

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 Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) (CRISPR-Cas) effector protein;
 - (b) a deaminase, optionally wherein the target nucleic acid is contacted with two or more deaminases; and
 - (c) a guide nucleic acid, wherein the deaminase is recruited to the Type V CRISPR-
 - 10 Cas effector protein (e.g., recruited via a protein to protein interaction, RNA to protein interaction, and/or chemical interaction), thereby modifying the target nucleic acid, optionally wherein the Type V CRISPR-Cas effector protein, the deaminase and guide nucleic acid are co-expressed.
- 15 2. A method of modifying a target nucleic acid, the method comprising:
contacting the target nucleic acid with:
 - (a) a Type V Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) (CRISPR-Cas) fusion protein comprising a Type V CRISPR-Cas effector
 - protein fused to a peptide tag;
 - 20 (b) a deaminase fusion protein comprising a deaminase fused to an affinity polypeptide that binds to the peptide tag, optionally wherein the target nucleic acid is contacted with two or more deaminase fusion proteins; and
 - (c) a guide nucleic acid, optionally wherein the Type V CRISPR-Cas fusion protein, the deaminase fusion protein and guide nucleic acid are co-expressed, thereby modifying the
 - 25 target nucleic acid.
3. A method of modifying a target nucleic acid, the method comprising:
contacting the target nucleic acid with:
 - (a) a Type V Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-
 - 30 associated (Cas) (CRISPR-Cas) fusion protein comprising a Type V CRISPR-Cas effector protein fused to an affinity polypeptide that binds to a peptide tag;
 - (b) a deaminase fusion protein comprising a deaminase fused to the peptide tag, optionally wherein the target nucleic acid is contacted with two or more deaminase fusion proteins; and

(c) a guide nucleic acid, optionally wherein the Type V CRISPR-Cas fusion protein, the deaminase fusion protein and guide nucleic acid are co-expressed, thereby modifying the target nucleic acid.

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

(a) a Type V Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) (CRISPR-Cas) effector protein;

10 (b) a recruiting guide nucleic acid comprising a guide RNA linked to an RNA
recruiting motif, and

(c) a deaminase fusion protein comprising a deaminase fused to an affinity polypeptide that binds to the RNA recruiting motif, optionally wherein the target nucleic acid is contacted with two or more deaminase fusion proteins; and

15 optionally wherein the Type V CRISPR-Cas effector protein, the deaminase fusion protein and the recruiting guide nucleic acid are co-expressed, thereby modifying the target nucleic acid.

20 5. The method of claim 2 or claim 3, wherein the peptide tag comprises 2 or more copies of the peptide tag (e.g., two or more epitopes).

6. The method of any one of claims 2, 3 or 5, wherein the peptide tag is a GCN4 peptide repeat unit (e.g., Sun-Tag), a c-Myc affinity tag, an HA affinity tag, a His affinity tag, an S affinity tag, a methionine-His affinity tag, an RGD-His affinity tag, a FLAG octapeptide, a strep tag or strep tag II, a V5 tag, and/or a VSV-G epitope.

25 7. The method of any one of claims 2, 3, 5, or 6, wherein the affinity polypeptide is an antibody.

8. The method of claim 7, wherein the antibody is a scFv antibody.

30 9. The method of claim 4, wherein the recruiting guide nucleic acid is linked to two or more RNA recruiting motifs, optionally wherein the two or more RNA recruiting motifs are the same RNA recruiting motif or different RNA recruiting motifs.

