oligonucleotides of the same physicochemical properties (e.g., the same GC content, T_m, length etc.) as the enriched set.

[0075] 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.

[0076] 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.

[0077] Methods of design and/or synthesis of a single stranded oligonucleotide may involve one or more of the steps of:

[0078] Identifying and/or selecting PRC2-associated region;

[0079] Designing a nucleic acid sequence having a desired degree of sequence identity or complementarity to a PRC2-associated region or a portion thereof;

[0080] Synthesizing a single stranded oligonucleotide to the designed sequence;

[0081] Purifying the synthesized single stranded oligonucleotide; and

[0082] Optionally mixing the synthesized single stranded oligonucleotide with at least one pharmaceutically acceptable diluent, carrier or excipient to form a pharmaceutical composition or medicament.

[0083] Single stranded oligonucleotides so designed and/or synthesized may be useful in method of modulating gene expression as described herein.

[0084] 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.

[0085] 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'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), or 2'-O—N-methylacetamido (2'-O-NMA). As another example, the nucleic acid sequence can include at least one 2'-O-methyl-modified nucleotide, and in some embodiments, all of the nucleotides include a 2'-O-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.

[0086] 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.

[0087] 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.

[0088] 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.

[0089] 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.

[0090] 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.

[0091] 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

[0092] 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: U.S. Pat. No. 7,399,845, U.S. Pat. No. 7,741,457, U.S. Pat. No. 8,022,193, U.S. Pat. No. 7,569,686, U.S. Pat. No. 7,335,765, U.S. Pat. No. 7,314,923, U.S. Pat. No. 7,335,765, and U.S. Pat. No. 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.

[0093] 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.