WHAT IS CLAIMED IS

1. A double-stranded, blunt-ended RNA molecule 22 or 23 basepairs in length comprising:

a) an active strand comprising SEQ ID NO:1 from 5' to 3' and

b) a fully complementary passenger strand comprising

i) modified nucleotides in the first and last two nucleotides of the passenger strand; and

ii) a terminal modification of the nucleotide at the 5' end.

2. The RNA molecule of claim 1, wherein the molecule is 23 basepairs in length and the active strand comprises SEQ ID NO:2.

3. The RNA molecule of claim 1, wherein the passenger strand comprises a modified nucleotide at positions 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 17, 18, 19, 20, 21, 22, and/or 23 relative to SEQ ID NO:4, wherein fewer than half of the total number of nucleotides in the passenger strand are modified nucleotides.

4. The RNA molecule of any of claims 1-3, wherein the passenger strand comprises modified nucleotides located at positions i) 1 and 2 and/or ii) 22 and 23 relative to SEQ ID NO:4.

5. The RNA molecule of any of claims 2-3, wherein the passenger strand comprises modified nucleotides located at positions i) 1 and 2 and ii) 22 and 23 relative to SEQ ID NO:4.

6. The RNA molecule of any of claims 1-5, wherein the passenger strand comprises a modified nucleotide located at positions i) 3 and 4 and/or ii) 19 and 20 relative to SEQ ID NO:4.

7. The RNA molecule of claim 6, wherein the passenger strand comprises a modified nucleotide located at positions i) 3 and 4 or ii) 19 and 20 relative to SEQ ID NO:4, but not at both positions i) and ii).

8. The RNA molecule of any of claims 4 – 7, wherein the passenger strand comprises modified nucleotides at positions 5 and 6 relative to SEQ ID NO:4.

9. The RNA molecule of any of claims 4 – 7, wherein the passenger strand comprises a modified nucleotide at positions 9 and 10 relative to SEQ ID NO:4.

10. The RNA molecule of any of claims 4 – 7, wherein the passenger strand comprises a modified nucleotide at positions 11 and 12 relative to SEQ ID NO:4.

11. The RNA molecule of any of claims 4 – 7, wherein the passenger strand comprises a modified nucleotide at positions 13 and 14 relative to SEQ ID NO:4.

12. The RNA molecule of any of claims 4 – 7, wherein the passenger strand comprises a modified nucleotide at positions 17 and 18 relative to SEQ ID NO:4.

13. The RNA molecule of claim 4, wherein the number of modified nucleotides in the passenger strand is four to eight.

14. The RNA molecule of claim 13, wherein the number of modified nucleotides in the passenger strand is five to seven.

15. The RNA molecule of claim 14, wherein the number of modified nucleotides in the passenger strand is six.

16. The RNA molecule of any of claims 1-15, wherein the passenger strand does not have a modified nucleotide located at positions 7, 8, 9, 15, and 16 relative to SEQ ID NO:4.

17. The RNA molecule of any of claims 1-16, wherein the passenger strand comprises a modified nucleotide at positions 1, 2, 21, 22, and 23 relative to SEQ ID NO:4.

18. The RNA molecule of any of claims 1-16, wherein the passenger strand comprises a modified nucleotide at positions 1, 2, 3, 4, 22, and 23 relative to SEQ ID NO:4.

19. The RNA molecule of any of claims 1-16, wherein the passenger strand comprises a modified nucleotide at positions 1, 2, 19, 20, 22, and 23 relative to SEQ ID NO:4.

20. The RNA molecule of any of claims 1-19, wherein the active strand comprises at least two modified nucleotides, wherein the modified nucleotides are not in the first two positions at the 5' end.

21. The RNA molecule of any of claims 1-19, wherein the active strand does not have a modified nucleotide in the first two positions at the 5' end.

22. The RNA molecule of claim 1, wherein the active strand does not comprise a modified nucleotide in the first or last two positions from the ends.

23. The RNA molecule of any of claims 20-22, wherein the active strand has modified nucleotides at positions 3, 4, 11, 12, 13, 14, 15, 16, 17, and/or 18 relative to SEQ ID NO:2.