10. The method of claim 4 or claim 9, wherein the RNA recruiting motif is a telomerase Ku binding motif (e.g., Ku binding hairpin) and the affinity polypeptide is a Ku polypeptide (e.g., Ku heterodimer); the RNA recruiting motif is a telomerase Sm7 binding motif and the affinity polypeptide is a Sm7 polypeptide; the RNA recruiting motif is an MS2 phage operator stem-loop and the affinity polypeptide is a MS2 Coat Protein (MCP); the RNA recruiting motif is a PP7 phage operator stem-loop and the affinity polypeptide is a PP7 Coat Protein (PCP); the RNA recruiting motif is an SfMu phage Com stem-loop and the affinity polypeptide is a Com RNA binding protein; the RNA recruiting motif is a Pumilio/fem-3 mRNA binding factor (PUF) and the affinity polypeptide is a PUF binding site (PBS) polypeptide; and/or the RNA recruiting motif is a synthetic RNA-aptamer and the affinity polypeptide is the corresponding aptamer ligand.
11. The method of any one of the preceding claims, wherein the Type V CRISPR-Cas effector protein comprises a mutation in a nuclease active site.
12. The method of any one of the preceding claims, wherein the deaminase is a cytosine deaminase and/or an adenine deaminase.
13. The method of any one of the preceding claims, wherein the two or more deaminase fusion proteins comprise the same or different deaminases.
14. The method of claim 13, wherein a first deaminase fusion protein of the two or more deaminase fusion proteins comprises a cytosine deaminase and a second deaminase fusion protein of the two or more deaminase fusion proteins comprises an adenine deaminase.
15. The method of any one of claims 12 to 14, wherein the cytosine deaminase is an apolipoprotein B mRNA editing catalytic polypeptide-like (APOBEC), a human activation induced deaminase (hAID), a FERNY deaminase, and/or a CDA1 deaminase, optionally wherein the cytosine deaminase comprises or is the sequence of any one of **SEQ ID NOs:23-32**.
16. The method of claim 15, wherein the cytosine deaminase is an APOBEC3A, optionally wherein the APOBEC3A comprises or is the sequence of (e.g., **SEQ ID NO:24**).

17. The method of any one of claims 12 to 16, wherein the adenine deaminase is TadA (tRNA-specific adenosine deaminase) and/or TadA* (evolved tRNA-specific adenosine deaminase), optionally wherein the adenine deaminase comprises or is the sequence of any one of **SEQ ID NOs:33-43**.
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18. The method of any one of the preceding claims, further comprising introducing a glycosylase inhibitor, optionally introducing two or more glycosylase inhibitors.
19. The method of claim 18, wherein the glycosylase inhibitor is a uracil-DNA glycosylase inhibitor (UGI), optionally wherein the UGI comprises or is the sequence of **SEQ ID NO:44**.
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20. The method claim 18 or claim 19, wherein the glycosylase inhibitor is recruited to the Type V CRISPR-Cas effector protein and/or the deaminase, optionally via a protein-protein interaction, RNA-protein interaction, or chemical interaction.
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21. The method of claim 18-20, wherein the glycosylase inhibitor is fused to the Type V CRISPR-Cas effector protein and/or the deaminase.
22. The method of any one of the preceding claims, wherein the Type V CRISPR-Cas effector protein, the Type V CRISPR-Cas fusion protein, the deaminase, and/or the deaminase fusion protein is encoded by a polynucleotide.
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23. The method of any one of claims 18 to 22, wherein the glycosylase inhibitor is encoded by a polynucleotide.
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24. The method of claim 22 or 23, wherein the polynucleotide encoding the Type V CRISPR-Cas effector protein, the polynucleotide encoding the deaminase, and the guide nucleic acid are comprised in one or more expression cassette(s) and/or vector(s).
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25. The method of any one of claims 22-24, wherein the polynucleotide encoding the Type V CRISPR-Cas fusion protein, the polynucleotide encoding the deaminase fusion protein, and the guide nucleic acid are comprised in one or more expression cassette(s) and/or vector(s).

