CLAIMS

WHAT IS CLAIMED IS:

1. An epigenetic editing system comprising:

(a) a fusion protein comprising:

a DNA-binding domain, and

a DNMT3L domain, wherein the DNMT3L domain is from a species selected from the group consisting of *Ailuropoda melanoleuca, Carlito syrichta, Meriones unguiculatus, Ochotona princeps, Neosciurus carolinensis, Bison bison, Equus przewalskii, Mus caroli and Pan troglodytes*; or

(b) a nucleic acid molecule encoding the fusion protein of (a).

2. The epigenetic editing system of claim 1, wherein the DNMT3L domain comprises an amino acid sequence that is at least 90% homologous to any one of SEQ ID NOs: 72-80 and 101-109.

3. The epigenetic editing system of claim 2, wherein the DNMT3L domain comprises an amino acid sequence of any one of SEQ ID NOs: 72-80 and 101-109.

4. The epigenetic editing system of claim 2, wherein the DNMT3L domain comprises an amino acid sequence that is at least 90% homologous to SEQ ID NO: 107.

5. The epigenetic editing system of claim 4, comprising an amino acid sequence of SEQ ID NO: 107.

6. The epigenetic editing system of any one of claims 1-5, wherein the fusion protein further comprises a repressor domain.

7. The epigenetic editing system of any one of claims 1-6, wherein the repressor domain comprises a KRAB domain.

8. The epigenetic editing system of claim 7, wherein the KRAB domain is derived from KOX1, ZIM3, ZFP28, or ZN627.

9. The epigenetic editing system of claim 7 or 8, wherein the KRAB domain is derived from the ZIM3.

10. The epigenetic editing system of claim 8 or 9, wherein the ZIM3 comprises an amino acid sequence that is at least 90% homologous to SEQ ID NO: 60 or 100.

11. The epigenetic editing system of any one of claims 10, wherein the fusion protein further comprises a DNMT3A domain.

12. The epigenetic editing system of claim 11, wherein the DNMT3A domain comprises an amino acid sequence that is at least 90% homologous to SEQ ID NO: 96.

13. The epigenetic editing system of claim 12, wherein the DNMT3A domain comprises an amino acid sequence of SEQ ID NO: 96.

14. The epigenetic editing system of any one of claims 1-13, wherein the fusion protein comprises two nuclear localization sequences (NLSs).

15. The epigenetic editing system of claim 14, wherein a first NLS of the two NLSs is positioned at the amino (N) terminus and a second NLS of the two NLSs is positioned at the carboxy (C) terminus of the fusion protein.

16. The epigenetic editing system of any one of claims 1-15, wherein the fusion protein comprises one or more peptide linkers.

17. The epigenetic editing system of claim 16, wherein the one or more peptide linkers comprise XTEN80 or XTEN16.

18. The epigenetic editing system of any one of claims 1-17, wherein the DNA-binding domain is a nuclease inactive Cas9 (dCas9) domain.

19. The epigenetic editing system of claim 18, wherein the dCas9 domain comprises an amino acid sequence that is at least 90% homologous to SEQ ID NO: 9.

20. The epigenetic editing system of any one of claims 1-19, further comprising one or more guide RNAs (gRNAs) or nucleic acid molecule(s) coding the gRNAs.