24. The RNA molecule of claim 23, wherein the active strand comprises modified nucleotides at positions 15 and 16 relative to SEQ ID NO:2.

25. The RNA molecule of claim 23, wherein the active strand comprises modified nucleotides at positions 3 and 4 relative to SEQ ID NO:2.

26. The RNA molecule of claim 23, wherein the active strand comprises modified nucleotides at positions 11 and 12 relative to SEQ ID NO:2.

27. The RNA molecule of claim 23, wherein the active strand comprises modified nucleotides at positions 11, 12, 13, and 14 relative to SEQ ID NO:2.

28. The RNA molecule of claim 23, wherein the active strand comprises modified nucleotides at positions 17 and 18 relative to SEQ ID NO:2.

29. The RNA molecule of any of claims 23-28, wherein the active strand comprises modified nucleotides at positions 11, 12, 15, and 16 relative to SEQ ID NO:2.

30. The RNA molecule of claim 29, wherein the active strand further comprises modified nucleotides at positions 13, 14, 17, and 18 relative to SEQ ID NO:2.

31. The RNA molecule of any of claims 23-28, wherein the active strand comprises modified nucleotides at positions 3, 4, 15, and 16 relative to SEQ ID NO:2.

32. The RNA molecule of any of claims 1-19, wherein the active strand does not have any modified nucleotides.

33. The RNA molecule of claim 29, wherein the passenger strand does not comprise any modified nucleotides except a 5' terminal modification.

34. The RNA molecule of claim 29, wherein the passenger strand comprises SEQ ID NO:4 and modified nucleotides at positions 1, 2, 20, 21, 22, and 23 relative to SEQ ID NO:4.

35. The RNA molecule of claim 29, wherein the passenger strand comprises SEQ ID NO:4 and modified nucleotides at positions 1, 2, 3, 4, 22, and 23 relative to SEQ ID NO:4.

36. The RNA molecule of any of claims 29, wherein the passenger strand comprises SEQ ID NO:4 and modified nucleotides at positions 1, 2, 19, 20, 22, and 23 relative to SEQ ID NO:4.

37. The RNA molecule of claim 30, wherein the passenger strand does not comprise any modified nucleotides except a 5' terminal modification.

38. The RNA molecule of claim 30, wherein the passenger strand comprises SEQ ID NO:4 and modified nucleotides at positions 1, 2, 20, 21, 22, and 23 relative to SEQ ID NO:4.

39. The RNA molecule of claim 30, wherein the passenger strand comprises SEQ ID NO:4 and modified nucleotides at positions 1, 2, 3, 4, 22, and 23 relative to SEQ ID NO:4.

40. The RNA molecule of any of claims 30, wherein the passenger strand comprises SEQ ID NO:4 and modified nucleotides at positions 1, 2, 19, 20, 22, and 23 relative to SEQ ID NO:4. [A-ID 206/P-ID 215]

41. The RNA molecule of claim 31, wherein the passenger strand does not comprise any modified nucleotides except a 5' terminal modification.

42. The RNA molecule of claim 31, wherein the passenger strand comprises SEQ ID NO:4 and modified nucleotides at positions 1, 2, 21, 22, and 23 relative to SEQ ID NO:4.

43. The RNA molecule of claim 31, wherein the passenger strand comprises SEQ ID NO:4 and modified nucleotides at positions 1, 2, 3, 4, 22, and 23 relative to SEQ ID NO:4.

44. The RNA molecule of any of claims 31, wherein the passenger strand comprises SEQ ID NO:4 and modified nucleotides at positions 1, 2, 19, 20, 22, and 23 relative to SEQ ID NO:4.

45. The RNA molecule of any of claims 1-44, wherein the terminal modification of the passenger strand comprises a lower alkylamine group.

