Claims

1. An isolated antisense oligonucleotide for inhibiting the activity of GLDC, wherein the oligonucleotide inhibits the expression of GLDC by inducing the skipping of an exon of a GLDC pre-mRNA or mature mRNA to induce cell cycle arrest or apoptosis, the antisense oligonucleotide comprises a sequence selected from any one of SEQ ID NOs: 1 to 94.

2. The antisense oligonucleotide according to claim 1, wherein the oligonucleotide inhibits the expression of GLDC or modify its expression products.

3. The antisense oligonucleotide according to any one of the preceding claims, wherein the oligonucleotide specifically hybridises to a target region of a GLDC pre-mRNA or mature mRNA, and the antisense oligonucleotide exerts a steric hindrance effect against one or more RNA-binding splicing regulators.

4. The antisense oligonucleotide according to claim 2, wherein the oligonucleotide prevents translation of the mRNA by steric hindrance.

5. The antisense oligonucleotide according to any one of the preceding claims, wherein the oligonucleotide specifically hybridises to an exon, intron or exon-intron boundary target region of a GLDC RNA, the target region is any one selected from the group comprising: exon 2, exon 3, exon 6, exon 7, exon 8, exon 9, exon 10, exon 12, exon 13, exon 15, exon 16, exon 19, exon 20, exon 21, intron 6, intron 7 and intron 8.

6. The antisense oligonucleotide according to any one of the preceding claims, wherein the antisense oligonucleotide comprising a modified polynucleotide backbone.

7. The antisense oligonucleotide according to claim 6, wherein the modified polynucleotide backbone comprises a modified moiety substituted for the sugar of at least one of the polynucleotides.

8. The antisense oligonucleotide according to claim 7, wherein the modified moiety selected from the group consisting of phosphorodiamidate morpholino oligomer (PMO), peptide-conjugated phosphorodiamidate morpholino oligomer (PPMO), and non-peptide dendrimeric octaguanidine moiety-tagged morpholino oligomer.

9. The antisense oligonucleotide according to any one of claims 6 to 8, wherein the modified polynucleotide backbone comprises at least one modified internucleotide linkage.

10. The antisense oligonucleotide according to claim 9, wherein the modified internucleotide linkage comprises a modified phosphate.

11. The antisense oligonucleotide according to claim 10, wherein the modified phosphate is selected from the group comprising of a non-bridging oxygen atom substituting a sulfur atom, a phosphonate, a phosphorothioate, a phosphodiester, a phosphoromorpholidate, a phosphoropiperazidate and a phosphoroamidate.

12. The antisense oligonucleotide according to any one of the preceding claims, wherein the antisense oligonucleotide comprises a backbone which is selected from the group comprising of ribonucleic acid, deoxyribonucleic acid, DNA phosphorothioate, RNA phosphorothioate, 2’-O-methyl-oligoribonucleotide and 2’-O-methyl-oligodeoxyribonucleotide, 2'-O-hydrocarbyl ribonucleic acid, 2´-O-hydrocarbyl DNA, 2'-O-hydrocarbyl RNA phosphorothioate, 2'-O-hydrocarbyl DNA phosphorothioate, 2'-F-phosphorothioate, 2'-F-phosphodiester, 2'-methoxyethyl phosphorothioate, 2-methoxyethyl phosphodiester, deoxy methylene(methylimino) (deoxy MMI), 2'-O-hydrocarby MMI, deoxy-methylphos-phonate, 2'-O-hydrocarbyl methylphosphonate, morpholino, 4'-thio DNA, 4'-thio RNA, peptide nucleic acid, 3'-amidate, deoxy 3'-amidate, 2'-O- hydrocarbyl 3'-amidate, locked nucleic acid, cyclohexane nucleic acid, tricycle-DNA, 2’fluoro-arabino nucleic acid, N3’-P5’ phosphoroamidate, carbamate linked, phosphotriester linked, a nylon backbone modification and mixtures of the aforementioned backbones.

13. The antisense oligonucleotide according to any one of the preceding claims, wherein the oligonucleotide is chemically linked to one or more conjugates that enhance the activity, cellular distribution, or cellular uptake of the antisense oligonucleotide.

