WE CLAIM:

1. A nucleic acid comprising a DNA sequence which encodes a short hairpin micro-RNA (shmiR), said shmiR comprising:

an effector sequence of at least 17 nucleotides in length;

an effector complement sequence;

a stemloop sequence; and

primary micro RNA (pri-miRNA) backbone;

wherein the effector sequence is substantially complementary to a RNA transcript set forth in any one of SEQ ID NOs: 22, 34 and 40.

2. The nucleic acid according to claim 1, wherein the shmiR is selected from the group consisting of:

a shmiR comprising an effector sequence set forth in SEQ ID NO:21 and an effector complement sequence set forth in SEQ ID NO:22;

a shmiR comprising an effector sequence set forth in SEQ ID NO:33 and an effector complement sequence set forth in SEQ ID NO:34; and

a shmiR comprising an effector sequence set forth in SEQ ID NO:39 and an effector complement sequence set forth in SEQ ID NO:40.

3. The nucleic acid according to claim 1 or claim 2, wherein the shmiR comprises, in a 5’ to 3’ direction:

(i) a 5’ flanking sequence of the pri-miRNA backbone;

the effector complement sequence;

the stemloop sequence;

the effector sequence; and

a 3’ flanking sequence of the pri-miRNA backbone; or

(ii) a 5’ flanking sequence of the pri-miRNA backbone;

the effector sequence;

the stemloop sequence;

the effector complement sequence; and

a 3’ flanking sequence of the pri-miRNA backbone.

4. The nucleic acid according to any one of claims 1 to 3, wherein:

(i) the stemloop sequence is the sequence set forth in SEQ ID NO: 75;

(ii) the pri-miRNA backbone is a pri-miR-30a backbone; or

(iii) the 5' flanking sequence of the pri-miRNA backbone is set forth in SEQ ID NO: 76 and the 3' flanking sequence of the pri-miRNA backbone is set forth in SEQ ID NO: 77; or

(iv) any combination of (i), (ii) and (iii).

5. The nucleic acid according to any one of claims 1 to 4, wherein:

(i) the shmiR comprises a sequence set forth in any one of SEQ ID NOs: 48, 54, and 57; or

(ii) the DNA sequence which encodes the shmiR is set forth in any one of SEQ ID NO: 64, 70, and 73.

6. A plurality of nucleic acids, comprising:

(a) at least one nucleic acid according to any one of claims 1 to 5; and

(b) at least one further nucleic acid comprising a DNA sequence which encodes a shmiR, said shmiR comprising:

an effector sequence of at least 17 nucleotides in length;

an effector complement sequence;

a stemloop sequence; and

pri-miRNA backbone;

wherein the effector sequence is substantially complementary to a RNA transcript set forth in any one of SEQ ID NOs: 22, 34 and 40;

wherein the shmiR encoded by the nucleic acid at (a) and the shmiR encoded by the nucleic acid at (b) comprise different effector sequences.

7. The plurality of nucleic acids according to claim 6, wherein the shmiRs at (a) and (b) are selected from the group consisting of:

a shRNA comprising an effector sequence set forth in SEQ ID NO:21 and an effector complement sequence set forth in SEQ ID NO:22;

a shRNA comprising an effector sequence set forth in SEQ ID NO:33 and an effector complement sequence set forth in SEQ ID NO:34; and

a shRNA comprising an effector sequence set forth in SEQ ID NO:39 and an effector complement sequence set forth in SEQ ID NO:40.

8. The plurality of nucleic acids according to claim 6, comprising:

a nucleic acid comprising a DNA sequence encoding a shmiR comprising an effector sequence set forth in SEQ ID NO:21 and an effector complement sequence set forth in SEQ ID NO:22;

a nucleic acid comprising a DNA sequence encoding a shmiR comprising an effector sequence set forth in SEQ ID NO:33 and an effector complement sequence set forth in SEQ ID NO:34; and

a nucleic acid comprising a DNA sequence encoding a shmiR comprising an effector sequence set forth in SEQ ID NO:39 and an effector complement sequence set forth in SEQ ID NO:40.

9. The plurality of nucleic acids according to any one of claims 6 to 8, wherein the shmiRs at (a) and (b) comprise, in a 5’ to 3’ direction:

(i) a 5’ flanking sequence of the pri-miRNA backbone;
the effector complement sequence;
the stemloop sequence;
the effector sequence; and
a 3’ flanking sequence of the pri-miRNA backbone; or

(ii) a 5’ flanking sequence of the pri-miRNA backbone;
the effector sequence;
the stemloop sequence;
the effector complement sequence; and
a 3’ flanking sequence of the pri-miRNA backbone.

10. The plurality of nucleic acids according to any one of claims 6 to 9, wherein:

(i) the stemloop sequence is the sequence set forth in SEQ ID NO: 75;

(ii) the pri-miRNA backbone is a pri-miR-30a backbone; or

(iii) the 5’ flanking sequence of the pri-miRNA backbone is set forth in SEQ ID NO: 76 and the 3’ flanking sequence of the pri-miRNA backbone is set forth in SEQ ID NO: 77; or

(iv) any combination of (i), (ii) and (iii).

11. The plurality of nucleic acids according to any one of claims 6 to 10, wherein:

(i) the shmiRs are selected from shmiRs comprising a sequence set forth in any one of SEQ ID NOs: 48, 54, and 57; or

(ii) the DNA sequences which encode the shmiRs are selected from the sequences set forth in SEQ ID NO: 64, 70, and 73.

12. A DNA-directed RNA interference (ddRNAi) construct comprising a nucleic acid according to any one of claims 1 to 5 or a plurality of nucleic acids according to any one of claims 6 to 11.

13. The ddRNAi construct according to claim 12, said ddRNAi construct comprising in a 5’ to 3’ direction:

(a) a nucleic acid encoding a shmiR comprising or consisting of the sequence set forth in SEQ ID NO:48:
a nucleic acid encoding a shmiR comprising or consisting of the sequence set forth in SEQ ID NO:57; and
a nucleic acid encoding a shmiR comprising or consisting of the sequence set forth in SEQ ID NO:54; or

(b) a nucleic acid comprising or consisting of the sequence set forth in SEQ ID NO:64;
a nucleic acid comprising or consisting of the sequence set forth in SEQ ID NO:73; and
a nucleic acid comprising or consisting of the sequence set forth in SEQ ID NO:70.

14. The ddRNAi construct according to claim 12 or 13, comprising a RNA pol III promoter upstream of the or each nucleic acid encoding a shmiR.

15. The ddRNAi construct of claim 14, wherein the or each RNA pol III promoter is selected from a U6 promoter selected from a U6-9 promoter, a U6-1 promoter and U6-8 promoter, and a H1 promoter.

16. The ddRNAi construct according to claim 15, said ddRNAi construct comprising:

(a) U6-9 promoter upstream of a nucleic acid comprising or consisting of the sequence set forth in SEQ ID NO:64:

(b) U6-1 promoter upstream of a nucleic acid comprising or consisting of the sequence set forth in SEQ ID NO:73; and

(c) U6-8 promoter upstream of a nucleic acid comprising or consisting of the sequence set forth in SEQ ID NO:70.

17. An expression vector comprising the ddRNAi construct of any one of claims 12 to 16.

18. The expression vector of claim 17, wherein the expression vector is a viral vector selected from the group consisting of an adeno-associated viral (AAV) vector, a retroviral vector, an adenoviral (AdV) vector and a lentiviral (LV) vector.