46. The RNA molecule of any of claims 1-45, wherein the modified nucleotides have sugar modifications .

47. The RNA molecule of claim 46, wherein the sugar modification is 2'-OMe.

48. A double-stranded RNA molecule of 20-23 basepairs in length, wherein the RNA molecule is blunt-ended at both ends, comprising an active strand having the sequence of

SEQ ID NO:2 and a separate and fully complementary passenger strand with a modified nucleotide at the 5' end,

wherein (i) the active strand comprises at least one modified internal nucleotide and/or (ii) the passenger strand comprises modified nucleotides in the first and last tow nucleotides and

wherein the double-stranded RNA molecule is more stable compared to a double-stranded, blunt-ended RNA molecule lacking any modification of an internal nucleotide.

49. A pharmaceutical composition comprising the RNA molecule of any of claims 1-48.

50. An RNA molecule according to any of claims 1-48 for use in providing miR-34a activity to a cell.

51. An RNA molecule according to any of claims 1-48 for use in decreasing cell proliferation.

52. An RNA molecule according to any of claims 1-48 for use in inducing apoptosis in a cell.

53. An RNA molecule according to any of claims 1-48 for use in a cancer therapy.

54. The RNA molecule of claim 53, for use in combination with an additional cancer therapy.

55. The use of claim 53, wherein the patient has been diagnosed with cancer.

56. A double-stranded, blunt-ended RNA molecule 23 or 24 basepairs in length comprising:

a) an active strand comprising

SEQ ID NO:5 from 5' to 3' ; and,

b) a fully complementary passenger strand comprising a terminal modification of the nucleotide at the 5' end

wherein the passenger strand comprises modified nucleotides in the first and last two nucleotides.

57. The RNA molecule of claim 56, wherein the molecule is 23 basepairs in length.

58. The RNA molecule of claim 56, wherein the passenger strand comprises a modified nucleotide at positions 1 (G), 2 (C), 3 (A), 21 (C), 22 (C), and/or 23 (U) relative to SEQ ID NO:6.

59. The RNA molecule of any of claims 56-58, wherein the passenger strand comprises modified nucleotides located at a subset of positions, wherein the subset is i) 1 (A), 2 (A), and 3 (C) and/or ii) 22 (C), and 23 (A) relative to SEQ ID NO:6.

60. The RNA molecule of any of claims 56-59, wherein the passenger strand comprises a modified nucleotide located at positions i) 1 (A), 2 (A), and 3 (C) relative to SEQ ID NO:6.

61. The RNA molecule of any of claims 56-60, wherein the passenger strand comprises a modified nucleotide located at positions ii) 22 (C), and 23 (A) relative to SEQ ID NO:6.

62. The RNA molecule of claim 59, wherein the passenger strand comprises a modified nucleotide located at positions 1 (A), 2 (A), 3 (C), 22 (C), and 23 (A) relative to SEQ ID NO:6.

63. The RNA molecule of claim 59, wherein the passenger strand comprises a modified nucleotide located at positions i) or ii) relative to SEQ ID NO:6, but not at both positions i) and ii).

64. The RNA molecule of any of claims 56 - 63, wherein the passenger strand further comprises a modified nucleotide located at positions 4 (A), 7 (A), 8 (G), 9 (C), 10 (U), 11 (A), 12 (A), 13 (C), 14 (U), 19 (U), and/or 21 (C) relative to SEQ ID NO:6.

65. The RNA molecule of any of claims 56, wherein the passenger strand does not have a modified nucleotide located at positions 5 (U), 6 (C), 15 (A), and/or 16 (C) relative to SEQ ID NO:6.

66. The RNA molecule of any of claims 56, wherein the number of modified nucleotides in the passenger strand is two to eight.

67. The RNA molecule of claim 66, wherein the number of modified nucleotides in the passenger strand is three to five.

68. The RNA molecule of any of claims 56, wherein the passenger strand comprises modified nucleotides at positions 1 (A), 2 (A), 3 (C), 17 (A), 18 (C), 21 (C), 22 (C), and 23 (A) relative to SEQ ID NO:6.

69. The RNA molecule of any of claims 56, wherein the passenger strand comprises modified nucleotides at positions 1 (A), 2 (A), 3 (C), 11 (A), 12 (A), 13 (C), 14 (U), 21 (C), 22 (C), and 23 (A) relative to SEQ ID NO:6.

