MODIFIED ANTIMIR-138 OLIGONUCLEOTIDES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of Singapore patent application No. 10201404535S, filed 31 July 2014, the contents of it being hereby incorporated by reference in its entirety for all purposes.

FIELD OF THE INVENTION

[0002] The present invention relates to biochemistry in particular biomarkers. In particular, the present invention relates to oligonucleotides that can regulate the expression of biomarker miR-138, pharmaceutical compositions and methods of using the biomarkers thereof.

BACKGROUND OF THE INVENTION

[0003] MicroRNAs (miRNAs) are endogenous small noncoding RNAs that regulate various physiological pathways such as cellular differentiation and proliferation via gene silencing. The microRNAs are thought to contribute to the initiation, progression and eventual metastasis of various proliferative diseases. For example, dysregulation of the expression of a miRNA may lead to aberrant expression of its target proteins, resulting in an altered phenotype in a cell. Impaired miRNA regulatory network is known to be one of the key mechanisms in the pathogenesis of proliferative diseases such as cancer. Thus, there is a need to provide molecules that have the potential to influence the expression of miRNA.

SUMMARY OF THE INVENTION

[0004] In one aspect, there is provided an oligonucleotide comprising one of the sequences selected from the group consisting of 5'-mC*mG*G*mCCmUmGAmUTmCAmCmAAmCAmCCmA*G*mC*mU-3' (SEQ ID NO: 13), and 5'-mC*mG*mG*mCmCTmGAmUTmCAmCAmACmACmCmCmA*mG*mC*mU-3' (SEQ ID NO: 10), wherein m is a 2'-O-methylation, * is a phosphorothioate linkage and underlined nucleotides represent a locked nucleic acid modification.

[0005] In another aspect, there is provided a pharmaceutical composition comprising an effective amount of the oligonucleotide as described herein, or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable carrier or diluent.

[0006] Also described herein is a method of treating a proliferative disease in a subject in need thereof comprising administering the oligonucleotide as described herein to the subject.

[0007] Also described herein is a use of an oligonucleotide as described herein in the manufacture of a medicament for treating proliferative disease in a subject in need thereof.

[0008] Also described herein is a method of reducing or inhibiting the activity of miR-138 in a cell comprising contacting the cell with the oligonucleotide as described herein.

Claims

1. An oligonucleotide comprising one of the sequences selected from the group consisting of
5’-mC*mG*G*mCCmUmGAmUTmCAmCmAAmCAmCCmA*G*mC*mU-3’ (SEQ ID NO: 13) and
5’-mC*mG*mG*mCmCTmGAmUTmCAmCAmACmACmCmA*mG*mC*mU-3’(SEQ ID NO: 10), wherein m is a 2’-O-methylation, * is a phosphorothioate linkage and underlined nucleotides represent a locked nucleic acid modification.

2. The oligonucleotide of claim 1, wherein the locked nucleic acid creates a bi-cyclic structure that locks the conformation of the ribose.

3. The oligonucleotide of claim 2, wherein the bi-cyclic structure is created by ribose moiety modification which creates a bridge connecting 2' oxygen to 4' carbon.

4. The oligonucleotide of claim 3, wherein the bridge is an ethylene, methylene or oxy-methylene bridge.

5. A pharmaceutical composition comprising an effective amount of the oligonucleotide of any one of claims 1 to 4, or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable carrier or diluent.