRN	145098960	145099005	-
384	chr6	UTRN	145106983	145107024	-
385	chr6	UTRN	145124174	145124220	-

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
386	chr6	UTRN	145128278	145128325	-
387	chr6	UTRN	145142105	145142152	-
388	chr6	UTRN	145149926	145149972	-
389	chr6	UTRN	145153110	145153155	-
390	chr6	UTRN	145155586	145155641	-
391	chr6	UTRN	145156956	145157020	-
392	chr6	UTRN	145161886	145161931	-
393	chr6	UTRN	145166490	145166527	-
394	chr6	UTRN	145167701	145167736	-
395	chr6	UTRN	145173585	145173627	-
396	chr6	UTRN	144606031	144610073	-
397	chr6	UTRN	144610926	144614972	-
398	chr6	UTRN	144626552	144630595	-
399	chr6	UTRN	144631946	144635970	-
400	chr6	UTRN	144648739	144652804	-
401	chr6	UTRN	144655045	144659093	-
402	chr6	UTRN	144694995	144699041	-
403	chr6	UTRN	144745612	144749674	-
404	chr6	UTRN	144745879	144749925	-
405	chr6	UTRN	144757816	144761863	-
406	chr6	UTRN	144766238	144770312	-
407	chr6	UTRN	144778036	144782082	-
408	chr6	UTRN	144780886	144784935	-
409	chr6	UTRN	144793766	144797789	-
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412	chr6	UTRN	144856769	144860809	-
413	chr6	UTRN	144859763	144863805	-
414	chr6	UTRN	144863560	144867594	-
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416	chr6	UTRN	144870146	144874179	-
417	chr6	UTRN	144871792	144875815	-
418	chr6	UTRN	144873726	144877775	-
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422	chr6	UTRN	144914606	144918629	-
423	chr6	UTRN	144951033	144955075	-

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
424	chr6	UTRN	144955938	144959985	-
425	chr6	UTRN	144958849	144962900	-
426	chr6	UTRN	144961737	144965802	-
427	chr6	UTRN	144978957	144983000	-
428	chr6	UTRN	144979226	144983271	-
429	chr6	UTRN	144979350	144983396	-
430	chr6	UTRN	144979507	144983542	-
431	chr6	UTRN	144981660	144985707	-
432	chr6	UTRN	145003066	145007095	-
433	chr6	UTRN	145003500	145007548	-
434	chr6	UTRN	145019339	145023384	-
435	chr6	UTRN	145034068	145038136	-
436	chr6	UTRN	145034766	145038820	-
437	chr6	UTRN	145036552	145040606	-
438	chr6	UTRN	145056056	145060096	-
439	chr6	UTRN	145057402	145061450	-
440	chr6	UTRN	145058834	145062905	-
441	chr6	UTRN	145060448	145064475	-
442	chr6	UTRN	145061125	145065160	-
443	chr6	UTRN	145061273	145065302	-
444	chr6	UTRN	145069318	145073359	-
445	chr6	UTRN	145077495	145081543	-
446	chr6	UTRN	145088227	145092266	-
447	chr6	UTRN	145093420	145097465	-
448	chr6	UTRN	145095191	145099232	-
449	chr6	UTRN	145096097	145100128	-
450	chr6	UTRN	145096960	145101005	-
451	chr6	UTRN	145104983	145109024	-
452	chr6	UTRN	145122174	145126220	-
453	chr6	UTRN	145126278	145130325	-
454	chr6	UTRN	145140105	145144152	-
455	chr6	UTRN	145147926	145151972	-
456	chr6	UTRN	145151110	145155155	-
457	chr6	UTRN	145153586	145157641	-
458	chr6	UTRN	145154956	145159020	-
459	chr6	UTRN	145159886	145163931	-
460	chr6	UTRN	145164490	145168527	-
461	chr6	UTRN	145165701	145169736	-

SEQ ID	Chrom	Gene	Chr. Start	Chr. End	Strand
462	chr6	UTRN	145171585	145175627	-

Single Strand Oligonucleotides (Antisense Strand of Target Gene)

SeqID range: 463-307980

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

CLAIMS

What is claimed is:

1. A single stranded oligonucleotide having a sequence 5'-X-Y-Z, wherein X is any nucleotide, Y is a nucleotide sequence of 6 nucleotides in length that is not a seed sequence of a human microRNA, and Z is a nucleotide sequence of 1-23 nucleotides in length, wherein the single stranded oligonucleotide is complementary with at least 8 consecutive nucleotides of a PRC2-associated region of a UTRN gene.

2. The single stranded oligonucleotide of claim 1, wherein the oligonucleotide does not comprise three or more consecutive guanosine nucleotides.