70. The RNA molecule of any of claims 56, wherein the passenger strand comprises modified nucleotides at positions 1 (A), 2 (A), 3 (C), 11 (A), 12 (A), 13 (C), 14 (U), 17 (A), 18 (C), 21 (C), 22 (C), and 23 (A) relative to SEQ ID NO:6.

71. The RNA molecule of any of claims 56-70, wherein the active strand comprises at least two modified nucleotides, wherein the modified nucleotides are not in the first two positions at the 5' end.

72. The RNA molecule of any of claims 56-70, wherein the active strand does not have a modified nucleotide in the first two positions at the 5' end.

73. The RNA molecule of claim 56, wherein the active strand does not comprise a modified nucleotide in the first or last two positions from the ends.

74. The RNA molecule of any of claims 71-73, wherein the active strand comprises modified nucleotides at positions 3 (G), 4 (C), 11 (G), 12 (U), 13 (A), 14 (G), 15 (C), 16 (C), 17 (U), and/or 18 (G) relative to SEQ ID NO:5.

75. The RNA molecule of claim 74, wherein the active strand comprises a modified nucleotide at positions 11 (G) and 12 (U) relative to SEQ ID NO:5.

76. The RNA molecule of claim 74, wherein the active strand comprises a modified nucleotide at positions 17 (U) and 18 (G) relative to SEQ ID NO:5.

77. The RNA molecule of claim 74, wherein the active strand comprises a modified nucleotide at positions 11 (G), 12 (U), 17 (U), and 18 (G) relative to SEQ ID NO:5.

78. The RNA molecule of claim 77, wherein the active strand further comprises a modified nucleotide at positions 3 (G), 4 (C), 13 (A), 14 (G), 15 (C), and/or 16 (C) relative to SEQ ID NO:5.

79. The RNA molecule of any of claims 74-78, wherein the passenger strand does not comprise any modified nucleotides.

80. The RNA molecule of claim 68, wherein the active strand comprises a modified nucleotide at positions 11 (G), 12 (U), 17 (U), and 18 (G) relative to SEQ ID NO:5.

81. The RNA molecule of claim 69, wherein the active strand comprises a modified nucleotide at positions 11 (G), 12 (U), 17 (U), and 18 (G) relative to SEQ ID NO:5.

82. The RNA molecule of any of claims 70, wherein the active strand comprises a modified nucleotide at positions 11 (G), 12 (U), 17 (U), and 18 (G) relative to SEQ ID NO:5.

83. The RNA molecule of any of claims 56-82, wherein the terminal modification of the passenger strand comprises a lower alkylamine group.

84. The RNA molecule of any of claims 56-83, wherein the modified nucleotides have modified sugars.

85. The RNA molecule of claim 84, wherein the sugar modification is 2'-OMe.

86. The double-stranded, blunt-ended RNA molecule of claim 56, further comprising a sugar modification of the nucleotides at one or more of positions 11 (A), 12 (A), 13 (C), 14 (U), 17 (A), and/or 18 (C) relative to SEQ ID NO:6.

87. A pharmaceutical composition comprising the RNA molecule of any of claims 56-85 and 86.

88. An RNA molecule according to any of claims 56-85 for use in providing miR-34c activity to a cell.

89. An RNA molecule according to any of claims 56-85 for use in decreasing cell proliferation.

90. An RNA molecule according to any of claims 56-85 for use in inducing apoptosis in a cell.

91. An RNA molecule according to any of claims 56-85 for use in a cancer therapy.

92. The RNA molecule of claim 91, for use in combination with an additional cancer therapy.

93. The RNA molecule of claim 91, wherein the patient has been diagnosed with cancer.

94. A double-stranded, blunt-ended RNA molecule 22 or 23 basepairs in length comprising:

a) an active strand comprising

SEQ ID NO:7 from 5' to 3'; and,

b) a fully complementary passenger strand comprising a terminal modification of the nucleotide at the 5' end,

wherein the passenger strand comprises modified nucleotides in the first and last two nucleotides.

95. The RNA molecule of claim 94, wherein the molecule is 23 basepairs in length.

96. The RNA molecule of claims 94-95, wherein the active strand comprises a modified nucleotide at position 3, 4, 11, 12, 13, 14, 15, 16, 17, and/or 18 in the active strand.