26. The method of any one of claims 22-25, wherein the polynucleotide encoding the Type V CRISPR-Cas effector protein, the polynucleotide encoding the deaminase fusion protein, and the recruiting guide nucleic acid are comprised in one or more expression
5 cassette(s) and/or vector(s).
27. The method of any one of claims 23 to 26, wherein the polynucleotide encoding the glycosylase inhibitor is comprised in an expression cassette or vector, optionally in the same expression cassette or vector comprising one or more of the polynucleotide encoding the
10 Type V CRISPR-Cas effector protein, the polynucleotide encoding the deaminase, and the guide nucleic acid, optionally in the same expression cassette or vector comprising one or more of the polynucleotide encoding the Type V CRISPR-Cas fusion protein, the polynucleotide encoding the deaminase fusion protein, and/or the guide nucleic acid, and/or optionally in the same expression cassette or vector comprising one or more of the
15 polynucleotide encoding the Type V CRISPR-Cas effector protein, the polynucleotide encoding the deaminase fusion protein, and/or the recruiting guide nucleic acid.
28. The method of any one of the preceding claims, wherein the Type V CRISPR-Cas effector protein is linked to a polypeptide of interest.
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29. The method of claim 28, wherein the polypeptide of interest comprises at least one polypeptide having nickase activity, recombinase activity, transposase activity, methylase activity, glycosylase (DNA glycosylase) activity, glycosylase inhibitor activity (e.g., uracil-DNA glycosylase inhibitor (UGI)), demethylase activity, transcription activation activity,
25 transcription repression activity, transcription release factor activity, histone modification activity, nuclease activity, single-strand RNA cleavage activity, double-strand RNA cleavage activity, restriction endonuclease activity (e.g., FokI), nucleic acid binding activity, methyltransferase activity, DNA repair activity, DNA damage activity, dismutase activity, alkylation activity, depurination activity, oxidation activity, pyrimidine dimer forming
30 activity, integrase activity, transposase activity, polymerase activity, ligase activity, helicase activity, and/or photolyase activity.
30. The method of claim 28 or claim 29, wherein the polypeptide of interest is encoded by a polynucleotide.

31. The method of any one of the preceding claims, wherein the Type V CRISPR-Cas effector protein is a Cas12a (Cpf1) polypeptide, Cas12b polypeptide, Cas12c (C2c3) polypeptide, Cas12d (CasY) polypeptide, Cas12e (CasX) polypeptide, Cas12g polypeptide, Cas12h polypeptide, Cas12i polypeptide, C2c4 polypeptide, C2c5 polypeptide, C2c8 polypeptide, C2c9 polypeptide, C2c10 polypeptide, Cas14a polypeptide, Cas14b polypeptide, and/or Cas14c polypeptide.
32. The method of any of the preceding claims, wherein the Type V CRISPR-Cas effector protein is a Cas12a (Cpf1) polypeptide, optionally wherein the Cas12a (Cpf1) polypeptide has a sequence of any one of **SEQ ID NOs:3-19** or that is encoded by a polynucleotide having a sequence of any one of **SEQ ID NOs:20-22**, optionally wherein the Cas12a polypeptide is a *Lachnospiraceae* bacterium ND2006 Cas12a (LbCas12a)(LbCpf1) polypeptide (e.g., having a sequence of any one of **SEQ ID NOs:3** or **9-11**), an *Acidaminococcus* sp. Cpf1 (AsCas12a) (AsCpf1) polypeptide(e.g., having a sequence of **SEQ ID NO:4**) and/or enAsCas12a polypeptide (e.g., encoded by a polynucleotide having a sequence of any one of **SEQ ID NOs:20-22**).
33. The method of any one of the preceding claims, wherein the target nucleic acid is in an organism, optionally an animal, a plant, a fungus, an archaeon, or a bacterium.
34. The method of claim 28, wherein the polynucleotide encoding the Type V CRISPR-Cas effector protein, the polynucleotide encoding the Type V CRISPR-Cas fusion protein, the polynucleotide encoding the deaminase, the polynucleotide encoding the deaminase fusion protein, the polynucleotide encoding the glycosylase inhibitor, and/or the polynucleotide encoding the polypeptide of interest are codon optimized for expression in the organism comprising the target nucleic acid.
35. A nucleic acid construct comprising:
- (a) a Type V Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) (CRISPR-Cas) fusion protein comprising a Type V CRISPR-Cas effector protein fused to a peptide tag;
 - (b) a deaminase fusion protein comprising a deaminase fused to an affinity polypeptide that binds to the peptide tag; and

(c) a guide nucleic acid.

36. A nucleic acid construct comprising:

5 (a) a Type V Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) (CRISPR-Cas) effector protein;

(b) a recruiting guide nucleic acid comprising a guide RNA linked to an RNA recruiting motif; and

(c) a deaminase fusion protein comprising a deaminase fused to an affinity polypeptide that binds to the RNA recruiting motif.