3. The single stranded oligonucleotide of claim 1 or 2, wherein the oligonucleotide does not comprise four or more consecutive guanosine nucleotides.

4. The single stranded oligonucleotide of any one of claims 1 to 3, wherein the oligonucleotide is 8 to 30 nucleotides in length.

5. The single stranded oligonucleotide of any one of claims 1 to 3, wherein the oligonucleotide is 8 to 10 nucleotides in length and all but 1, 2, or 3 of the nucleotides of the complementary sequence of the PRC2-associated region are cytosine or guanosine nucleotides.

6. The single stranded oligonucleotide of any one of claims 1 to 6, wherein at least one nucleotide of the oligonucleotide is a nucleotide analogue.

7. The single stranded oligonucleotide of claim 6, wherein the at least one nucleotide analogue results in an increase in Tm of the oligonucleotide in a range of 1 to 5 °C compared with an oligonucleotide that does not have the at least one nucleotide analogue.

8. The single stranded oligonucleotide of any one of claims 1 to 7, wherein at least one nucleotide of the oligonucleotide comprises a 2' O-methyl.

9. The single stranded oligonucleotide of any one of claims 1 to 8, wherein each nucleotide of the oligonucleotide comprises a 2' O-methyl.

10. The single stranded oligonucleotide of any one of claims 1 to 8, wherein the oligonucleotide comprises at least one ribonucleotide, at least one deoxyribonucleotide, or at least one bridged nucleotide.

11. The single strand oligonucleotide of claim 10, wherein the bridged nucleotide is a LNA nucleotide, a cEt nucleotide or a ENA modified nucleotide.

12. The single stranded oligonucleotide of any one of claims 1 to 6, wherein each nucleotide of the oligonucleotide is a LNA nucleotide.

13. The single stranded oligonucleotide of any one of claims 1 to 6, wherein the nucleotides of the oligonucleotide comprise alternating deoxyribonucleotides and 2'-fluoro-deoxyribonucleotides.

14. The single stranded oligonucleotide of any one of claims 1 to 6, wherein the nucleotides of the oligonucleotide comprise alternating deoxyribonucleotides and 2'-0-methyl nucleotides.

15. The single stranded oligonucleotide of any one of claims 1 to 7, wherein the nucleotides of the oligonucleotide comprise alternating deoxyribonucleotides and ENA nucleotide analogues.

16. The single stranded oligonucleotide of any one of claims 1 to 7, wherein the nucleotides of the oligonucleotide comprise alternating deoxyribonucleotides and LNA nucleotides.

17. The single stranded oligonucleotide of any one of claims 13 to 16, wherein the 5' nucleotide of the oligonucleotide is a deoxyribonucleotide.

18. The single stranded oligonucleotide of any one of claims 1 to 6, wherein the nucleotides of the oligonucleotide comprise alternating LNA nucleotides and 2'-O-methyl nucleotides.

19. The single stranded oligonucleotide of claim 18, wherein the 5' nucleotide of the oligonucleotide is a LNA nucleotide.

20. The single stranded oligonucleotide of any one of claims 1 to 8, wherein the nucleotides of the oligonucleotide comprise deoxyribonucleotides flanked by at least one LNA nucleotide on each of the 5' and 3' ends of the deoxyribonucleotides.

21. The single stranded oligonucleotide of any one of claims 1 to 20, further comprising phosphorothioate internucleotide linkages between at least two nucleotides.

22. The single stranded oligonucleotide of claim 21, further comprising phosphorothioate internucleotide linkages between all nucleotides.

23. The single stranded oligonucleotide of any one of claims 1 to 22, wherein the nucleotide at the 3' position of the oligonucleotide has a 3' hydroxyl group.

24. The single stranded oligonucleotide of any one of claims 1 to 23, wherein the nucleotide at the 3' position of the oligonucleotide has a 3' thiophosphate.

25. The single stranded oligonucleotide of any one of claims 1 to 24, further comprising a biotin moiety conjugated to the 5' nucleotide.

26. A single stranded oligonucleotide comprising a region of complementarity that is complementary with at least 8 consecutive nucleotides of a PRC2-associated region of a UTRN gene, wherein the oligonucleotide has at least one of:

a) a sequence that is 5'X-Y-Z, wherein X is any nucleotide and wherein X is anchored at the 5' end of the oligonucleotide, Y is a nucleotide sequence of 6 nucleotides in length that is not a human seed sequence of a microRNA, and Z is a nucleotide sequence of 1 to 23 nucleotides in length;

b) a sequence that does not comprise three or more consecutive guanosine nucleotides;

c) a sequence that has less than a threshold level of sequence identity with every sequence of nucleotides, of equivalent length to the second nucleotide sequence, that are between 50 kilobases upstream of a 5'-end of an off-target gene and 50 kilobases downstream of a 3'-end of the off-target gene;

d) a sequence that is complementary to a PRC2-associated region that encodes an RNA that forms a secondary structure comprising at least two single stranded loops; and/or

e) a sequence that has greater than 60% G-C content.

