CLAIMS

1. A fusion protein comprising, from N-terminus to C-terminus:

(i) a DNA methyltransferase domain, a nuclease-deficient RNA-guided DNA endonuclease enzyme, and a Krüppel associated box domain; or

(ii) a Krüppel associated box domain, a nuclease-deficient RNA-guided DNA endonuclease enzyme, and a DNA methyltransferase domain.

2. The fusion protein of claim 1, wherein the nuclease-deficient RNA-guided DNA endonuclease enzyme is a nuclease-deficient Class II CRISPR endonuclease.

3. The fusion protein of claim 1, wherein the DNA methyltransferase domain comprises a Dnmt3A protein and a Dnmt3L protein (a Dnmt3A-3L domain).

4. The fusion protein of claim 1, wherein the fusion protein comprises, from N-terminus to C-terminus, the DNA methyltransferase domain, the nuclease-deficient RNA-guided DNA endonuclease enzyme, and the Krüppel associated box domain.

5. The fusion protein of claim 4, wherein the nuclease-deficient RNA-guided DNA endonuclease enzyme is dCas9 and the DNA methyltransferase domain comprises a Dnmt3A protein and a Dnmt3L protein (a Dnmt3A-3L domain); wherein the dCas9 is covalently linked to the Dnmt3A-3L domain via an XTEN linker.

6. The fusion protein of claim 1, wherein the fusion protein comprises, from N-terminus to C-terminus, the Krüppel associated box, the nuclease-deficient RNA-guided DNA endonuclease enzyme, an XTEN linker, and the DNA methyltransferase domain.

7. The fusion protein of claim 1, wherein the nuclease-deficient RNA-guided DNA endonuclease enzyme is dCas9 and the DNA methyltransferase domain comprises a Dnmt3A protein and a Dnmt3L protein (a Dnmt3A-3L domain).

8. The fusion protein of claim 7, wherein the dCas9 is covalently linked to the Dnmt3A-3L domain via a XTEN linker and wherein the Krüppel associated box domain is covalently linked to the dCas9 via a peptide linker.

9. The fusion protein of claim 1, wherein the nuclease-deficient RNA-guided DNA endonuclease enzyme is covalently linked to the Krüppel associated box domain via a peptide linker.

10. The fusion protein of claim 1, wherein the nuclease-deficient RNA-

guided DNA endonuclease enzyme is covalently linked to the DNA methyltransferase domain via a peptide linker.

11. The fusion protein of claim 1, wherein the Krüppel associated box domain in (ii) is covalently linked to the DNA methyltransferase domain via an XTEN linker.

12. The fusion protein of claim 5, wherein the XTEN linker comprises about 16 to 80 amino acid residues.

13. The fusion protein of claim 1, further comprising a nuclear localization signal peptide.

14. The fusion protein of claim 1, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 12, 13, 14, or 15.

15. A nucleic acid sequence encoding the fusion protein of claim 1.

16. A complex comprising: (i) a fusion protein of claim 1; and (ii) a polynucleotide comprising: (a) a DNA-targeting sequence that is complementary to a target polynucleotide sequence; and (b) a binding sequence for the nuclease-deficient RNA-guided DNA endonuclease enzyme, wherein the nuclease-deficient RNA-guided DNA endonuclease enzyme is bound to the polynucleotide via the binding sequence.

17. A vector comprising a nucleic acid sequence encoding the fusion protein of claim 1.

18. A cell comprising the fusion protein of claim 1.

19. A method of silencing a target nucleic acid sequence in a harvested cell, comprising: (i) delivering a first polynucleotide encoding a fusion protein of claim 1 to a harvested cell containing the target nucleic acid; and (ii) delivering to the cell a second polynucleotide comprising: (a) a DNA-targeting sequence that is complementary to the target nucleic acid sequence; and (b) a binding sequence for the nuclease-deficient RNA-guide DNA endonuclease enzyme.