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37. A Type V Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) (CRISPR-Cas) system comprising:

(a) a Type V CRISPR-Cas fusion protein comprising a Type V CRISPR-Cas effector protein fused to a peptide tag;

15 (b) a deaminase fusion protein comprising a deaminase fused to an affinity polypeptide that binds to the peptide tag; and

(c) a guide nucleic acid comprising a spacer sequence and a repeat sequence, wherein the guide nucleic acid is capable of forming a complex with the Type V CRISPR-Cas effector protein of the Type V CRISPR-Cas fusion protein and the spacer sequence is capable of
20 hybridizing to a target nucleic acid, thereby guiding the Type V CRISPR-Cas fusion protein to the target nucleic acid, and wherein the deaminase fusion protein is recruited to the Type V CRISPR-Cas fusion protein and target nucleic acid by the binding of the affinity polypeptide to the peptide tag that is fused to the Type V CRISPR-Cas fusion protein, whereby the system is capable of modifying (e.g., cleaving or editing) the target nucleic acid.

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38. A Type V Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) (CRISPR-Cas) system comprising:

(a) a Type V CRISPR-Cas effector protein;

30 (b) a recruiting guide nucleic acid comprising a guide RNA linked to an RNA recruiting motif; and

(c) a deaminase fusion protein comprising a deaminase fused to an affinity polypeptide that binds to the RNA recruiting motif, wherein the recruiting guide nucleic acid comprises a spacer sequence and a repeat sequence, wherein the recruiting guide nucleic acid is capable of forming a complex with the Type V CRISPR-Cas effector protein and the guide

RNA is capable of hybridizing to a target nucleic acid, thereby guiding the Type V CRISPR-Cas effector protein to the target nucleic acid, and wherein the deaminase fusion protein is recruited to the Type V CRISPR-Cas effector protein and target nucleic acid by the binding of the affinity polypeptide to the RNA recruiting motif that is fused to the recruiting guide
5 nucleic acid, whereby the system is capable of modifying (e.g., cleaving or editing) the target nucleic acid.

39. The nucleic construct of claim 35 or claim 36, or the CRISPR-Cas system of claim 37 or claim 38, wherein the Type V CRISPR-Cas effector protein is a Cas12a (Cpf1)
10 polypeptide, Cas12b polypeptide, Cas12c (C2c3) polypeptide, Cas12d (CasY) polypeptide, Cas12e (CasX) polypeptide, Cas12g polypeptide, Cas12h polypeptide, Cas12i polypeptide, C2c4 polypeptide, C2c5 polypeptide, C2c8 polypeptide, C2c9 polypeptide, C2c10 polypeptide, Cas14a polypeptide, Cas14b polypeptide, and/or Cas14c polypeptide.

15 40. The nucleic acid construct of claim 35 or claim 36, or the CRISPR-Cas system of claim 37 or claim 38, wherein the Type V CRISPR-Cas effector protein is a Cas12a (Cpf1) polypeptide, optionally wherein the Cas12a (Cpf1) polypeptide has a sequence of any one of **SEQ ID NOs:3-19** or that is encoded by a polynucleotide having a sequence of any one of **SEQ ID NOs:20-22**, optionally wherein the Cas12a polypeptide is a *Lachnospiraceae*
20 bacterium ND2006 Cas12a (LbCas12a)(LbCpf1) polypeptide (e.g., having a sequence of any one of **SEQ ID NOs:3** or **9-11**), an *Acidaminococcus sp.* Cpf1 (AsCas12a) (AsCpf1) polypeptide(e.g., having a sequence of **SEQ ID NO:4**) and/or enAsCas12a polypeptide (e.g., encoded by a polynucleotide having a sequence of any one of **SEQ ID NOs:20-22**).

25 41. An expression cassette comprising the nucleic acid construct of any one of claims 35, 36, 39, or 40.

42. An expression cassette comprising the CRISPR-Cas system of any one of claims 37 to
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43. A cell comprising the nucleic acid construct of any one of claims 35, 36, 39, or 40, or the expression cassette of claim 41.

44. A cell comprising the CRISPR-Cas system of any one of claims 37 to 40 or the expression cassette of claim 42.