CLAIMS

1. A fusion protein comprising a clustered regularly interspersed short palindromic repeats (CRISPR) protein linked to at least one nucleosome interacting protein domain,
wherein the CRISPR protein is a type II CRISPR/Cas9 nuclease or nickase, or the CRISPR protein is a type V CRISPR/Cpf1 nuclease or nickase, and
wherein the fusion protein further comprises at least one nuclear localization signal, at least one cell-penetrating domain, at least one marker domain, or a combination thereof, and
wherein the at least one nucleosome interacting protein domain is a high mobility group (HMG) box (HMGB) DNA binding domain; a HMG nucleosome-binding (HMGN) protein; a central globular domain from histone H1; a DNA binding domain from a chromatin remodeling complex protein chosen from switch/sucrose non-fermentable (SWI/SNF) complex, imitation switch (ISWI) complex, chromodomain-helicase-DNA binding (CHD) complex, nucleosome remodeling and deacetylase (NuRD) complex, INO80 complex, SWR1 complex, or RSC complex; or a combination thereof.

2. The fusion protein of claim 1, wherein the CRISPR protein is a type II CRISPR/Cas9 protein modified to lack all nuclease activity and linked to a non-nuclease domain, or a type V CRISPR/Cpf1 protein modified to lack all nuclease activity and linked to a non-nuclease domain.

3. The fusion protein of claim 2, wherein the non-nuclease domain has cytosine deaminase activity, histone acetyltransferase activity, transcriptional activation activity, or transcriptional repressor activity.

4. The fusion protein of any preceding claim, wherein at least one nucleosome interacting protein domain is HMGB1 box A domain, HMGN1 protein, HMGN2 protein, HMGN3a protein, HMGN3b protein, histone H1 central globular

domain, imitation switch (ISWI) protein DNA binding domain, chromodomain-helicase-DNA protein 1 (CHD1) DNA binding domain, or a combination thereof.

5. The fusion protein of any preceding claim, wherein the at least one nucleosome interacting protein domain is linked to the CRISPR protein directly via a chemical bond, indirectly via a linker, or a combination thereof, and/or wherein the at least one nucleosome interacting protein domain is linked to the CRISPR protein at its N-terminus, C-terminus, an internal location, or a combination thereof.

6. The fusion protein of any preceding claim, comprising at least one nuclear localization signal.

7. The fusion protein of claim 1, wherein the CRISPR protein is *Streptococcus pyogenes* Cas9 (SpCas9), *Streptococcus thermophilus* Cas9 (StCas9), *Streptococcus pasteurianus* (SpaCas9), *Campylobacter jejuni* Cas9 (CjCas9), *Staphylococcus aureus* (SaCas9), *Francisella novicida* Cas9 (FnCas9), *Neisseria cinerea* Cas9 (NcCas9), *Neisseria meningitis* Cas9 (NmCas9), *Francisella novicida* Cpf1 (FnCpf1), *Acidaminococcus sp*. Cpf1 (AsCpf1), or *Lachnospiraceae* bacterium ND2006 Cpf1 (LbCpf1).

8. The fusion protein of claim 1, wherein the fusion protein has an amino acid sequence having at least 90% sequence identity with SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, or SEQ ID NO:79;
optionally wherein the fusion protein has an amino acid sequence as set forth in SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74,

SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, or SEQ ID NO:79.

9. A nucleic acid encoding the fusion protein of any preceding claim, optionally which is codon optimized for translation in a eukaryotic cell, and/or optionally which is part of a viral vector, a plasmid vector, or a self-replicating RNA.

10. A complex comprising at least one fusion protein of any of claims 1-8 and at least one guide RNA.

11. A kit comprising the fusion protein according to any one of claims 1-8, the nucleic acid according to claim 9 or the complex according to claim 10.

12. A eukaryotic cell comprising the fusion protein according to any one of claims 1-8, the nucleic acid according to claim 9 or the complex according to claim 10.

13. A method for increasing efficiency of targeted genome or epigenetic modification in a eukaryotic cell, the method comprising introducing into the eukaryotic cell:
(a) at least one fusion protein or nucleic acid encoding at least one fusion protein, each fusion protein comprising a CRISPR protein linked to at least one nucleosome interacting protein domain, wherein the CRISPR protein (i) has nuclease or nickase activity or (ii) is modified to lack all nuclease activity and is linked to a non-nuclease domain, wherein the CRISPR protein is a type II CRISPR/Cas9 protein or a type V CRISPR/Cpf1 protein, and wherein the at least one fusion protein further comprises at least one nuclear localization signal, at least one cell-penetrating domain, at least one marker domain, or a combination thereof;
(b) at least one guide RNA or nucleic acid encoding at least one guide RNA;
wherein the CRISPR protein of the at least one fusion protein is targeted to a target chromosomal sequence and the at least one nucleosome interacting

protein domain of the at least one fusion protein alters nucleosomal or chromatin structure such that the at least one fusion protein has increased access to the target chromosomal sequence, thereby increasing efficiency of targeted genome or epigenetic modification,
wherein the at least one nucleosome interacting protein domain is a high mobility group (HMG) box (HMGB) DNA binding domain; a HMG nucleosome-binding (HMGN) protein; a central globular domain from histone H1; a DNA binding domain from a chromatin remodeling complex protein chosen from switch/sucrose non-fermentable (SWI/SNF) complex, imitation switch (ISWI) complex, chromodomain-helicase-DNA binding (CHD) complex, nucleosome remodeling and deacetylase (NuRD) complex, INO80 complex, SWR1 complex, or RSC complex; or a combination thereof, and
wherein the method does not comprise a method for treatment of the human or animal body by surgery or therapy.

14. The method of claim 13, wherein the non-nuclease domain has cytosine deaminase activity, histone acetyltransferase activity, transcriptional activation activity, or transcriptional repressor activity.

15. The method of any of claim 13 or claim 14, wherein the at least one nucleosome interacting protein domain is linked to the CRISPR protein directly via a chemical bond, indirectly via a linker, or a combination thereof; and/or wherein the at least one nucleosome interacting protein domain is linked to the CRISPR protein at its N-terminus, C-terminus, an internal location, or a combination thereof.

16. The method of any of claims 13-15, wherein the at least one fusion protein comprises at least one nuclear localization signal.

17. The method of any of claims 13-16, wherein the nucleic acid encoding the at least one fusion protein is codon optimized for translation in the eukaryotic

cell, and/or wherein the nucleic acid encoding the at least one fusion protein is part of a viral vector, a plasmid vector, or a self-replicating RNA.

18. The method of any of claims 13-17, wherein the method further comprises introducing into the eukaryotic cell at least one donor polynucleotide, the donor polynucleotide comprising at least one donor sequence.

19. The method of any of claims 13-18, wherein the eukaryotic cell is *in vitro* or *in vivo*, and/or wherein the eukaryotic cell is a mammalian cell or a human cell.