

THAT WHICH IS CLAIMED IS:

1. A method of modifying a target nucleic acid, the method comprising:
contacting the target nucleic acid with

5 (a) a Type V CRISPR-Cas effector protein or a Type II CRISPR-Cas effector protein;

(b) a reverse transcriptase, and

(c) an extended guide nucleic acid (e.g., extended Type II or Type V CRISPR RNA, extended Type II or Type V CRISPR DNA, extended Type II or Type V crRNA, extended Type II or Type V crDNA), wherein the extended guide nucleic acid further
10 comprises a structured RNA motif, thereby modifying the target nucleic acid.

2. The method of claim 1, wherein the structured RNA motif is located at the 3' end of the extended guide nucleic acid.

3. The method of claim 1 or claim 2, wherein the structured RNA motif is AsCpf1BB (**SEQ ID NO:189**), BoxB (**SEQ ID NO:190**), pseudoknot (decoy) (**SEQ ID NO:95**, **SEQ ID NO:203**), pseudoknot (tEvoPreQ1) (**SEQ ID NO:191**), fimpknot (**SEQ ID NO:192**), mpknot (**SEQ ID NO:193**), MS2 (**SEQ ID NO:194**), PP7 (**SEQ ID NO:195**), SLBP (**SEQ ID NO:196**),
20 TAR (**SEQ ID NO:197**), and/or ThermoPh (**SEQ ID NO:198**).

4. The method of any one of claims 1-3, wherein the structured RNA motif is a pseudoknot.

5. The method of claim 4, wherein the pseudoknot is a tEvoPreQ1 pseudoknot comprising
25 the nucleic acid sequence of **SEQ ID NO:158** or an EvoPreQ1 Pseudoknot comprising the nucleic acid sequence of **SEQ ID NO:191**.

6. The method of claim 4, wherein the pseudoknot comprises the nucleic acid sequenced of **SEQ ID NO:95** or **SEQ ID NO:203**.

7. The method of any one of claims 1 to 6, wherein the extended guide nucleic acid further comprises:

(i) a Type V CRISPR nucleic acid or Type II CRISPR nucleic acid (crRNA, crDNA) and/or a Type V CRISPR nucleic acid or Type II CRISPR nucleic acid and a tracr nucleic acid;
5 and

(ii) an extended portion comprising a primer binding site and a reverse transcriptase template (RT template) (RTT) and the RTT is a length of about 35 nucleotides to about 75 nucleotides and the PBS is a length of about 30 nucleotides to about 80 nucleotides, optionally wherein the PBS is a length of about 8, 16, 24, 32, 40, 48, 56, 64, 72, or 80 nucleotides and the RTT is a length of
10 about 36, 40, 44, 47, 50, 52, 55, 63, 72 or 74 nucleotides.

8. The method of claim 7, wherein the Type V CRISPR-Cas effector protein or the Type II CRISPR-Cas effector protein is a fusion protein and/or the reverse transcriptase is a fusion protein, wherein the Type V CRISPR-Cas fusion protein or Type II CRISPR-Cas fusion protein,
15 the reverse transcriptase fusion protein and/or the extended guide nucleic acid is fused to one or more components that recruit the reverse transcriptase to the Type V CRISPR-Cas effector protein or Type II CRISPR-Cas effector protein, optionally the one or more components recruit via protein-protein interactions, protein-RNA interactions, and/or chemical interactions, wherein the Type V CRISPR-Cas fusion protein or Type II CRISPR-Cas fusion protein is fused to a
20 chromatin modulating peptide.

9. The method of claim 8, wherein the chromatin modulating peptide is fused to the C-terminus and/or the N-terminus of the Type V CRISPR-Cas fusion protein or Type II CRISPR-Cas fusion protein.

10. The method of claim 8 or claim 9, wherein the Type V CRISPR-Cas fusion protein or Type II CRISPR-Cas fusion protein is fused at its N-terminus to a reverse transcriptase and the chromatin modulating peptide is fused to the N-terminus of the reverse transcriptase.

11. The method of any one of claims 8-10, wherein the chromatin modulating peptide is CHD1, H1G, HB1, and HN1.

12. The method of claim 11, wherein CHD1 is **SEQ ID NO:199**, H1G is **SEQ ID NO:200**, HB1 is **SEQ ID NO:201**, and HN1 is **SEQ ID NO:202**.
- 5 13. The method of any of the preceding claims, wherein the reverse transcriptase is fused to one or more single stranded RNA binding domains (RBDs), thereby improving the thermostability, processivity and template affinity of the reverse transcriptase.
- 10 14. The method of claim 13, wherein the one or more single stranded RNA binding domains are fused to the N-terminus of the reverse transcriptase, optionally wherein the reverse transcriptase is further fused at its C-terminus to the N-terminus of the Type II CRISPR-Cas effector protein and/or Type V CRISPR-Cas effector protein.
- 15 15. The method of any one of the preceding claims, further comprising contacting the target nucleic acid with a single stranded DNA binding protein (ssDNA binding protein).
16. The method of claim 15, wherein the ssDNA binding protein is fused to the Type II V CRISPR-Cas effector protein or Type V CRISPR-Cas effector protein.
- 20 17. The method of claim 16, wherein the ssDNA binding protein is fused to the C-terminus of the Type II or Type V CRISPR-Cas effector protein.
18. The method of claim 16, wherein the ssDNA binding protein is fused to the N-terminus of the Type II or Type V CRISPR-Cas effector protein.
- 25 19. The method of any of claims 15 to 18, wherein the ssDNA binding protein is hRad51 (optionally, hRad51_S208E_A209D), hRad52, BsRecA, EcRecA, T4ssB and/or Brex27.
- 30 20. The method of any one of the preceding claims, further comprising reducing double strand breaks by introducing a chemical inhibitor of non-homologous end joining (NHEJ), by introducing a CRISPR guide nucleic acid or an siRNA targeting an NHEJ protein to transiently

knock-down expression of the NHEJ protein, or by introducing a polypeptide that prevents NHEJ, wherein the polypeptide that prevents NHEJ is a Gam protein and the Gam protein is fused to the reverse transcriptase and/or the CRISPR-Cas effector protein, optionally the Gam protein is fused to the N-terminus of the reverse transcriptase and/or the N-terminus of the
5 CRISPR-Cas effector protein.

21. The method of claim 20, wherein the Gam protein is *Escherichia* phage Mu Gam protein, optionally the Gam protein comprise the amino acid sequence of **SEQ ID NO:147**.