14. The antisense oligonucleotide according to any one of the preceding claims, wherein the oligonucleotide modulates one or more of activity; or level of pre-mRNA, matured mRNA and protein expression.

15. The antisense oligonucleotide according to any one of claims 1 to 14 for use in treating a GLDC-expressing cancer patient.

16. The antisense oligonucleotide according to claim 15, wherein the patient is administered a further anti-cancer agent or treatment.

17. The antisense oligonucleotide according to any one of claims 15 or 16 wherein the cancer is any one selected from the group comprising: non-small cell lung carcinoma (NSCLC), breast cancer, ovarian cancer, colon cancer, melanoma, testis cancer, thyroid cancer, and glioma, carcinoid and phyllode tumours.

18. A pharmaceutical composition comprising the antisense oligonucleotide according to any one of claims 1 to 17 and a pharmaceutically acceptable carrier.

19. The composition according to claim 18, wherein the composition is suitable for parenteral administration either naked or complexed with a delivery agent to a patient.

20. The composition according to claim 19, wherein the carrier is selected from the group comprising of a nanoparticle, such as a polymeric nanoparticle; a liposome, such as pH-sensitive liposome, an antibody conjugated liposome; a viral vector, a cationic lipid, a polymer, a UsnRNA, such as U7 snRNA and a cell penetrating peptide.

21. The composition according to any one of claims 18 to 20, wherein the antisense oligonucleotide is administered orally, or rectal, or transmucosal, or intestinal, or

intramuscular, or subcutaneous, or intramedullary, or intrathecal, or direct intraventricular, or intravenous, or intravitreal, or intraperitoneal, or intranasal, or intraocular.

22. Use of an antisense oligonucleotide according to any one of claims 1 to 14 in the manufacture of a medicament for treating cancer.

23. The use according to claim 22, wherein the oligonucleotide modulates one or more of activity; or level of pre-mRNA, matured mRNA and protein expression.

24. The use according to claim 23, wherein the oligonucleotide inhibits the expression of GLDC or modify its expression products.

25. The use according to any one of claims 22 to 24, wherein the cancer is non-small cell lung carcinoma (NSCLC).

26. A method for selecting a therapeutic strategy for a patient with cancer, the method comprising assessing the level of GLDC nucleic acid, protein or activity in a sample, wherein if the level of GLDC nucleic acid, protein or activity in the sample is an elevated level, then the therapeutic strategy comprises treating the patient with an inhibitor of GLDC activity, the inhibitor comprises an antisense oligonucleotide according to any one of claims 1 to 14.

27. The method according to claim 26, further comprising the step of selecting a treatment regime making use of the information on the level of GLDC nucleic acid, protein or activity in the sample.

28. The method according to any one of claims 26 or 27, wherein the sample is obtained from the patient and the sample is a tissue sample in which cancer is suspected or in which cancer has been found, or contains cells from said tissue.

29. A method of inducing exon-skipping of a GLDC pre-mRNA, the method comprising delivering to a cell the antisense oligonucleotide according to any one of claims 1 to 17, or

the composition according to any one of claim 18 to 21, thereby inducing exon-skipping of the GLDC pre-mRNA.

30. The method according to claim 29, wherein any one of exon 2, exon 3, exon 6, exon 7, exon 8, exon 9, exon 10, exon 12, exon 13, exon 15, exon 16, exon 19, exon 20, or exon 21 is skipped.

31. The method according to any one of claims 29 or 30, wherein the cell is a human cell.

32. The method according to claim 31, wherein the human cell is a cancer cell, the cancer is any one selected from the group comprising: haematological malignancies, lung cancer, breast cancer, prostate cancer, stomach cancer, testis cancer, larynx cancer, liver cancer, uterus cancer, colorectal cancer, melanoma, glioblastoma, sarcomas, and retinoblastoma.

33. A kit comprising the antisense oligonucleotide of any one of claims 1 to 17, optionally in a container, and a package insert, package label, instructions or other labelling.