27.. The single stranded oligonucleotide of claim 26, wherein the oligonucleotide has the sequence 5'X-Y-Z and wherein the oligonucleotide is 8-50 nucleotides in length.

28. A composition comprising a single stranded oligonucleotide of any one of claims 1 to 27 and a carrier.

29. A composition comprising a single stranded oligonucleotide of any one of claims 1 to 28 in a buffered solution.

30. A composition of claim 28, wherein the oligonucleotide is conjugated to the carrier.

31. The composition of claim 30, wherein the carrier is a peptide.

32. The composition of claim 30, wherein the carrier is a steroid.

33. A pharmaceutical composition comprising a composition of any one of claims 28 to 32 and a pharmaceutically acceptable carrier.

34. A kit comprising a container housing the composition of any one of claims 28 to 33.

35. A method of increasing expression of a UTRN gene in a cell, the method comprising delivering the single stranded oligonucleotide of any one of claims 1 to 27 into the cell.

36. The method of claim CI, wherein delivery of the single stranded oligonucleotide into the cell results in a level of expression of a UTRN gene that is at least 50% greater than a level of expression of the UTRN gene in a control cell that does not comprise the single stranded oligonucleotide.

37. A method increasing levels of a UTRNgene in a subject, the method comprising administering the single stranded oligonucleotide of any one of claims 1 to 27 to the subject.

38. A method of treating a condition associated with decreased levels of a UTRN gene in a subject, the method comprising administering the single stranded oligonucleotide of any one of claims 1 to 27 to the subject.

39. The method of claim 38, wherein the condition is a muscular dystrophy, including DMD, BMD, and myotonic dystrophy.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/041452

A. CLASSIFICATION OF SUBJECT MATTER

C12N 15/11(2006.01)i, C12N 15/12(2006.01)i, A61K 48/00(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C12N 15/11; A61K 31/7105; A61K 31/712; A61K 48/00; C12N 15/12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & keywords: human microRNA, polycomb repressive complex2, PRC2, utrophin, UTRN

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2009-134710 A2 (THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA) 05 November 2009 See claims 1 and 11.	1-3,26,27
A	DI CERTO, MARIA GRAZIA et al., "The artificial gene Jazz, a transcriptional regulator of utrophin, corrects the dystrophic pathology in mdx mice ", Human molecular genetics, 2010, Vol. 19, No. 5, pp. 752-760. See abstract; page 753.	1-3,26,27
A	WO 2008-103763 A2 (SEQUENOM, INC.) 28 August 2008 See claims 1-3.	1-3,26,27
A	MIURA, PEDRO et al., "Utrophin upregulation for treating Duchenne or Becker muscular dystrophy: how close are we?", Trends in Molecular Medicine, Vol. 12, No. 3, March 2006, pp. 122-129. See abstract; page 123.	1-3,26,27
A	US 2012-0046345 A1 (COLLARD, JOSEPH et al.) 23 February 2012 See paragraphs [0083]-[0086] ; claim 1.	1-3,26,27

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 July 2013 (29.07.2013)	**29 July 2013 (29.07.2013)**

Name and mailing address of the ISA/KR
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/041452

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons::

1. ☒ Claims Nos.: 37-39
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 37-39 pertain to methods for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.

2. ☒ Claims Nos.: 7,1 1,19,22,30-32,36, 39
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Claims 7,1 1,19,22,30-32,36 and 39 are unclear since they refer to claims which are not searchable due to not being drafted in accordance with the second and third sentence of Rule 6.4(a).

3. ☒ Claims Nos.: 4-6,8-10,12-18,20-21,23-25,28-29,33-35,37-38
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. Ill Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required addtional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/US2013/041452

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009-134710 A2	05/11/2009	US 2012-0122953 Al	17/05/2012
		Wo 2009-134710 A3	30/12/2009
WO 2008-103763 A2	28/08/2008	wo 2008-103761 A2	28/08/2008
		wo 2008-103761 A9	22/01/2009
		wo 2008-103763 A3	25/03/2010
US 2012-0046345 Al	23/02/2012	CA 2761248 Al	11/11/2010
		CN 102459597 A	16/05/2012
		EP 2427554 A2	14/03/2012
		EP 2427554 A4	22/05/2013
		JP 2012-525852 A	25/10/2012
		KR 10-2012-0013425 A	14/02/2012
		KR 2012-0013425 A	14/02/2012
		wo 2010-129861 A2	11/11/2010
		wo 2010-129861 A3	12/05/2011