Claims

1. A composition comprising an RNA interference (RNAi) trigger for inhibiting the expression of an Hif2α gene, wherein the RNAi trigger comprises a sense strand and an antisense strand, wherein the antisense strand comprises the base sequence (5′ → 3′) of UUUCAUGAAAUCGUUACGUUG (SEQ ID NO. 41), wherein the sense strand comprises a core sequence of 16 or more consecutive nucleobases that is at least substantially complementary to the antisense strand sequence, and wherein the sense strand and/or antisense strand independently comprises one or more modified nucleotides.

2. The composition of claim 1, wherein both the sense strand and the antisense strand each independently comprises one or more modified nucleotides or nucleotide mimics.

3. The composition of claim 1, wherein the modified nucleotide is selected from the group consisting of: 2′-O-methyl modified nucleotide, nucleotide comprising a 5′-phosphorothioate group, 2′-deoxy-2′-fluoro modified nucleotide, 2′-deoxy-modified nucleotide, locked nucleotide, abasic nucleotide, deoxythymidine, inverted deoxythymidine, 2′-amino-modified nucleotide, 2′-alkyl-modified nucleotide, morpholino nucleotide, and non-natural base comprising nucleotide.

4. The composition of claim 3, wherein the sense strand contains one, two, or three 2′-deoxy-2′-fluoro modified nucleotides at positions 11, 12, and/or 13 from the 3′ end.

5. The composition of claim 3, wherein the antisense strand contains a 2′-deoxy-2′-fluoro modified nucleotide at position 2 from the 5′ end.

6. The composition of claim 3, wherein the antisense strand contains a 2′-deoxy-2′-fluoro modified nucleotide at position 14 from the 5′ end.

7. The composition of claim 3, wherein the antisense strand contains one, two, three, or four 2′-deoxy-2′-fluoro modified nucleotides at positions 4, 6, 8, 10, and 12 from the 5′ end.

8. The composition of claim 1, wherein the RNAi trigger comprises one or more phosphorothioate internucleoside linkages.

9. The composition of claim 8, wherein the sense strand comprises one or two phosphorothioate internucleoside linkages.

10. The composition of claim 8, wherein the antisense strand comprises one, two, three, or four phosphorothioate internucleoside linkages.

11. The composition of claim 1, further comprising one or more additional therapeutics or treatments.

12. The composition of claim 1, further comprising a pharmaceutically acceptable excipient.

13. The composition of claim 1, wherein the composition is packaged in a kit, container, pack, dispenser, pre-filled syringes, or vials.

14. The composition of claim 1, wherein the antisense strand further comprises a 3′ extension of 1-6 nucleotides in length.

15. The composition of claim 14, wherein the 3′ extension of the antisense strand comprises uAu, uGu, udTsdT, usdTsdT, UfAu, Aua, Afsusa, UAU, uAfu, uau, udAu, uscu, usgu, uscsu, cAu, aUa, aua, u(invdA)u, cag, agu, gcg, caa, usasu, uAMTM, or usTMsAM.

16. The composition of claim 1, wherein a targeting group is conjugated to the RNAi trigger.

17. The composition of claim 16, wherein the targeting group comprises a compound selected from the group consisting of: integrin-binding compound, $\alpha_v\beta_3$ integrin-binding, RGD ligand, RGD peptide, and RGD mimic.

18. The composition of claim 1, wherein a delivery polymer is conjugated to the RNAi trigger.

19. The composition of claim 1, wherein a linking group is conjugated to the RNAi trigger.

20. The composition of claim 1, wherein the antisense strand comprises the base sequence (5′ → 3′) of UUUCAUGAAAUCGUUACGUUG (SEQ ID NO. 41) and said sequence is located at positions 1-21 from the 5′ end of the antisense strand.

21. The composition of claim 1, wherein the sense strand of the RNAi agent comprises the base sequence (5′ → 3′) of ACGUAACGAUUUCAUGAAA (SEQ ID NO: 50).

22. The composition of claim 1, wherein the sense strand of the RNAi agent comprises the base sequence (5′ → 3′) of ACGUAACGAUUUCAUGAAAT (SEQ ID NO: 51).

23. The composition of claim 1, wherein the sense strand of the RNAi agent comprises the base sequence (5′ → 3′) of ACGUAACGAUUUCAUGAAU (SEQ ID NO: 53).

24. The composition of claim 1, wherein the sense strand of the RNAi agent comprises the base sequence (5′ → 3′) of CAACGUAACGAUUUCAUGA (SEQ ID NO: 58).

25. The composition of claim 1, wherein the sense strand of the RNAi agent comprises the base sequence (5′ → 3') of CAACGUAACGAUUUCAUGAAA (SEQ ID NO: 59).

26. The composition of claim 1, wherein the sense strand of the RNAi agent comprises the base sequence (5′ → 3') of UAUACGUAACGAUUUCAUGAAAT (SEQ ID NO: 72).

27. The composition of claim 1, wherein the sense strand of the RNAi agent is 16 to 30 nucleotides in length.

28. The composition of claim 27, wherein the antisense strand of the RNAi agent is 21 to 30 nucleotides in length.

29. A method for inhibiting Hif2α expression in an isolated cell or isolated tissue, the method comprising administering to the isolated cell or isolated tissue, an effective amount of the composition of claim 1.

30. The method of claim 29, wherein the cell or tissue is a renal cell carcinoma.

31. An RNAi trigger for inhibiting the expression of an Hif2α gene, wherein the RNAi trigger comprises a sense strand and an antisense strand, wherein the antisense strand comprises the base sequence (5′ → 3') of UUUCAUGAAAUCGUUACGUUG (SEQ ID NO. 41), wherein said sequence is located at positions 1-21 from the 5' end of the antisense strand, wherein the sense strand comprises a core sequence of 16 or more consecutive nucleobases that is at least substantially complementary to the antisense strand sequence, and wherein the sense strand and/or antisense strand independently comprises one or more modified nucleotides.