97. The RNA molecule of any of claims 94-96, wherein the active strand comprises at least two modified internal nucleotides.

98. The RNA molecule of claim 97, wherein the active strand comprises no more than 11 modified internal nucleotides.

99. The RNA molecule of any of claims 94-98, wherein the passenger strand comprises at least one modified internal nucleotide.

100. The RNA molecule of claim 99, wherein the passenger strand comprises a modified nucleotide at position 1, 2, 3, 4, 9, 10, 11, 12, 13, 14, 19, 21, and/or 22 in the passenger strand.

101. The RNA molecule of any of claims 94-100, wherein the passenger strand does not have a modified nucleotide at position 15 and/or 16.

102. The RNA molecule of any of claims 94-101, wherein the passenger strand comprises SEQ ID NO:3.

103. The RNA molecule of claim 102, wherein the passenger strand comprises a modified nucleotide at position 1, 2, 3, 5, 6, 9, 10, 11, 12, 13, 14, 17, 18, 19, 20, 21, and/or 22 in the passenger strand.

104. The RNA molecule of any of claims 94-101, wherein the active strand comprises SEQ ID NO:5.

105. The RNA molecule of claim 104, wherein the passenger strand comprises a modified nucleotide at position 1, 2, 3, 4, 7, 8, 9, 10, 11, 12, 13, 14, 19, 21, 22, and/or 23 in the passenger strand.

106. The RNA molecule of any of claims 94-105, wherein the active strand comprises the sequence of SEQ ID NO:9.

107. The RNA molecule of any of claims 94-106, wherein the active strand comprises SEQ ID NO:9 from 5' to 3'.

Claims

1. A double-stranded, blunt-ended RNA molecule 22 or 23 basepairs in length comprising:

a) an active strand comprising SEQ ID NO: 1 from 5′ to 3′ and

b) a fully complementary passenger strand comprising:

i) modified nucleotides in the first and last two nucleotides of the passenger strand and

ii) a terminal modification of the nucleotide at the 5′ end.

2. The RNA molecule of claim 1, wherein the molecule is 23 basepairs in length and the active strand comprises SEQ ID NO: 2.

3. The RNA molecule of claim 1, wherein the passenger strand comprises a modified nucleotide at positions 1, 2, 3, 4, 5, 6, 10, 11, 12, 13, 14, 17, 18, 19, 20, 21, 22, and/or 23 relative to SEQ ID NO:4, wherein fewer than half of the total number of nucleotides in the passenger strand are modified nucleotides.

4. The RNA molecule of claim 1, wherein the passenger strand does not have a modified nucleotide located at positions 7, 8, 9, 15, and 16 relative to SEQ ID NO: 4.

5. The RNA molecule of claim 1, wherein the active strand comprises at least two modified nucleotides, wherein the modified nucleotides are not in the first two positions at the 5′ end.

6. The RNA molecule of claim 5, wherein the active strand has two modified nucleotides at positions 3, 4, 11, 12, 13, 14, 15, 16, 17, and/or 18 relative to SEQ ID NO: 2.

7. The RNA molecule of claim 1, wherein the modified nucleotides have sugar modifications.

8. The RNA molecule of claim 7, wherein the sugar modification is 2′-OMe.

9. The RNA molecule of claim 1, wherein the passenger strand comprises 4, 5, 6, 7, or 8 modified nucleotides.

10. The RNA molecule of claim 9, wherein the passenger strand comprises 6 modified nucleotides.

11. The RNA molecule of claim 1, wherein the passenger strand comprises 4, 5, 6, 7, or 8 modified nucleotides, wherein the modified nucleotides have sugar modifications.

12. The RNA molecule of claim 1, wherein the terminal modification of the nucleotide at the 5′ end of the passenger strand is a C4-C12 amine linker.

13. The RNA molecule of claim 12, wherein the terminal modification of the nucleotide at the 5′ end of the passenger strand is a C6 amine linker.

14. The RNA molecule of claim 1, wherein the active strand is unmodified.