20. A method of silencing a target nucleic acid sequence in a harvested cell, the method comprising delivering a complex to a harvested cell containing the target nucleic acid; wherein the complex comprises: (i) a fusion protein of claim 1; and (ii) a polynucleotide comprising: (a) a DNA-targeting sequence that is complementary to a target polynucleotide sequence; and (b) a binding sequence for the nuclease-deficient RNA-guided DNA

endonuclease enzyme, wherein the nuclease-deficient RNA-guided DNA endonuclease enzyme is bound to the polynucleotide via the binding sequence.

21. The fusion protein of claim 1, wherein the nuclease-deficient RNA-guided DNA endonuclease enzyme is dCas9 which comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:23; ddCas12a which comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:34; dLbCfp1 which comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:35; or dFnCfp1 which comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:36.

22. The fusion protein of claim 1, wherein the Krüppel associated box domain comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:16.

23. The fusion protein of claim 3, wherein the Dnmt3A protein comprises an amino acid sequence with at least 85% sequence identity to SEQ ID NO:26, and the Dnmt3L protein comprises an amino acid sequence with at least 85% sequence identity to SEQ ID NO:28.

24. The fusion protein of claim 1, wherein the fusion protein comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:15.

25. The fusion protein of claim 1, wherein the nuclease-deficient RNA-guided DNA endonuclease enzyme is selected from the group consisting of dCas9, ddCpf1, ddCas12a, ddLbCpf1 and ddFnCpf1.

26. A fusion protein comprising, a DNA methyltransferase domain, a nuclease-deficient RNA-guided DNA endonuclease enzyme, and a Krüppel associated box domain; wherein

(1) the nuclease-deficient RNA-guided DNA endonuclease enzyme is dCas9 which comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:23; ddCas12a which comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:34; dLbCfp1 which comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:35; or dFnCfp1 which comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:36;

(2) the Krüppel associated box domain comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO:16; and

(3) the DNA methyltransferase domain comprises a Dnmt3A protein, a Dnmt3L protein, or a Dnmt3A protein and a Dnmt3L protein; wherein the Dnmt3A protein comprises an amino acid sequence with at least 85% sequence identity to SEQ ID NO:26, and the Dnmt3L protein comprises an amino acid sequence with at least 85% sequence identity to SEQ ID NO:28.

27. The fusion protein of claim 26, wherein the Krüppel associated box domain comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO:16.

28. The fusion protein of claim 27, wherein the Krüppel associated box domain comprises an amino acid sequence having at least 95% sequence identity to SEQ ID NO:16.

29. The fusion protein of claim 28, wherein the Krüppel associated box domain comprises an amino acid sequence having at least 99% sequence identity to SEQ ID NO:16.

30. The fusion protein of claim 26, wherein the Dnmt3A protein comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO:26.

31. The fusion protein of claim 30, wherein the Dnmt3A protein comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO:26.

32. The fusion protein of claim 31, wherein the Dnmt3A protein comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO:26.

33. The fusion protein of claim 26, wherein the Dnmt3L protein comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO:28.

34. The fusion protein of claim 33, wherein the Dnmt3L protein comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO:28.

35. The fusion protein of claim 34, wherein the Dnmt3L protein comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO:28.

36. The fusion protein of claim 26, wherein the dCas9 comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO:23.

37. The fusion protein of claim 36, wherein the dCas9 comprises an amino acid sequence having at least 95% sequence identity to SEQ ID NO:23.

38. The fusion protein of claim 37, wherein the dCas9 comprises an amino acid sequence having at least 99% sequence identity to SEQ ID NO:23.

39. The fusion protein according to claim 25, wherein the Krüppel associated box domain comprises an amino acid sequence of SEQ ID NO: 16, the Dnmt3A protein comprises an amino acid sequence of SEQ ID NO: 26, the Dnmt3L protein comprises an amino acid sequence of SEQ ID NO: 28 and the dCas9 comprises an amino acid sequence of SEQ ID NO: 23.

40. The fusion protein according to claim 39, wherein the fusion protein comprises, from N-terminus to C-terminus, a DNA methyltransferase domain, a nuclease-deficient RNA-guided DNA endonuclease enzyme, and a Krüppel associated box domain.